Breaking barriers, personalizing pathways: psychological health and self-management of people with chronic kidney disease

Cardol, C.K.

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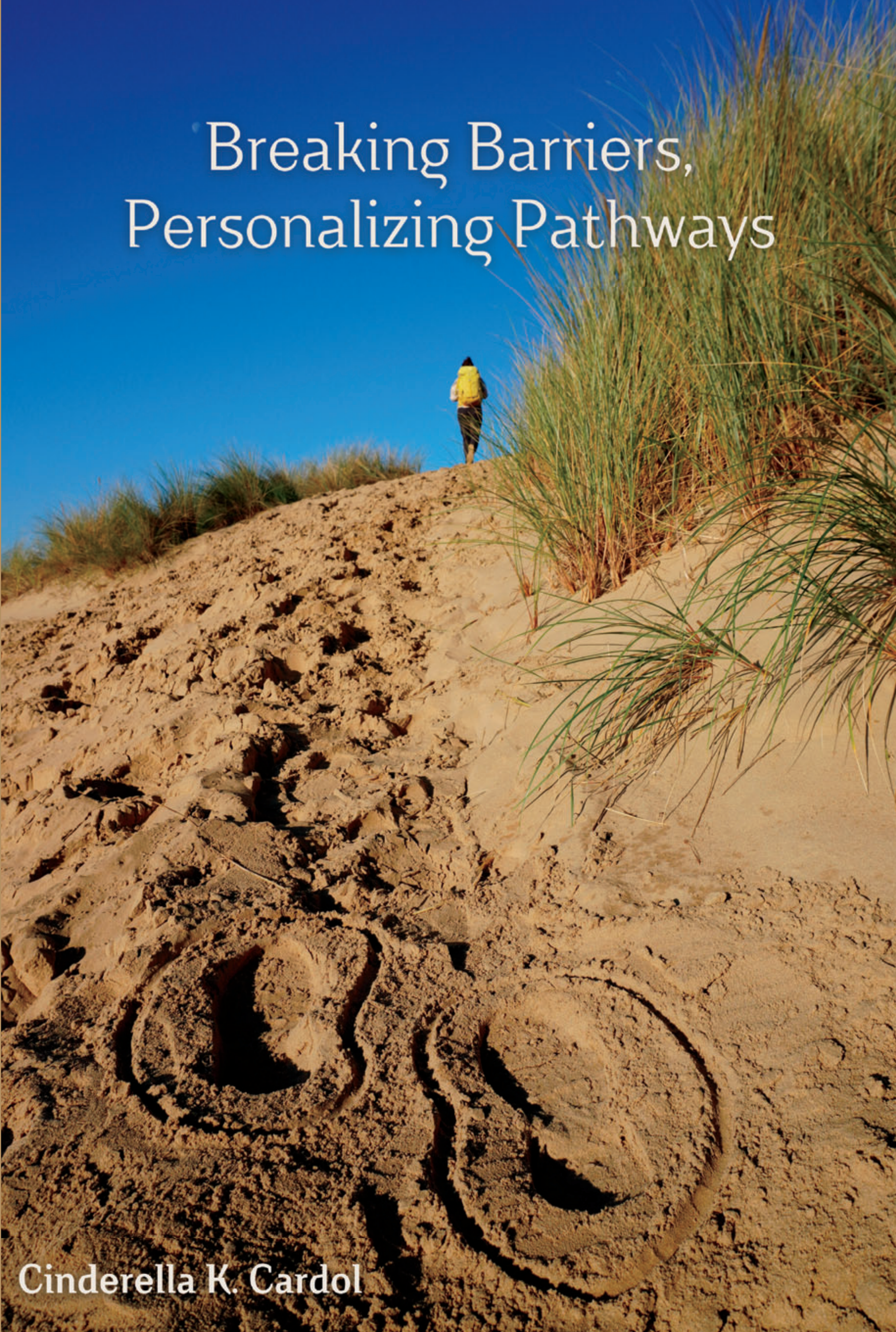

Psychological health and self-management of people with chronic kidney disease

Cinderella K. Cardol

Breaking Barriers, Personalizing Pathways

Psychological health and self-management of people with chronic kidney disease

Cinderella Katinka Cardol

Author: C.K. Cardol (Katja)
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Breaking Barriers, Personalizing Pathways

Psychological health and self-management of people with chronic kidney disease

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Chapter 1

General Introduction

Chronic Kidney Disease

Chronic kidney disease (CKD) is a highly prevalent condition, contributing substantially to the worldwide disease burden.[1] From all causes of death, kidney diseases have risen to the 10th leading cause.[2] Globally in 2017, 1.2 million people died from CKD and an additional 1.4 million from cardiovascular complications attributable to CKD.[1]

CKD is defined as glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2 or markers of kidney damage (e.g., protein loss in urine called albuminuria, or history of kidney transplantation), present for three months or longer.[3] The disease occurs from a variety of causes, of which hypertension and diabetes are most common.[3] CKD can be classified based on cause, decreasing GFR and increasing albuminuria and grouped into four risk categories to indicate disease severity and predict prognosis: low risk, moderately increased risk, high risk, and very high risk.[3] Prognosis also depends on multimorbidity:[3,4] Many patients have one or multiple other chronic conditions in addition to their CKD–25% even have three or more additional diseases.[4] Common comorbidities are hypertension, diabetes, heart failure, chronic pulmonary disease, and atrial fibrillation.[4]

Disease Progression and Medical Treatment

Kidneys have crucial functions, including the removal of waste products from the body, the regulation of the balance of fluids and minerals, and the involvement in hormonal processes that aid blood pressure regulation, red blood cell production, and bone metabolism.[5] Therefore, the more CKD progresses (i.e., worsening GFR or albuminuria), the more fluids and toxins accumulate in the body that make symptoms and health complications arise, such as cardiovascular events. Treatment of CKD is mainly focused on stabilizing kidney function and preventing cardiovascular diseases. Up to the moderately increased risk category, treatment is often provided by general practitioners and limited to antihypertensive medication and healthy lifestyle recommendations.[5] Usually, patients with more severe CKD are treated by a nephrologist and have frequent (e.g., 6- or 3-monthly) hospital visits to monitor and manage their kidney function. Many people do not experience symptoms until approximately 30% of their kidney function is left. From then onward, common disease-related symptoms include fatigue, loss of strength, stiff joints, weight loss, sleep difficulties, and pain, and patients experience a lowered physical and mental health-related quality of life.[6]

When the GFR is below 15 (i.e., kidney failure), most people require kidney replacement therapy to prolong life, that is, kidney transplantation or dialysis.[5] Kidney transplantation is a surgery to place a healthy kidney from a deceased or living donor into the patient's body, to take over the kidney function.[7] Even though quality of life improves after transplantation, kidney function does not recover completely and can still deteriorate, that is, patients still have CKD.[3] In addition, they receive strict and lifelong immunosuppressive medication prescriptions. These medications can have many side effects and most patients still experience burdensome symptoms, including muscle soreness, fatigue, xeroderma, numbness, and shortness of breath.[8] Still, kidney transplantation is preferred over dialysis treatment, as kidney transplant recipients often have better long-term outcomes (e.g., survival) and quality of life than patients receiving dialysis. However, due to contraindications to transplant procedures or medications and long waiting lists, not all patients are able to receive a kidney transplantation and therefore need to be treated with dialysis.[9] Dialysis is an intensive treatment to remove waste products and fluids from the blood and thus to partially take over the kidney function.[5] Patients often need to dialyze three times a week for three to four hours, and most of them need to go to the hospital to do so.[10] Kidney failure and dialysis have a large impact on patients' quality of life and symptom burden, for instance, many patients experience severe fatigue.[11,12] Although kidney replacement therapy is needed for only 1% of people with CKD, its costs are high and make CKD the most expensive of chronic diseases.[3]

CKD Self-Management

In addition to medical treatment provided by health professionals, people with CKD can take a certain degree of control over their disease themselves. In order to slow down the loss of kidney function, reduce cardiovascular burden and mortality risks, and prevent kidney failure,[13-15] the adoption of a healthy lifestyle and adherence to medication prescriptions are crucial parts of disease self-management.[3,16] Adherence refers to "the extent to which a person's behavior in taking medication, following a diet, or executing lifestyle changes, corresponds with the agreed recommendations from a health care provider."[17(p3)] In the current dissertation, we focus on adherence behaviors of patients who are not receiving dialysis treatment, including kidney transplant recipients. Kidney failure and dialysis treatment are more burdensome and require different disease management behaviors (e.g., stringent fluid restrictions), whereas most self-management recommendations for kidney transplant recipients and other patients with a CKD diagnosis who are not on dialysis (i.e., GFR $\geq$15) are similar and have the same purposes to prevent or reduce disease burden.[3,16] Key recommended behaviors are dietary adherence, physical activity, weight maintenance, medication adherence, and non-smoking.[3,18]

Dietary adherence. A first key health behavior is adherence to a healthy diet. The exact dietary requirements are usually complex and vary significantly by CKD severity and comorbidities, and can for instance comprise protein, potassium, or phosphorus restrictions to reduce their accumulation into the blood, or nutritional supplements (e.g., vitamins and minerals) to improve nutritional status if a patient's diet alone does not suffice.[18] A main recommendation for practically every patient is the restriction of sodium intake to <100 mmol (or <2300 milligrams) a day. This corresponds with less than half a teaspoon of total daily salt consumption. An excess of sodium is a risk factor for elevated blood pressure (BP) and proteinuria,[19] and dietary sodium restriction significantly reduces both.[20,21] Based on the association between proteinuria reduction and long-term outcomes, improved dietary sodium management has been expected to lead to a 25% improvement in clinical kidney and cardiovascular outcomes, such as kidney function loss and cardiovascular events.[21]

Physical activity. A second health behavior patients with CKD should take into account, is physical activity, which is defined as "any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level."[22(p618)] Physical activity can take place in any context, including work, leisure, and household activities, as well as sports or exercise. Exercise is a planned and repetitive form of physical activity, with the aim to improve or maintain physical fitness and health.[22] The recommended amount of physical activity is at least 150 minutes per week.[3] Regular physical activity and exercise could lead to decreased morbidity, weight loss, and improved physical functioning and quality of life,[3,23] whereas inactive and sedentary behaviors are strongly associated with a decreased quality of life, poor clinical outcomes, and increased mortality.[13,24,25]

Weight maintenance. A factor related to dietary adherence and physical activity is weight maintenance, usually measured by the proxy body mass index (BMI) in the range of 18.5–24.9 kg/m^2 for a healthy weight. Being underweight (BMI <18.5 29.9 kg/m^2) is a risk factor for mortality,[18] and being overweight (BMI 25–29.9 kg/m^2) or obese (BMI ≥30 kg/m^2) have been associated with cardiovascular risks, proteinuria, and kidney failure.[18,26,27] Weight reduction has been related to a decrease in albuminuria and stability of eGFR.[28]

Medication adherence. Most patients with CKD receive medication prescriptions, often including antihypertensive medication to improve blood pressure and reduce albuminuria.[5] In addition, kidney transplant recipients need to adhere to strict immunosuppressant medication regimens to avoid graft rejection.[3] Medication adherence is the process by which patients take their medications as prescribed, whereas late or non-initiation (i.e., a patient does not take the first dose of a prescribed medication), sub-optimal implementation (i.e., a patient's actual dosing does not correspond to the prescribed dosing regimen), and early discontinuation (i.e., a patient stops taking prescribed medication) are all forms of non-adherence.[29] Nonadherence increases risks of CKD progression, cardiovascular events, and kidney or transplant failure, including the requirement of transplantation or dialysis.[30-32]

Non-smoking. Another important risk behavior in kidney disease is tobacco smoking. Smoking increases blood pressure and heart rate, and both never and former smokers have reduced risks of CKD progression, cardiovascular events, and mortality compared to current smokers.[13] Smoking may cause irreversible kidney damage, while cessation can slow down the decline of renal function and reduce cardiovascular morbidity and mortality.[25,33]

Alcohol use. Alcohol consumption is often assumed to be an unhealthy risk behavior, but is currently not included in CKD management guidelines, due to conflicting findings regarding protective as well as harmful effects of light-to-moderate alcohol drinking (a maximum of 1–2 drinks per day) on health and kidney damage.[18,34] Also, there is no clear evidence for associations between high alcohol consumption (more than two drinks per day) and adverse CKD outcomes, such as proteinuria or kidney failure.[35]

Non-Adherence to Self-Management Recommendations

Although the benefits of adherence to the behavioral recommendations as described above are clear, a large proportion of patients do not fully succeed. In recent studies among patients with CKD not on dialysis, about 78% of the patients had a suboptimal diet, limited physical activity was reported by 34–47% of patients, 73% were overweight or obese, medication non-adherence ranged from 12 to 67%, and 13–17% were current smokers.[25,36,37] Specifically among kidney transplant recipients, in recent research 50–80% did not follow dietary recommendations (e.g., no restrictions in sodium or protein intake), 89% did not engage in regular physical activity, 49% were overweight or obese, 10–42% were not fully adherent to their immunosuppressive and other prescribed medication, and 11% currently smoked.[38,39]

Barriers to Self-Management: CKD-Related Stressors

Many people with CKD thus experience difficulties to adhere to all recommended self-management tasks. Self-management requires specific knowledge, skills, and changes of probably deep-seeded habits. In addition, patients need to cope with other disease-related stressors, including the burden of diagnosis, hospital visits and medical procedures, and often also with physical symptoms and comorbidities.[5] Moreover, living with a CKD diagnosis does not only affect bodily symptoms and physical outcomes, but can also have a major impact on other life domains, including disrupted and uncertain future perspectives, changes in social and work participation, and affected emotional wellbeing and mental health.[40] Also, health-related quality of life, referring to the impact that a disease and its treatment have on various life domains, generally decreases.[41,42] In other words, as for most chronic diseases, CKD comes with many acute and ongoing physical, psychological, and social stressors to cope with and adjust to.[43]

Adjustment to stressors. Many evidence-based models exist that explain how patients adjust to chronic disease-related stressors. Recently, Carroll and colleagues synthesized adjustment models into the transdiagnostic theoretical model of adjustment to long-term conditions (TMA-LTC; Figure 1).[44] The TMA-LTC proposes that such often uncontrollable and long-lasting disease stressors can disrupt patients' emotional equilibrium.[44] In accordance with Leventhal and colleagues' Common-Sense Model of Self-Regulation,[45] the TMA-LTC explains that patients' ability to return to equilibrium in response to stressors, that is, the achievement of good psychological adjustment, largely depends on their self-regulation: Adjustment requires (1) accurate and helpful interpretations of the disease and symptoms (e.g., perceived control versus helplessness, acceptance versus denial); (2) cognitive, behavioral, and emotional responses that are appropriate to the situation (e.g., positive health behaviors versus overactivity or excessive rest, expression of emotions versus non-disclosure); and (3) an ability to evaluate and adapt coping mechanisms.[44,45] The model in Figure 1 shows barriers and facilitators to adjustment, which explain why some people adjust well whereas others experience significant distress. In addition, patients' responses to stressors can be influenced by socio-demographic (e.g., socioeconomic status, cultural influences), intrapersonal (e.g., optimism, perfectionism), interpersonal (e.g., social support), environmental (e.g., availability of healthcare), and disease-specific contexts (e.g., symptom severity, treatment) that apply to their personal situation, which could either hinder or facilitate adjustment.[43,44]

Psychological distress. If patients fail to adequately adjust to stressors and do not return to a state of equilibrium, they may develop psychological complaints. With a prevalence of 21–34%, a considerable part of the CKD population not receiving dialysis suffers from symptoms of depression or anxiety, often referred to as psychological distress.[46,47] Importantly, psychological distress has been associated with adverse health outcomes in CKD, including disease progression, hospitalization, and mortality.[4,47] One of the explanations for these adverse outcomes among psychologically distressed patients is that distress may be associated with non-adherence to the recommended self-management behaviors.[47]

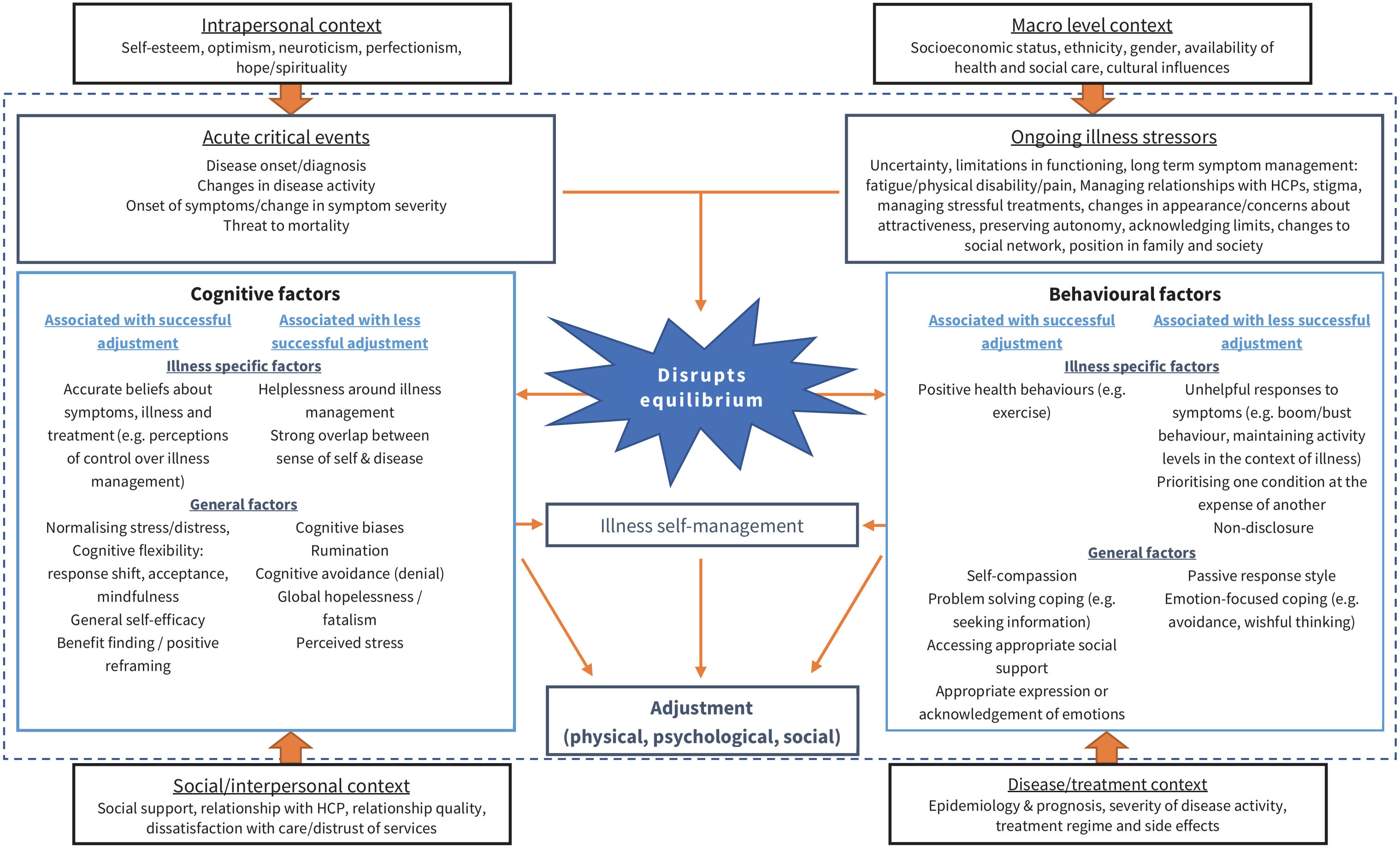

Figure 1. Transdiagnostic theoretical model of adjustment to long-term conditions (TMA-LTC). Reprinted with permission from "An evidence-based theory of psychological adjustment to long-term physical health conditions: Applications in clinical practice," by S. Carroll, Z. Moon, J. Hudson, K. Hulme, and R. Moss-Morris, 2022, *Psychosomatic Medicine, 84*(5), p. 552 (10.1097/PSY.0000000000001076). HCP: Healthcare Professional.

The association between psychological distress and self-management may be a two-way street. On the one hand, as shown in the TMA-LTC in Figure 1, the unhelpful cognitions and behaviors in response to stressors may lead to inadequate disease self-management, which could contribute to unsuccessful adjustment including psychological distress.[44] On the other hand, an unhelpful response to disease-related stressors can induce psychological distress directly and can go along with problems in self-efficacy, unhelpful cognitions and perceptions regarding coping abilities, and social isolation, which in turn lead to avoidance behaviors and hinder compliance with self-management requirements.[48,49] The intertwinement of psychological distress and self-management is alarming, as a vicious cycle of increasing adverse outcomes may occur (Figure 2): Disease-related stressors induce psychological distress; psychological distress could hamper self-management; poor self-management contributes to disease progression and adverse health outcomes; those outcomes are additional stressors that may induce or worsen psychological distress, which may further refrain patients from engaging in self-management behaviors.[48,50]

Research among other chronically ill populations indeed indicates that psychological distress may form a major barrier for self-management.[49,51,52] Notably, regardless of the high rates of psychological distress among patients with CKD, relatively little evidence exists regarding its association with self-management in this population.[36] To understand and successfully break the vicious cycle and improve outcomes, a focus on both possibly intertwined factors seems beneficial, that is, on psychological distress as well as self-management behaviors.

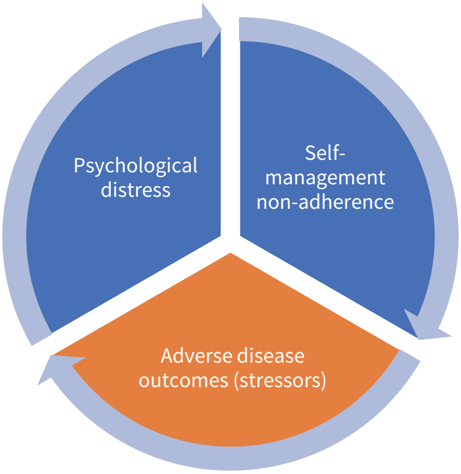

Figure 2. The potential associations between psychological distress, self-management, and adverse disease outcomes in chronic kidney disease.

Facilitating Self-management by Providing Personalized Care

Given the proposed interrelatedness of psychological distress and self-management, multicomponent interventions aiming to improve both should probably lead to better health outcomes.[23,48,51,53] However, treatment programs usually have a rather one-sided focus on either improving psychological functioning[54] or enhancing adherence to self-management recommendations[55] and often, psychological support is provided by mental healthcare services, separated from physical hospital care.[53,56] Important nuances unique to living with a chronic disease may be overlooked in mental healthcare, being predominantly designed for primary mental health disorders instead of physical conditions.[44] Also, this fragmented care can make patients feel stigmatized; they may perceive referrals to mental healthcare as being labeled with a psychological disorder on top of their chronic disease diagnosis.[57] Instead, psychological support integrated in regular CKD care would aid to normalize that psychological distress is an expected response to a disease-related distressing situation. Importantly, a one-sided focus on physical health and self-management in hospital care could also cause psychological contributors to non-adherent behaviors to remain unrecognized, as no routine assessments of psychological distress take place and both patients and health professionals tend to be hesitant to talk about psychological complaints.[40,53,58] That is, information regarding psychological health may be perceived as private or sensitive by health professionals,[58] or patients' may feel that their worries do not match the priorities of their healthcare providers, who are perceived to focus mainly on laboratory results and physical outcomes instead of actual wellbeing experienced by patients themselves.[40] To improve early recognition, communication, and support, combined or integrated interventions are needed that aid in identifying and reducing personal psychological barriers, facilitating coping resources, and that could thus break the vicious cycle of increasing psychological distress, non-adherence, and adverse health outcomes. To achieve effective, feasible, and acceptable interventions, design and content could benefit from several characteristics: person-centeredness,[59] a care pathway of screening and treatment,[43] and use of electronic health (eHealth) solutions.[60] Each of these characteristics will be explained below.

Person-centered care. Rather than offering each patient the same standardized intervention, personalized interventions are increasingly used and investigated.[43,61] Review and trial results show that personalization could result in stronger and more sustainable intervention effects compared to standardized treatment, as well as better adherence, motivation, and satisfaction of patients.[59,62] Every person is unique, which implies a large variability in patients' functioning, their characteristics, and situational context. This variability requires interventions that are tailorable to each individual's goals, values, needs, and preferences.[17,63] Personalized interventions are based on the four principles of patient- or person-centered care. Person-centered care can be described as (1) *holistic*, meaning that all domains of patients' health and wellbeing are taken into account, including physical and mental health; (2) *individualized*, which means that individuals' unique needs, priorities, and specific health concerns are considered; (3) *respectful*, that is, patients are treated with respect and have the right to make choices regarding their own health and treatment; and (4) *empowering*, which means that patients' autonomy and self-confidence are encouraged.[64] To achieve adequate personalization or intervention tailoring to the needs and characteristics of both the chronic disease population and the individual patient,[65] early involvement of and co-creation with patients, health professionals, and other stakeholders in the development process is crucial.[60,66]

Screening. A first step to personalization of care pathways is screening for difficulties that patients may experience, including psychological distress and suboptimal self-management. Screening procedures can serve multiple functions: First, personally relevant problems can be identified, to avoid that they remain unreported.[40] Second, visualization of screening results can facilitate conversations between patients and their health professionals.[58] Third, results can be used to offer adequate support to patients who need it, i.e., to fit further steps to a person's individual difficulties, preferences, and needs.[43,58] Fourth, at the start of such personalized support, screening tools can aid to understand and map patients' presenting problems, barriers, and facilitators (e.g., components of the TMA-LTC that are associated with more or less successful adjustment to stressors, see also Figure 1), as well as to guide goal setting.[43,44] Fifth, routine screening measurements can be done to monitor health and functioning over time.[43,62]

For screening tools to serve these functions and strengthen their overarching purpose of personalization, patient-reported and personalized assessments could be included.[63,67] In clinical practice, personalized instruments are useful to assess patients' personal priorities for improvement and to aid in goal setting.[67] Also, progress can be monitored as experienced by patients themselves in areas that matter to them, or which they actually intended to improve in their treatment trajectories.[40] Additionally, in research settings, personalized assessments allow researchers to evaluate whether interventions are not only effective for the average patient or the studied sample as a whole, but also whether the effects are personally relevant to individual patients.[63]

Treatment. As a second step to personalized care, individuals whose screening results indicate adjustment problems should receive support that matches their needs and priorities.[43] Specifically, in case of co-occurring psychological distress and self-management non-adherence, multicomponent treatment could be offered to target both. Cognitive-behavioral therapy (CBT) has been found to be effective in enhancing psychological functioning and achieving behavior change among populations with chronic diseases.[68-70] This therapy is based on the cognitive model, which describes the interactions between thoughts or cognitions, emotions and physical sensations, and behaviors.[71,72] Unhelpful cognitions of people with CKD may regard, for instance, a low perceived understanding of their kidney disease, negative consequences on their lives, or a perceived lack of control,[73,74] and have been associated with reduced quality of life,[73] medication nonadherence,[74] and disease progression.[75] Such maladaptive illness perceptions and treatment beliefs (e.g., “Physical activity worsens my disease” or “I’m unable to change my habits”) could be changed with the use of cognitive techniques, for example by examining the evidence for and against an untrue thought to challenge its accuracy. In addition to cognitive techniques, unhelpful behaviors may be changed using behavioral techniques, such as behavioral activation to increase physical activity and to maintain a balance between activity and rest.[44] In terms of the TMA-LTC described before (Figure 1), by restructuring thinking patterns and changing maladaptive behaviors with CBT, patients adopt more helpful cognitive and behavioral coping responses to disease-related stressors, which helps them to return to a state of emotional equilibrium and achieve successful adjustment.[44]

In addition to the indirect improvement of self-management by targeting psychological adjustment, self-management behavior change can be further targeted directly by applying behavior change techniques in order to enhance patients’ self-regulation skills.[45,76,77] As an example, recent trials evaluated dietary self-management interventions that were self-regulation theory-based.[78,79] Self-regulation theories evolved from cognitive-behavioral learning theory.[77] Multiple intervention principles are similar to CBT and the approaches can be easily combined. Self-regulation has been defined by Maes and Karoly (2005) as a behavioral process aimed at the attainment and maintenance of personal goals.[80] Patients focus on personally meaningful and urgent goals that originate from themselves instead of being imposed by the therapist, which enhances intrinsic motivation.[71,81] That is, when goals are personally relevant, self-chosen, and rewarding, they are likely to be pursued and thus better self-management is most likely to be achieved and maintained.[77,81] Again, personalization is essential, which can be warranted by one of the key principles of CBT and self-regulation: the collaborative relationship between patient and therapist, with the aims to help patients effectively define their own problems and goals, and to assist them in gaining the skills needed to achieve the desired psychological adjustment and self-management behaviors.[71,80] It is important to set and concurrently target psychological and self-management goals, given the associations between psychological distress and self-management explained before (Figures 1 and 2), which imply that improving one could facilitate the other and vice versa.[48,53,82] In sum, a two-sided treatment approach can focus on both psychological distress symptoms and self-management behaviors, which would have the most beneficial long-term effects on patients' health and disease.[70]

eHealth. To integrate personalized care pathways in CKD care, there is growing evidence for electronic health (eHealth) solutions as adequate modalities of delivery.[60] Research shows that eHealth interventions usually have a high feasibility, acceptability, and feasibility, for multiple reasons.[60] For patients, using eHealth applications from home can reduce stigma associated with psychotherapy and makes newly learned habits relatively easy to practice in their usual environments, compared to face-to-face care in a healthcare setting.[57,83] For health professionals, eHealth applications provide an efficient way of obtaining insights in patients' health and support needs.[56] Many self-management programs for patients with chronic diseases are blended, that is, they consist of online elements (e.g., online messaging, education, or exercises) complemented with face-to-face therapist guidance.[65] There is considerable evidence for the effectiveness of eHealth interventions. For instance, Internet-delivered guided cognitive-behavioral therapy (iCBT) has been found to reduce psychological distress, depressive, anxiety symptoms in other chronically ill populations, and to be just as effective as face-to-face therapy.[10,84] For patients with chronic kidney disease, multiple systematic reviews show that a great variety of eHealth interventions (e.g., online interactive educational programs, electronic medication and blood pressure monitoring devices, video consultations, and combinations) are effective in improving self-management outcomes such as medication adherence.[60,85] Figure 3 depicts an example of a personalized eHealth care pathway with screening and treatment.

Aims and Outline of This Dissertation

In sum, the considerable prevalence of psychological distress, together with the high non-adherence rates to recommended self-management behaviors, may lead to adverse health outcomes among people with CKD not on dialysis. Personalized, multicomponent eHealth interventions with the aims to recognize and treat problems in both psychological functioning and self-management seem needed. Such interventions should lead to better health outcomes: enhanced emotional wellbeing and disease management, improvements in outcomes that are personally meaningful to the individual, and finally better mental and physical health and quality of life. However, no personalized and theory-based interventions with an explicit focus on both psychological treatment with CBT as well as self-management support have been developed and investigated specifically for patients with CKD not on dialysis. Therefore, the aim of this dissertation was to develop and evaluate the effectiveness of a personalized eHealth care pathway, including:

1) a screening tool with questionnaires and results visualized in personalized profile charts. Main screening purposes were to identify patients who experience psychological distress and suboptimal self-management, to tailor treatment, and to monitor progress,
2) blended and guided treatment which integrates iCBT and self-management support. Main treatment purposes were to treat psychological distress, to diminish barriers and promote facilitators for adherence to self-management recommendations, and to support patients in adopting and maintaining healthy and adherent behaviors.

As presented in **Chapter 2**, we conducted a focus group study with patients and health professionals in four Dutch medical centers, to identify which barriers and facilitators for engaging in self-management behaviors people with CKD experience, as well as to explore which specific intervention strategies are needed to address those. Based on the findings, complemented with co-creation methods to fit the needs and preferences of patients with chronic diseases, we systematically developed the eHealth care pathway as described in **Chapter 3**. Subsequently, for the cross-sectional survey study in **Chapter 4**, patients were invited to complete the screening component of this eHealth care pathway, to assess how many people with CKD not on dialysis experience psychological distress, depressive, or anxiety symptoms and difficulties in dietary adherence, physical activity, medication adherence, weight maintenance, and non-smoking. We investigated whether those psychological and self-management problems were linearly or proportionally associated with each other. Patients who did report a combination of psychological distress and suboptimal self-management additionally completed a personalized outcome instrument of which the development and psychometric properties are evaluated in **Chapter 5**, to define their priorities for improvement and monitor personally meaningful change that may be achieved in personalized treatment. Patients with psychological and self-management difficulties were also invited to participate in the randomized controlled trial described in **Chapter 6**, with the aim to investigate the personalized treatment effectiveness in reducing psychological distress symptoms, and in improving physical and mental health-related quality of life, self-efficacy for disease management, chronic condition self-management, and personalized functioning and self-management outcomes compared with a care as usual control condition. Last, in **Chapter 7** the most important findings of this dissertation are outlined, together with recommendations for future research and for clinical practice.

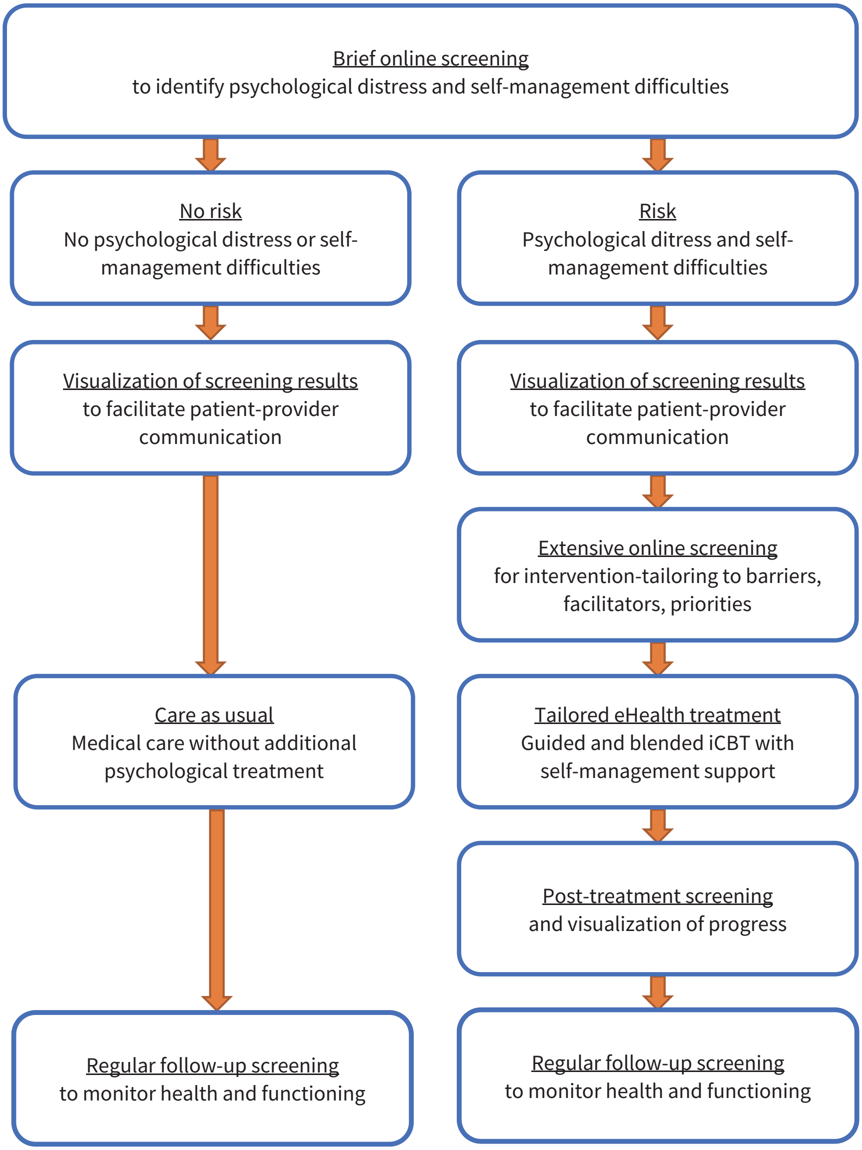

Figure 3. Example of a personalized eHealth care pathway for patients with chronic kidney disease.

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Chapter 2

Psychosocial barriers and facilitators for adherence to a healthy lifestyle among patients with chronic kidney disease: a focus group study

Cinderella K. Cardol, Karin Boslooper-Meulenbelt, Henriët van Middendorp, Yvette Meuleman, Andrea W.M. Evers, and Sandra van Dijk

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Abstract

Background

Progression of chronic kidney disease (CKD) may be delayed if patients engage in healthy lifestyle behaviors. However, lifestyle adherence is very difficult and may be influenced by problems in psychosocial functioning. This qualitative study was performed to gain insights into psychosocial barriers and facilitators for lifestyle adherence among patients with CKD not receiving dialysis.

Methods

Eight semi-structured focus groups were conducted with a purposive sample of 24 patients and 23 health care professionals from four Dutch medical centers. Transcripts were analyzed using thematic analysis. Subsequently, the codes from the inductive analysis were deductively mapped onto the Theoretical Domains Framework (TDF).

Results

Many psychosocial barriers and facilitators for engagement in a healthy lifestyle were brought forward, such as patients' knowledge and intrinsic motivation, emotional wellbeing and psychological distress, optimism, and disease acceptance. The findings of the inductive analysis matched all fourteen domains of the TDF. The most prominent domains were 'social influences' 'and 'environmental context and resources', reflecting how patients' environments hinder or support engagement in a healthy lifestyle.

Conclusions

The results indicate a need for tailored behavioral lifestyle interventions to support disease self-management. The TDF domains can guide development of adequate strategies to identify and target individually experienced psychosocial barriers and facilitators.

Keywords Lifestyle adherence; Psychosocial determinants; Self-management interventions; Chronic kidney disease (CKD); Qualitative research; Focus groups; Thematic analysis; Theoretical Domains Framework (TDF).

Background

For patients in the non-dialysis-dependent stages of chronic kidney disease (CKD), engaging in a healthy lifestyle is crucial, as it can postpone further loss of kidney function and prevent cardiovascular complications.[1] Key lifestyle behaviors in CKD include engaging in regular physical activity, refraining from smoking, maintaining a healthy weight, and adhering to dietary regimens and medication prescriptions.[2] Unfortunately, engaging in healthy lifestyle habits is difficult for most patients. A large observational cohort study showed that only 2% of the patients with mild-to-moderate CKD achieved all four lifestyle recommendations assessed.[1] Almost a quarter of the patients were regular smokers, nearly half of the cohort reported limited physical activity, approximately 80% did not meet dietary regimens, and a similar percentage were overweight or obese.[1]

One of the possible explanations for this non-adherence to a healthy lifestyle is that modifying lifestyle is not the only challenge that patients face. The integration of kidney disease and its medical management into daily life requires extensive coping skills, such as accepting the diagnosis and prognosis, as well as coping with physical symptoms and social implications of CKD.[3] Consequently, many patients experience diminished psychosocial functioning, even patients in early stages of CKD.[4-6] For example, recent studies showed that one-quarter to a third of patients with CKD not receiving dialysis are affected by psychological distress, that is, symptoms of depression or anxiety–such as sadness, loss of interest, irritability, nervousness, or restlessness.[4,5]

Identification and treatment of psychosocial problems is important, since psychosocial functioning determines how patients cope with chronic disease and their ability to change lifestyle habits.[7] Psychosocial influences on self-management and lifestyle behaviors can range from internal (e.g., behaviors, cognitions, and emotions) to coping with external (i.e., social and environmental) determinants. For instance, depression and anxiety symptoms and a lack of social support have been associated with medication non-adherence in kidney transplant recipients.[8] Such knowledge on psychosocial factors that hinder or facilitate the engagement in healthy lifestyle behaviors is imperative for the development of effective lifestyle interventions to aid patients with CKD. Yet, relatively few studies have explored the barriers and facilitators for successful adherence to lifestyle guidelines in this population. Also, the existing literature predominantly focused on adherence to dietary regimens, mainly among patients treated with hemodialysis.[9-11] As the dialysis treatment for patients with kidney failure is more burdensome and requires different lifestyle adaptations (e.g., stringent fluid restrictions) compared to disease management for patients with CKD not receiving dialysis, barriers and facilitators may also differ between the two CKD populations.[2] On the contrary, except for a strict adherence to immunosuppressive medications after kidney transplantation, most general lifestyle recommendations for kidney transplant recipients and other patients with CKD not receiving dialysis are similar, especially after the postoperative recovery period.[2,12,13] Also, the lifestyle measures have similar purposes for both groups, that is, to delay disease progression and to lower cardiovascular risk.[2,12,13]

Most studies among patients with CKD did not use a theoretical framework such as the Theoretical Domains Framework (TDF).[14,15] This framework synthesizes a number of behavior change theories into 14 domains that determine behavior, such as skills, reinforcement, social influences, and emotion. The TDF has been used in qualitative studies among populations with other chronic diseases, including those that address lifestyle change.[15,16] The TDF may be helpful to disentangle and structure barriers and facilitators, and importantly, the TDF domains can be translated to evidence-based intervention strategies and behavior change techniques (BCTs) to address barriers and promote the desired lifestyle behaviors.[14,15] Last, to our knowledge, few studies included the perspectives of health professionals. It is important to explore the barriers and facilitators for lifestyle adherence that health professionals observe among their patients, since they experience what works for whom. For successful implementation of lifestyle interventions in health care settings, health professionals should find them beneficial to their daily practice.[17] When exploring both patients and health professionals' perspectives, similarities and differences can be revealed and incorporated into an intervention design.[9]

This study entails a further exploration of factors that are related to the key lifestyle behaviors in CKD: keeping a healthy diet and weight, engaging in regular physical activity, refraining from smoking, and adhering to medication prescriptions.[2] To gain in-depth insight into patients and health professionals' perspectives on psychosocial influences on adherence to a healthy lifestyle, a semi-structured focus group study was conducted among patients and health professionals and data were mapped onto the TDF. This study had two aims: (1) to identify psychosocial barriers and facilitators for engaging in a healthy lifestyle among patients with CKD not receiving dialysis, and (2) to explore which intervention strategies are needed to address such barriers and facilitators.

Methods

Setting

This focus group study is part of the E-health Guidance in identifying and Overcoming psychological barriers for Adopting a healthy Lifestyle among patients with chronic kidney disease (E-GOAL) study (Netherlands Trial Registry, study number: NL7338), which entails the development and evaluation of a self-management electronic health intervention. In line with the exploratory nature of the study, focus groups instead of individual interviews were conducted, as participant interaction could create a chain of thoughts and ideas and the group dynamics may provide a breadth of perspectives and information.[18] Four focus groups with patients and four with health professionals took place between August 2017 and February 2018 in four medical centers distributed throughout The Netherlands, of which three university medical centers and one non-academic center. The study was approved by the Medical Research Ethics Committee Leiden The Hague Delft (MREC LDD P17.090) and was performed in accordance with the 1964 Helsinki declaration and its later amendments. The COnsolidated criteria for REporting Qualitative research (COREQ)[19] were followed.

Participant Selection and Recruitment

We used purposive sampling to include a heterogeneous sample in order to explore a wide range of perspectives.[20] For this purpose, health professionals were asked to recruit Dutch-speaking patients of 18 years or older, with spread in sociodemographic characteristics (i.e., in age and gender), different non-dialysis-dependent CKD stages (including kidney transplant recipients >1 year ago), and diverse experiences with adapting lifestyle behaviors (i.e., regarding different lifestyle domains, level of difficulty to adhere to a healthy lifestyle, and amount of professional support received). Patients were invited to participate by their nephrologist or nurse practitioner during hospital visits. To gain insights from different occupational perspectives, health professionals of all relevant occupations in CKD care (e.g., nephrologists, nurse practitioners, and dieticians) were invited to participate via email by a nephrologist from the research team who worked at the participating departments. Participation was voluntary and without compensation, except for reimbursement of patients' travel expenses (full compensation of public transport or mileage allowance). Participants received verbal and written information regarding study purposes and procedures and provided written informed consent prior to participation.

Participants were recruited until six to ten individuals for each focus group were scheduled at a convenient date and time to maximize attendance. Twelve patients were eventually unable to attend (for nine of them the scheduled date was inconvenient, two patients cancelled due to health reasons, and one patient cancelled due to personal circumstances). Five health professionals were unable to attend on the scheduled date due to work-related obligations. Focus groups were held until data saturation (i.e., until no new themes were brought forward). In case of last-minute cancellations, it was decided to proceed with a focus group if at least four participants were present, to maintain sufficient opportunity for group discussion.

Data Collection and Content

The focus group sessions lasted between 1.5 and 2.5 hours and were moderated by the first author, a female PhD candidate in medical psychology, who had received training in conducting and analyzing focus group discussions. The author had limited interactions by email or phone with participants before the focus group sessions, except for four participating nephrologists, with whom she already had a professional relationship. The participants were informed that the moderator was a researcher working on a lifestyle program to support patients with CKD. An instructed observer (female) took field notes on group dynamics and nonverbal communication. The sessions were audio recorded with permission of the participants.

A semi-structured focus group question guide was developed in accordance with the project aims and literature guidelines,[20,21] partly based on a previous study of the research group.[9] The focus group guide was refined in collaboration with a patient with CKD, who provided feedback on question structure, interpretation, and comprehensibility of wording. Open-ended questions were included in the semi-structured focus groups, allowing the exploration of themes as they arose. The moderator probed responses and stimulated in-depth discussions and engagement of all participants. Participants answered questions about 1) the perceived consequences and difficulties to adjust to CKD, 2) experiences regarding the adherence to a healthy lifestyle. This included the perceived barriers and facilitators in general and for each of the specific lifestyle recommendations, 3) the role of psychosocial barriers and facilitators and, specifically, psychological distress, and 4) their ideas about how to target psychosocial barriers and facilitators in a support program. To introduce our assumption that psychosocial issues and psychological distress may play an important role, after an open discussion of all themes, two translated quotations about the psychological impact of chronic disease from qualitative studies among other chronically ill populations were shown, and participants were invited to discuss whether they recognized these. A summary of the focus group guide is shown in Table A1 (Supplementary File 1). By the end of the sessions, participants individually wrote down a top-3 of barriers and facilitators they considered most important. Furthermore, they completed a short questionnaire on sociodemographic characteristics.

Data Analysis

The focus group moderator and observer discussed the main themes in a debriefing directly after each focus group. Suiting the exploratory purpose of the study, the transcripts were analyzed using a thematic analysis approach. Analysis was conducted following the six phases outlined by Braun and Clarke,[22] and with use of Atlas.ti version 7.5.6 software. In the first phase, the first author transcribed the sessions verbatim, based on recordings and field notes. The author reviewed all transcripts and marked first ideas for codes. Unclear statements were clarified by contacting the concerning participants, to ensure that their perspectives were adequately represented. Phase 2 comprised inductively coding the transcripts by categorizing all relevant data under codes. Phase 3 involved combining different codes into themes. In phase 4, the themes were reviewed and then deductively classified into the 14 domains of the TDF (v2).[14,15] The TDF entails a synthesis of 14 main behavior change determinants from key theories, e.g. knowledge, intentions, environmental context and resources, and behavioral regulation.[14] The TDF is validated for use in behavior change research,[15] and has been used to understand determinants of behavior change among patients with CKD.[16,23] The TDF was used because the themes fitted its domains well and the framework was helpful to disentangle and structure the findings. In phase 5, the TDF domain definitions were used to describe the content and refine the themes within each domain. Last, in the sixth phase, the current article was written. In this phase, similarities and differences between patients and health professionals' focus groups were taken into account in two ways: First, the Atlas.ti software was used to mark to which focus group the data within each domain and theme belonged, which made differences and parallels between the two participant groups visible. Second, the top-3 barriers and facilitators considered most important by each participant were analyzed: Three points were given to a theme a participant found most important, two to their second, and one to their third choice. Then, all top-3 barriers and facilitators were categorized into the TDF domains. Percentages of the points given to each domain were calculated for the full sample, and also per participant category. Finally, to structure the results section of the report, an existing categorization of the fourteen TDF domains was used,[15] into three overarching components that are considered essential for behavior and behavior change to occur: Capability, Opportunity, and Motivation (the 'COM-B' system).[14]

In both the inductive and deductive coding stages, triangulation across three investigators—all experienced in qualitative data analysis—repeatedly took place. The first author analyzed all transcripts in accordance with the six phases, from transcription to manuscript drafting. The second author (a female physician researcher and PhD candidate in nephrology) and the last author (a female researcher in health psychology) independently coded three transcripts (phase 2), sorted codes into themes (phase 3), and allocated those to the domains of the TDF (phase 4). For the top-3 barriers and facilitators, the first and last author independently categorized all barriers and facilitators into the TDF domains. In each phase, the researchers frequently discussed the identified codes, themes, and allocation of themes to the TDF domains, to resolve any inconsistencies and coding problems and revise the generated themes. This was done to minimize interpretive bias due to prior understandings of the phenomena under study. Also, the full manuscript was revised by all other authors. Finally, all study participants were sent a copy of a summary report and were invited to provide feedback, which was provided by one participant and incorporated in the results. Quotations were translated from Dutch to English for publication purposes. For patient quotations, patients' disease statuses were indicated by their CKD stages, including a "T" to indicate kidney transplant recipients (e.g., CKD stage 3T).

Results

Table 1. Sample characteristics of patients with CKD (*n*=24) and health professionals (*n*=23) per focus group.

Participants	No. of Participants	Age Range	Education Level		Gender		CKD stage range	Kidney Transplantation	
			Low	High	Male	Female		Yes	No
Patients	6	55–85	4	1[a]	4	2	4–5	1	5
Patients	7	35–74	4	3	5	2	2–4	7	0
Patients	7	37–79	4	3	6	1	1–5	0	7
Patients	4	48–69	1	3	3	1	2–4	3	1
Professionals	6	42–62	0	6	1	5			
Professionals	6	25–61	0	6	1	5			
Professionals	5	35–57	0	5	2	3			
Professionals	6	34–61	1	5	2	4			

[a] One patient did not complete this question. Abbreviations: CKD, chronic kidney disease; No., number. Low education includes primary, pre-vocational and vocational education; high education includes advanced levels of secondary and tertiary education.

Sample characteristics

The final sample consisted of four focus groups with patients ($n = 24$) and four with health professionals ($n = 23$). Each focus group involved four to seven participants. As shown in Tables 1 and B1 (Supplementary File 2), the patients had a mean age of 62.2 years (range

35.8–85.0 years) and the majority (75.0%) were male. About half of the patients had a kidney function (estimated glomerular filtration rate) of <30 ml/min per 1.73 m^2, and almost half had received a kidney transplant. The health professionals had a mean age of 48.4 years (range 25.3–62.7 years) and the majority (73.9%) were female. In each of the focus groups with health professionals, at least one nephrologist, dietician, nurse practitioner, and social worker were present.

Barriers and Facilitators

A summary of the results can be found in Table 2, including the main barriers and facilitators that were brought forward, structured into the 14 overarching TDF domains and three COM-B components. Also, the similarities and differences between themes discussed by patients and by health professionals are shown.

Capability

Knowledge

Both patients and health professionals emphasized the relevance of patients' knowledge about lifestyle guidelines. Health professionals reported that patients often have inaccurate beliefs on how to engage in a healthy lifestyle, overestimate its financial burden, and tend to overrate the healthiness of their current lifestyle:

> "…they were not at all aware that they took so little steps a day … They were like 'Oh, I thought I would be closer to those 10.000'." (Dietician)

In line with this, many patients emphasized the complexity of especially medication prescriptions and dietary restrictions, as well as the need to learn what a healthy lifestyle comprises:

> "I would eat half a melon easily. The professor called it 'wrong fruit' … with too many sugars and so on. Before I did not know. Ignorance." (Patient, male, CKD stage 5)

Memory, Attention and Decision Processes

Health professionals were concerned that patients would get confused by the great amount of often contradictory information, especially for healthy diets and food choices:

"People are really being overwhelmed, they search themselves as well, of course. In a mishmash of information in which they can't find their way." (Dietician)

Skills

Both patients and health professionals emphasized the ability to use creativity in learning new lifestyle behaviors:

> "I'm able to cook in such a way that my guests don't miss salt. I've learned many alternatives." (Patient, female, CKD stage 4)

Health professionals stated that interpersonal skills are required, mainly assertiveness, for instance to ask or search for additional information, to ask for support, and to indicate needs:

> "It's facilitating when a patient asks questions to us as health professionals. So we should train them to ask for what really matters to them." (Nephrologist)

In line with this, most patients mentioned the importance of the ability to handle social pressure and refuse unhealthy food or cigarettes. Accordingly, some even avoided social gatherings to refrain from unhealthy seductions. Furthermore, some patients made sure that they only had healthy products available at home, as they found it hard to resist temptations:

> "When it's 4 PM, you become tired, and you think 'screw that apple', and you open the drawer and think 'well, what shall I choose?' What's available … you grab it more easily." (Patient, female, CKD stage 2T)

Behavioral Regulation

To automatize healthy lifestyle behaviors, patients and health professionals emphasized consciously breaking habits, creating new routines, and linking new behaviors to existing habits. Health professionals underlined that breaking long-lasting habits is problematic, as it is more comfortable and easy to maintain old habits:

> "Then you suddenly have to change something you have been used to doing for 20 years, to lighten a cigarette when you're a bit stressed." (Social worker)

Furthermore, disease progress and comorbidities (mainly diabetes) demand patients to frequently adapt their routines of diet and medication intake. Additionally, specifically for medication adherence, deviating from usual routines makes it difficult to remember performing the healthy behavior:

> "Sometimes when you go out shopping and it takes longer, then you eat something elsewhere, and then you forget or miss your medication. That takes me by surprise sometimes." (Patient, male, CKD stage 4)

Table 2. Main themes (barriers/facilitators for lifestyle adherence) from focus groups, structured into TDF and COM-B.

COM-B component	TDF Domain (definition)	Themes patients	Themes health professionals
Capability (Patients' psychological and physical capacity to engage in a healthy lifestyle)	**Knowledge** (An awareness of the existence of something)	Knowledge of healthy lifestyle	Knowledge of healthy lifestyle; Beliefs about healthy lifestyle; Beliefs about financial burden
	Memory, Attention and Decision Processes (The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives)	-	Confusion due to information overload
	Skills (An ability or proficiency acquired through practice)	Creativity; Coping with temptations/social pressure	Creativity; Assertiveness
	Behavioral Regulation (Anything aimed at managing or changing objectively observed or measured actions)	Breaking habits; Creating routines	Breaking habits; Creating routines
Opportunity (All factors external to patients that encourage or discourage healthy lifestyle behaviors)	**Environmental Context and Resources** (Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior)	Disease characteristics; Material support tools; Characteristics of health care system; Societal characteristics	Disease characteristics; Material support tools; Characteristics of health care system; Societal characteristics; Competing tasks; Psychiatric or cognitive problems
	Social Influences (Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors)	Instrumental/emotional support by social environment; Peer pressure	Instrumental/emotional support by social environment; Peer pressure; Professional support

COM-B component	TDF Domain (definition)	Themes patients	Themes health professionals
Motivation (Patients' reflective and automatic brain processes that energize and direct behavior, such as habitual processes, emotional responding, and analytical decision-making)	**(Social/Professional) Role & Identity** (A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting)	-	Obedience; Conscientiousness
	Beliefs about Capabilities (Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use)	-	Locus of control; Self-efficacy
	Optimism (The confidence that things will happen for the best or that desired goals will be attained)	Focusing at opportunities; Acceptance; Resilience	Focusing at opportunities; Acceptance
	Emotion (A complex reaction pattern, involving experiential, behavioral, and physiological elements, by which the individual attempts to deal with a personally significant matter or event)	Depressive feelings; Stress; Anxiety	Depressive feelings; Stress; Anxiety
	Beliefs about Consequences (Acceptance of the truth, reality, or validity about outcomes of a behavior in a given situation)	Beliefs about consequences of lifestyle behaviors; Previous experiences with consequences	Beliefs about consequences of lifestyle behaviors; Previous experiences with consequences
	Reinforcement (Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus)	Noticeable effects; Healthy behaviors experienced as punishment	Noticeable effects; Unhealthy behaviors as short-term reward; Punishing unhealthy behaviors
	Intentions (A conscious decision to perform a behavior or resolve to act in a certain way)	Intrinsic motivation; Higher-order purposes	Intrinsic motivation; Higher-order purposes
	Goals (Mental representations of outcomes or end states that an individual wants to achieve)	Flexibility; Discipline	Goal setting

Note. Parts of this Table are adapted from "Validation of the theoretical domains framework for use in behavior change and implementation research.", by J. Cane, D. O'Connor, and S. Michie, 2012, *Implementation Science, 7*(37), p. 13-15. Copyright 2012 by Cane et al. Adapted with permission. TDF: Theoretical Domains Framework; COM-B: Capability, Opportunity, Motivation – Behavior.

Opportunity

Environmental Context and Resources

In all focus groups, characteristics of disease were mentioned to influence patients' engagement. Disease symptoms, such as fatigue and a lack of energy, make lifestyle adaptations and specifically physical activity difficult. At the same time, some participants stated that a lack of physical symptoms may form a barrier to perceive the urgency to engage in a healthy lifestyle. Health professionals saw this mainly among patients in early, asymptomatic disease stages, but a few transplant recipients also experienced this barrier:

> "That's what makes it [lifestyle adherence] so difficult. I have a kidney function of 18% now, but I do not feel anything [symptoms]." (Patient, male, CKD stage 4T)

A few patients but mainly health professionals pointed out the role of competing tasks, for instance caused by irregularity or busyness at work on top of suffering from a chronic disease. These competing tasks force patients to prioritize, which is often at the expense of a healthy lifestyle, especially of physical activity:

> "… and that they [patients] want to use their last bit of energy to work because they really want to maintain that, for instance." (Nephrologist)

In most focus groups with health professionals, psychiatric illness, addiction, and cognitive decline among patients were believed to hinder a healthy lifestyle, due to insufficient capabilities to change habits, or a lack of insight in their disease and consequences of their behavior.

The use of material resources or tools was mentioned by both patients and health professionals to facilitate lifestyle adherence, such as scales, planners, alarms, medicine boxes, and blood pressure monitors. With regard to the health care system, many health professionals mentioned the short duration of hospital visits, the lack of regular follow-up visits, and the consultation of different health professionals at each visit as barriers to adequately promote their patients' behavior change in a patient-centered way:

> "But if you want to achieve that [behavior change] you need to explain why it is important, … and also check with the patient like 'how are you going to do that in the upcoming three months, what are the social-context goals you want to achieve'. Yeah then another half an hour has passed, that is impossible." (Nephrologist)

To overcome these barriers, participants stressed the importance of additional health care support, such as dietetics, physiotherapy, psychotherapy, and social work:

> "Nothing is as difficult as behavior change. If you only look at yourself, you can be very motivated, but then to set it in motion and maintain it [is difficult]. You should

> deploy much more psychotherapists, to make sure that people also get the tools to start behavior change." (Nurse practitioner)

Regarding barriers from a societal perspective, some participants were critical about the amounts of high-sodium foods in restaurants and supermarkets. Health professionals were concerned about the increase of sedentary behavior in work settings.

Social Influences

In all focus groups with health professionals, the role of their own support was extensively discussed. Many health professionals pointed out the importance of bonding, positive stimulation, regular evaluation, reinforcing progression, and repetition of relevant themes. They all believed that patient-centered care is necessary to achieve that patients engage in a healthy lifestyle. Within patient-centered care, health professionals adapt their communication style and information provision to patients' personal needs, barriers and facilitators, intellectual abilities, and health literacy, and focus on whatever topic patients find most urgent:

> "Sometimes I try to explain sodium but then they mix it up a bit and talk about potassium the whole time, then I think, well then I'll explain potassium. That is important. To treat what's on a patient's mind at that moment." (Dietician)

Health professionals stressed the importance of emotional and instrumental support by family members, especially regarding smoking and diet. It was believed that living alone and social isolation encourage unhealthy behavior. In addition, they were very concerned about reluctance of family members to participate in patients' lifestyle behavior change:

> "It isn't only about changing the patients, it's also about changing their system. You don't even see their system, that's even more difficult to change." (Nephrologist)

Conversely, few patients experienced barriers from their social environment. Some argued that family members do not participate in their lifestyle regimens, or that they are sometimes too pitying or meddlesome. However, most patients were rather positive about family support, especially by partners and children. They indicated that they feel supported when their loved ones think along, keep an eye on their behavior, and participate, especially in healthy eating:

> "…my wife always says immediately 'what's inside', in packages and bags … she looks up menus on the internet. … I always say 'there's two persons ill, you're not ill alone'." (Patient, male, CKD stage 4T)

In almost all patient focus groups as well as by some health professionals, owning a dog and the opportunity to encounter others and engage in social interaction were mentioned to be important facilitators that encourage going out for a walk or bike ride. With regard to social learning and peer pressure, a few health professionals stated that the wish to fit in can be detrimental if patients are surrounded by unhealthy examples of others:

> "It is actually 'not done' if you say 'I don't want to eat that' at a birthday party, or 'I'm quitting smoking' or 'I won't visit you tonight because I'll go for a run' … you will be judged on that a little. Or you will get comments about it, which won't make it easier." (Dietician)

Also, it was mentioned by health professionals that in some cultures, it is common to use a lot of sodium, and it may be impolite to refuse food. Conversely, patients tended to focus on facilitating effects of peer pressure:

> "In the past, you fitted in if you smoked, but if you smoke nowadays, you don't fit in anymore." (Patient, male, CKD stage 5)

Motivation

(Social/Professional) Role & Identity

Health professionals described patients that succeed in adhering to a healthy lifestyle to be often very obedient, structured, and conscientious:

> "The perfectionists they generally achieve more." (Nephrologist)
>
> "…you just tell them what they have to do, and then they do it exactly. There are also people who behave that way as a part of their personality. … You just say 'walk 3 times a day' and they do it." (Social worker)

Beliefs about Capabilities

Health professionals emphasized that it is hard to adapt lifestyle habits for patients with an external locus of control. They argued that some patients believe their doctor or partner is responsible for their disease progress or lifestyle, and that they cannot influence their condition themselves:

> "When someone says 'Yes, but my wife cooks'. Then you already know that it will be very hard to get through." (Dietician)

Similarly, according to some health professionals, patients may lack self-efficacy or have pessimistic beliefs about the complexity of lifestyle behaviors; yet only a few patient participants expressed uncertainty about their own capabilities.

Optimism

Participants in all focus groups stressed the importance of optimism, that is, looking at opportunities and alternative possibilities instead of focusing on physical limitations or lifestyle restrictions:

> "I see one patient…, he lost two legs in one year. … I thought he would arrive here as a wreck. Well he came in, in that wheel chair, and he said: 'I'm still able to cook and I love doing that.' The man's eyes literally beamed." (Nephrologist)

Patients stressed that their optimism facilitates disease acceptance and resilience. In line with this, both patients and health professionals believed that patients need to accept their condition and lifestyle regimens in order to achieve lifestyle changes:

> "Well, what I do, I do not focus on the things which I can't do anymore, I look at the things I still *can* do." (Patient, male, CKD stage 4T)

Emotion

Some participants recognized that experienced limitations due to CKD and a lack of disease acceptance may contribute to depressive feelings. In most focus groups, the role emotions was already discussed as a barrier for healthy lifestyle behaviors before the quotations from previous studies were shown: Participants agreed that feeling down or depressed forms a barrier to engage in healthy lifestyle behaviors, e.g., physical activity, since depressive feelings are often accompanied by a lack of energy, motivation, persistence, or an inability to see opportunities. Many stated that causes of depressive feelings may also be unrelated to disease, such as work-related problems or an inclination to be pessimistic. A few participants added that chronic disease may make it even more difficult to cope with adversities in other life domains:

> "These people already have limitations. Then a setback is even more difficult to handle. More difficult to stay motivated and maintain your lifestyle in order." (Social worker)

Participants indicated that engaging in healthy behaviors could also be hampered by stress. To deal with stressful situations and to feel less stressed, unhealthy behaviors are being used as coping strategies, especially unhealthy eating and smoking:

> "When things happen of which you think, back then I thought it was really true but, that you believe it helps to smoke a cigarette. … especially when things fall short, you 'need' some consolation. And you receive that false consolation by a cigarette." (Patient, female, CKD stage 2T)

Furthermore, participants agreed that anxiety may either hinder or facilitate behavior change. On the one hand, anxiety regarding disease may contribute to an "ostrich policy":

> "Head in the sand, also anxiety, I was very anxious. … I did everything that was unhealthy." (Patient, male, CKD stage 3T)

On the other hand, concerns about future perspective and especially the occurrence of sudden negative health-related events (e.g., experiencing a heart attack) may cause fear that motivates patients to prevent future complications.

Beliefs about Consequences

Beliefs about side effects were important barriers for medication-taking behavior. As a facilitator, some participants argued that awareness about the consequences of unhealthy behavior and the effects of a healthy lifestyle may be enhanced by patients' experiences with dialysis or a kidney transplant themselves or by their relatives:

> "My first wife died due to kidney failure, so I know what it is, I saw the entire deterioration process, and that does not make you happy. So you do everything to prevent that from happening." (Patient, male, CKD stage 2)
>
> "… unless you have something hereditary with grandmother, grandfather, brother, sister who are already in a later stage, then you are more aware of it [the importance of healthy behavior]." (Nurse practitioner)

Specifically, kidney transplant recipients expressed a drive to prevent graft rejection:

> "Immunosuppressive drugs, you just take them because the last thing you want is the kidney to be rejected." (Patient, female, CKD stage 2T)

Reinforcement

According to some health professionals, unhealthy behavior, for instance smoking or snacking, provides a short-term reward, while a few patients experienced healthy behavior as some kind of punishment:

> "Everything that tastes good, is forbidden." (Patient, male, CKD stage 5T)

Most participants reported that noticeable effects, such as visible weight loss, a better physical condition, or a reduction in medication prescriptions, are rewarding and facilitate healthy behavior:

> "Results help, either weight loss, or waist circumference diminishes, or you see at such a device at the gym that you got more muscle mass. And [it helps] when you eventually feel it as well. But that small intermediate step of a centimeter, or a kilogram less, or a bit more muscle mass or less fat mass … that helps." (Dietician)

However, participants stated that it is not always possible to make progress visible or to influence measurement results by adapting lifestyle behavior, due to underlying disease factors:

> "Suddenly my body produces a protein while I try so incredibly hard, I follow the dietician's advice…" (Patient, male, CKD stage 3)
>
> "I think that is very difficult in our patient group … you slowly get worse. You quit smoking, but you don't get better, you still have difficulties climbing the stairs because your kidney function deteriorates." (Nurse practitioner)

Some health professionals argued that it helps when unhealthy behavior is punished, for instance by making it more difficult to receive a transplant when a patient does not quit smoking.

Intentions

Most participants agreed that a strong intrinsic motivation is needed for patients to engage in behavior change. They stated that in order to succeed, a lifestyle change should be enjoyable and rewarding:

> "For example she [social worker] arranged a vegetable garden for me. … In the past I was always active with plants, with the garden. So in that time I had a great experience. That helps to engage in physical activity, growing vegetables yourself, getting to know people. That helped me." (Patient, male, CKD stage 3T)

Furthermore, participants stated that lifestyle adaptations should be linked to higher-order values and purposes that are personally important for the patients:

> "The purpose is not quitting smoking, the purpose is doing fun things with the grandchildren." (Social worker)

Goals

Some patients valued freedom and flexibility in the implementation of lifestyle advices, rather than being too strict:

> "One day I do not use salt at all, the other day a little more … that is how I try to do it." (Patient, female, CKD stage 4)

While health professionals stressed the importance of setting concrete and personally feasible behavioral goals, patients did not mention goal setting specifically. Actually, they stated that discipline should be sufficient to maintain a healthy lifestyle. Some even added that they just want to stay alive and fight for that:

> “When you get an advice, you do everything you can to fight for it. You start from the position ‘I want to go on’ and then you try your best.” (Patient, female, CKD stage 5)

Ranking of Barriers and Facilitators

Patients as well as health professionals considered barriers and facilitators related to patients’ social and physical environment most important, among which social support by a patient’s partner and others, peer pressure, and physical limitations or complaints. Other themes often ranked by patients were intrinsic motivation, discipline, and an optimistic attitude; whereas health professionals found knowledge about disease and lifestyle, goal setting, disease acceptance, and intrinsic motivation most important. In Figure 1, a ranking of themes categorized in accordance with the TDF domains is shown.

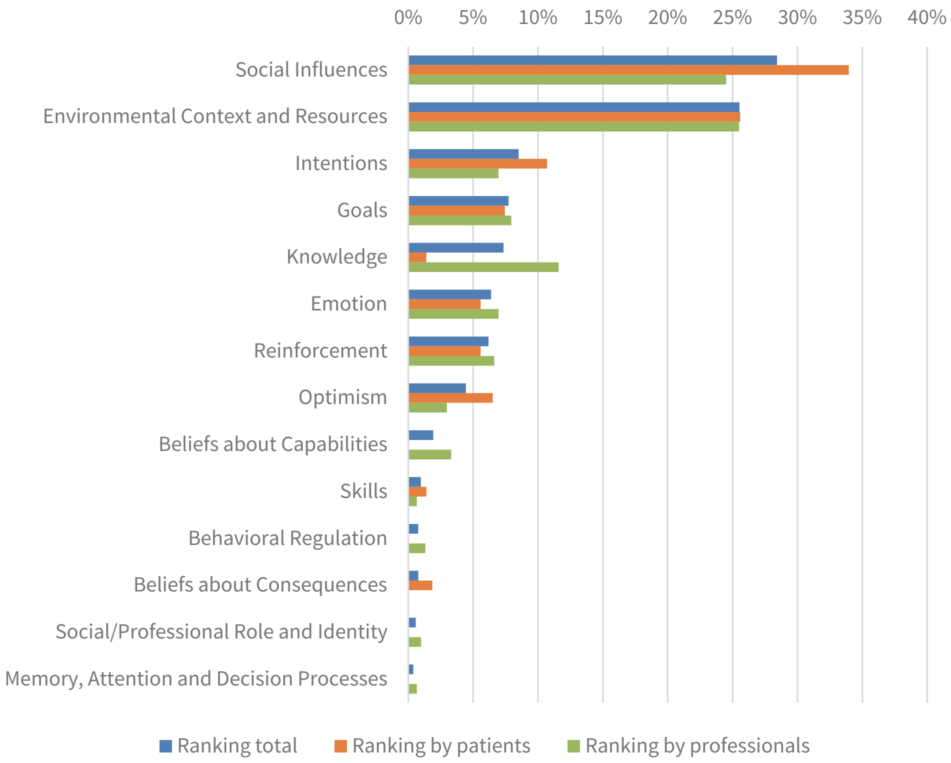

Figure 1. Importance of themes that determine lifestyle adherence in chronic kidney disease ranked by participants. *Note.* Percentages of the points given to themes within each domain of the Theoretical Domains Framework (TDF) are shown, from the total sample and per participant category.

Intervention Strategies

Patients suggested that a support program to target the barriers and facilitators should be patient-centered, in order to provide information and support that is tailored to their personal situation and preferences. Additionally, such a program should provide very clear information on what behaviors are healthy, including concrete examples. Especially in one focus group, patients proposed intensive guidance, for instance by a personal coach. Some patients found contact with fellow patients, for example in organized gatherings, useful in order to learn from each other's experiences, whereas others were hesitant about listening to peers with negative experiences or pessimistic perceptions.

Health professionals had diverse ideas about prerequisites of intervention strategies, such as a positive, empowering approach and repetition of information. Health professionals agreed with patients on a tailored, patient-centered program, and added the importance of small, feasible steps. Some mentioned the utility of psychological intervention strategies for behavior change:

> "…if you have a positive self-image, self-esteem, if you are optimistic, happy, then everything will be easier and everything [lifestyle changes] will succeed better. People who are ponderous, not necessarily depressed, are more pessimistic. … Nowadays many initiatives exist, books, internet, coaching, many people have a coach to pay attention to these kinds of things." (Nephrologist)

Discussion

With regard to the first aim of this qualitative study, multiple psychosocial barriers and facilitators were revealed across all fourteen domains of the TDF, that may determine the adherence to a healthy lifestyle among patients with CKD not receiving dialysis. Patients and health professionals agreed on the importance of patients' social and physical environments, intrinsic motivation, and emotional wellbeing. Furthermore, patients stressed discipline and optimism as main determinants, whereas health professionals emphasized knowledge, beliefs about capabilities, and goal setting. As a second research aim, a number of intervention strategies to overcome barriers and promote facilitators were identified in this study. Both patients and health professionals stressed that, since the experienced barriers and facilitators may differ per individual, intervention strategies should be patient-centered and tailored. Tailored interventions could target multiple barriers and facilitators and are personalized to individual needs.[24,25] Below, the main TDF domains of barriers and facilitators, as well as matching intervention strategies and BCTs that were brought forward by patients and health professionals, will be discussed.

Both patients and health professionals extensively stressed the importance of the degree to which patients' environments provide the opportunity to engage in a healthy lifestyle. In line with previous studies among CKD populations, this implies that intervention strategies should involve the physical and social environment.[26-28] Health professionals argued that patients' social environments often hinder engagement in a healthy lifestyle, whereas patients perceived their social network as facilitating. Both perspectives imply the need for BCTs that promote social support.[14] As previously described in research among patients with chronic diseases,[29] including patients with chronic kidney disease,[30] we found that especially partners and other family members play an integral role in disease management and support. Therefore, it is vital to involve them in behavior change interventions for patients. Possible ways to achieve this suggested by participants included stimulating relatives to join patients' behavior changes or teaching patients interpersonal skills to indicate their needs and ask for the support they prefer. Also, participants suggested practical environmental resources, i.e., material tools that aid to fit lifestyle adaptations into patients' personal situation and daily life.[14] For example, planning tools could be used to schedule resting time between physical activities in order to evenly distribute energy levels and diminish fatigue burden.

Regarding motivational barriers and facilitators, participants agreed on the role of a strong intrinsic motivation. This may sometimes be lacking among patients in non-transplant and asymptomatic stages of CKD, who may perceive adherence to lifestyle guidelines to be less urgent. However, enhancing motivation alone is not sufficient to achieve behavior change, as other factors also play an important role herein: Health professionals mentioned in consistence with literature that patients' capabilities to change their lifestyle may be limited by a lack of knowledge about what a healthy lifestyle comprises.[27,31] Therefore, a combined approach of BCTs is recommended to enhance both motivation and knowledge,[32] which would support patients to put healthy lifestyle behaviors into practice. For instance, in a small intervention study among patients with CKD not receiving dialysis guided by a health psychologist, motivational interviewing techniques to improve intrinsic motivation were combined with education to increase knowledge, tailored to patients' stages of behavior change.[33] The study showed promising results on medication adherence and emotional wellbeing. The current findings also suggest a need for tailoring behavior change techniques to patients' stages of behavior change. For example, the BCT of setting personally relevant and feasible goals, which was mainly mentioned by health professionals, may be especially useful to enhance motivation and facilitate the adoption of new behavior in early stages. In contrast, patients stressed the importance of discipline, which should be promoted in later stages to facilitate long-term maintenance of healthy behaviors, for instance by listing and using personal strengths that may aid a patient in persisting (i.e., BCT ‘valued self-identity’).[14]

Regarding emotional wellbeing, patients and health professionals agreed on the negative impact of psychological distress, including symptoms of depression, anxiety, and stress. A link between psychological distress and non-adherence to lifestyle recommendations is not surprising, as psychological distress symptoms are related to reduced levels of energy, motivation, self-efficacy, self-regulatory resources, and social support, which all may form strong barriers for engagement in a healthy lifestyle.[7,11] Intervention strategies in chronic disease evaluated in published research usually focus either on diminishing psychological distress or on improving lifestyle behaviors.[34] It is desirable to target both in an integrated way, for instance by providing self-management support using cognitive-behavioral therapy specialized for adjustment to chronic disease.[17] In integrated interventions, patients can be stimulated to set goals and engage in behaviors that both diminish psychological distress and improve healthy lifestyle behaviors.[7] For example, not only BCTs could be deployed that directly target lifestyle behaviors, such as enhancing motivation or knowledge, but also that seek to reduce negative and enhance positive emotions to facilitate performance of the desired behaviors, e.g., by cognitive restructuring of negative thoughts and beliefs.[14]

This study has several strengths. To our knowledge, this is the first qualitative study in which barriers and facilitators for engaging in a healthy lifestyle were explored across the full range of lifestyle recommendations in CKD care. Since perspectives of patients and health professionals working with different CKD stages were involved, including kidney transplant patients, it can be argued whether the results can be generalized to populations with various disease courses and characteristics (e.g., symptomatic or not). On the one hand, some of the barriers and facilitators found were rather specific for the CKD population, such as those related to the gradual disease progress with asymptomatic early stages and burdensome treatments in severe end stages, including the often complex dietary restrictions and medication prescriptions that vary across stages. Also, some facilitators were specifically relevant for (potential) kidney transplant recipients, such as adherence to healthy lifestyle behaviors driven by a motivation to enhance their eligibility for transplantation or to prevent graft rejection. These disease-specific themes should be taken into account when supporting patients with CKD not receiving dialysis. On the other hand, patients with CKD often suffer from comorbidities (e.g., type 2 diabetes mellitus) and many themes, such as psychological distress, did not seem disease-specific and have been found applicable to other chronically ill populations for which engaging in healthy lifestyle behavior is also essential, such as for patients with diabetes or cardiovascular diseases.[35-37] Furthermore, participants in our study have different education levels, suggesting that the findings may also be applicable to under-served groups with low education levels and possibly low health literacy, since education level has been found predictive of health literacy.[38] As we did not measure health literacy or other chronic conditions in the current study, additional research could further investigate generalization to different populations and health behaviors.

Some limitations should be taken into account. As a possible source of bias in data collection, one could argue that the relevance of psychological distress may have been overestimated due to the quotations shown and the specific question about this theme. However, in most focus groups, the importance of psychological distress was already discussed by participants as a consequence of living with CKD and as a barrier for healthy lifestyle behaviors before the quotations and specific question were used. Furthermore, adherence to a healthy diet was more prevalently discussed than the other relevant lifestyle behaviors. This result may indicate that dietary adherence is the most important and complex lifestyle behavior in this population. However, the frequent discussion of dietary adherence may also be explained by the presence of a dietician in each focus group among health professionals (whereas in only one focus group, a physiotherapist participated), and the fact that dietetics is the only specialized hospital lifestyle support that is common in Dutch CKD care. Regarding data analysis, the inductively created codes fitted the TDF well and a main advantage of using this meta behavior change framework is its systematic synthetization of a large amount of behavior change theories, which taps into the challenges of translating theories into practice and minimizes the risk of missing relevant constructs.[29,39] However, some challenges were experienced when mapping the data onto the TDF. Foremost, not all domains are mutually exclusive and mainly the 'environmental context and resources' domain seemed rather broad and not very well conceptualized.[40] Therefore, this domain was experienced to be a receptacle of a wide range of themes and thus could seem over-represented. Furthermore, the TDF was originally developed for health professionals' behavior,[41] and difficulties were experienced when translating some domains to patients' behavior, for instance with 'social/professional role & identity'. These challenges were solved by comparing our categorizations to other studies focused on kidney patient disease management behaviors that used the TDF.[16,23] Additionally, we applied constant researcher triangulation and discussion, in order to reach interpretation consistency and a satisfactory inter-rater reliability.[20,21]

The results, which show a great variety of psychosocial barriers and facilitators that may differ per individual patient, imply that tailored psychosocial intervention strategies could be a promising approach to support patients with CKD in lifestyle behavior change. To be able to support patients in their personal needs, first, psychosocial and lifestyle-related difficulties of an individual patient should be detected. However, it may be difficult to assess psychosocial barriers that are not readily observable and patients may hesitate to disclose personal information in a routine hospital visit.[42,43] Among patients in our focus groups, little discussion of support by their health care providers took place, which may indeed indicate a gap of discussing personal barriers and facilitators for healthy lifestyle behaviors in patient-provider communication. This lack of discussion may lead to misunderstandings and discrepancies between patient needs and actual support from health professionals, especially since our findings show that determinants perceived as important by health professionals, such as knowledge, do not always align with determinants that matter to patients themselves. In addition, health professionals mentioned the low frequency and duration of contact moments as a barrier to adapt their aid to their patients' needs. A suitable first step in tailored intervention design may therefore be a screening instrument including the main TDF domains by which patients could indicate personal barriers and facilitators. Such a tool could aid health professionals to accurately and efficiently address potential barriers in consults, adjust lifestyle advices to their patients' situation, monitor and reinforce progress, and refer patients to more specialized support or treatment when needed.[17,44] As a second step, such a specialized and tailored treatment could be developed by translating the TDF domains to intervention strategies and BCTs that fit the target behavior and population best.[14] To guide these steps, the Behavior Change Wheel, a framework for intervention design, could be used.[14] As an example, we refer to the steps taken in the development of the E-GOAL eHealth care pathway, described elsewhere,[45] in which we matched the insights of the current focus group study to intervention content. For instance, to promote the TDF domain reinforcement, we included the BCTs 'self-reward' and 'material rewards', in an exercise to select a personally relevant contingent reward to reinforce progress in the desired behavior change. Noteworthy, many barriers, facilitators, and intervention strategies identified in this study were found valuable for multiple lifestyle behaviors relevant in CKD management, and previous research proposed that the interrelatedness of different lifestyle behaviors warrants an integrated approach.[27] This suggests that a single intervention could be adapted to the lifestyle behavior of patients' preference. Development, evaluation, and implementation of such an integrated intervention should preferably take place in a research setting in close collaboration with patients, health professionals, and other stakeholders in clinical practice, to investigate its feasibility, acceptability, cost-effectiveness, and effectiveness in improving patients' lifestyle and health outcomes.

Conclusions

This focus group study presents a broad range of barriers and facilitators that determine engagement in healthy lifestyle behaviors among patients with CKD not receiving dialysis. The great amount of mainly environmental, motivational, and emotional barriers experienced by patients, may explain why many of them do not succeed in adhering to the CKD lifestyle recommendations. Participants in this study stressed the impact of psychosocial barriers and facilitators for lifestyle adherence, such as psychological distress, which may have been somewhat overlooked in previous research. Furthermore, the current study identified intervention strategies to overcome barriers and promote facilitators, as the TDF domains can be translated to matching BCTs. Developing and investigating interventions that address psychosocial barriers and facilitators, and that combine screening and treatment, allows for better tailoring to patients' needs, by identifying and treating individually experienced psychosocial barriers for adherence to lifestyle guidelines.

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Supplementary File 1

Question Guide of the Focus Groups

Table A1. Question guide of the focus groups.

1. What are the most important lifestyle adaptations you made or think you should make? *(only in patient focus groups)*

2. What do you perceive as the most important consequences of (your) kidney disease?

3. Facilitators: what helps or has helped you/your patients to engage in a healthy lifestyle?

4. Barriers: what makes or has made it difficult for you/your patients to engage in a healthy lifestyle?

5. What barriers and facilitators are specific to a healthy diet/a healthy weight/physical activity/no smoking/medication adherence?

6. We think that psychological factors may play a role. *Example quotations shown:*

"I think a lot of the time that's what can make the whole self-management thing so difficult to stick to, it's the thing of wanting to be your old self."[a]

"*…these little conditions, they stop you doing things, and then your motivation, if you're feeling down and you're depressed, then your motivation's not there.*"[b]

Do you recognize this? Why?

7. If you would have the opportunity to design your own program to support patients with CKD in targeting the mentioned barriers and facilitators, what should be included in such a program?

[a](Gordon et al., 2017, p.e212); [b]Coventry, Fisher, Kenning, Bee, & Bower, 2014, p. 7)

Supplementary File 2

Sample Characteristics

Table B1. Sample characteristics of patients with CKD (*n* = 24) and health professionals (*n* = 23).

Characteristics	Patients		Professionals	
Mean age (SD)	62.2	(13.7)	48.4	(11.5)
Male gender *n* (%)	18	(75.0)	6	(26.1)
Country of birth Netherlands *n* (%)	20	(83.3)	21	(91.3)
Married/partnered *n* (%)	20	(83.3)	20	(87.0)
Having children *n* (%)	20	(83.3)	13	(56.5)
Level of education *n* (%)[a]				
Low (primary, pre-vocational and vocational)	13	(56.5)	1	(4.3)
High (advanced secondary and tertiary)	10	(43.5)	22	(95.7)
Work status *n* (%)[a]				
Full-time	3	(13.0)	12	(52.2)
Part-time	3	(13.0)	11	(47.8)
Voluntary work	5	(21.7)		
School/studies	1	(4.3)		
Home/retired	8	(34.8)		
Disabled due to health	3	(13.0)		
Kidney transplantation *n* (%)	11	(45.8)		
CKD stage *n* (%)				
1	1	(4.2)		
2	4	(16.7)		
3	8	(33.3)		
4	6	(25.0)		
5	5	(20.8)		
Mean years in CKD treatment (SD)	11.6	(8.1)		
Health care profession *n* (%)				
Internist-nephrologist			7	(30.4)
Dietician			6	(26.1)
Social worker			4	(17.4)
Nurse practitioner			4	(17.4)
Nurse			1	(4.3)
Physiotherapist			1	(4.3)

[a] One patient did not complete this question. Abbreviations: CKD, chronic kidney disease.

Chapter 3

Detecting and treating psychosocial and lifestyle-related difficulties in chronic disease: Development and treatment protocol of the E-GOAL eHealth care pathway

Cinderella K. Cardol, Judith Tommel, Henriët van Middendorp,
Yvette Ciere, Jacob K. Sont, Andrea W.M. Evers, and Sandra van Dijk

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Abstract

Background

Many patients with lifestyle-related chronic diseases find it difficult to adhere to a healthy and active lifestyle, often due to psychosocial difficulties. The aim of the current study was to develop an eHealth care pathway aimed at detecting and treating psychosocial and lifestyle-related difficulties that fits the needs and preferences of individual patients across various lifestyle-related chronic diseases.

Methods

Each intervention component was developed by (1) developing initial versions based on scientific evidence and/or the Behavior Change Wheel; (2) co-creation: acquiring feedback from patients and health professionals; and (3) refining to address users' needs.

Results

In the final eHealth care pathway, patients complete brief online screening questionnaires to detect psychosocial and lifestyle-related difficulties, i.e., increased-risk profiles. Scores are visualized in personal profile charts. Patients with increased-risk profiles receive complementary questionnaires to tailor a 3-month guided web-based cognitive behavioral therapy intervention to their priorities and goals. Progress is assessed with the screening tool.

Conclusions

This systematic development process with a theory-based framework and co-creation methods resulted in a personalized eHealth care pathway that aids patients to overcome psychosocial barriers and adopt a healthy lifestyle. Prior to implementation in healthcare, randomized controlled trials will be conducted to evaluate its cost-effectiveness and effectiveness on psychosocial, lifestyle, and health-related outcomes.

Keywords Lifestyle adherence; Psychosocial adjustment; Chronic disease management; Intervention development; eHealth; Screening; Web-based cognitive-behavioral therapy; Tailored personalized treatment; Behavior Change Wheel; Co-creation

Introduction

Lifestyle-related chronic diseases—such as type 2 diabetes, cancers, and cardiovascular, kidney, and chronic respiratory diseases[1,2]—form the leading causes of death, accounting for 71% of global mortality in 2016.[2] Although these diseases largely differ regarding treatment regimens, disease-specific guidelines have one thing in common: They stress that this mortality could be greatly lowered if patients with such lifestyle-related diseases would adhere to a set of key healthy lifestyle behaviors,[3] including engaging in regular physical activity, keeping a healthy weight and diet, refraining from smoking, and adhering to medication prescriptions.[1,4] Engaging in these behaviors could also diminish cardiovascular complications, hospitalizations, comorbidities, and physical as well as psychological disease burden.[3] However, sustained adherence to healthy lifestyle behaviors is only achieved by a minority of patients: In multiple cohort studies, less than 5% of patients reached all lifestyle guidelines, even including individuals who already had experienced a coronary heart disease or stroke event.[5,6]

These findings show that it is very difficult to adjust to chronic disease and adopt an active, healthy lifestyle. It requires challenging coping skills, such as accepting diagnosis and prognosis, managing physical and social implications, and changing long-standing habits. These challenges influence patients' psychosocial functioning: Many experience psychological distress, that is, symptoms of depression or anxiety, including sadness, loss of interest, irritability, nervousness, or restlessness.[7-9] Psychological distress symptoms often go hand in hand with deficits in energy, self-regulatory resources, memory, motivation, optimism, self-efficacy, and social support. These problems in patients' psychosocial functioning may form strong barriers for engagement in a healthy lifestyle.[10-12] For instance, recent systematic reviews showed that depressive symptoms among patients with type 2 diabetes were negatively associated with physical activity and dietary adherence,[13] and that both depressive and anxiety symptoms predicted medication non-adherence among kidney transplant recipients.[14] Additionally, many pulmonary and cardiac patients seem to avoid physical activity due to fears about physical symptoms, such as not being able to breathe or having a cardiac event.[15] Thus, adequate psychosocial adjustment to chronic disease may be a prerequisite for lifestyle adherence.

Even though psychological distress may hamper the uptake of a healthy lifestyle, most existing support strategies focus either solely on diminishing psychological distress or only on improving lifestyle behaviors. On the one hand, mental healthcare mainly focuses on treating psychological distress symptoms, but their interaction with chronic somatic disease and its lifestyle management is not always sufficiently taken into account; on the other hand, lifestyle interventions in the medical setting tend to pay insufficient attention to psychological burden that may hinder the engagement in a healthy lifestyle.[16,17] It would be valuable to integrate support strategies for both psychological distress and lifestyle in chronic disease: This could not only diminish psychosocial barriers to improve adherence to healthy lifestyle behaviors, but vice versa, the uptake of healthy and active lifestyle behaviors could also help to reduce psychological distress.[10] For instance, enhancing mood may establish the energy and motivation needed to engage in physical activity, and in turn, activity may alleviate anxiety and depressive symptoms.[18] Literature suggests that integrated treatments, aimed at bi-directional improvements in psychosocial functioning and lifestyle management, could be more effective than one-sided interventions in improving physical as well as psychological outcomes and patients' quality of life.[10,13,17]

A first step to support patients with both psychosocial and lifestyle adjustments is to identify patients who experience difficulties in these areas, and are therefore at increased risk for poor mental and physical health outcomes, such as low positive affect, quality of life, and disease progression or complications.[19,20] However, the literature shows that, in busy clinical practice, it is challenging for medical health professionals to assess and discuss their patients' psychosocial difficulties and cues that may indicate non-adherence, which may not be readily observable.[21] Patients and providers may normalize psychosocial difficulties as a "logical" consequence of chronic disease, or even attribute psychological symptoms to physical health conditions.[22] Both could lead to under-diagnosis and under-treatment of psychological health problems. For instance, in a recent study among patients with cardiopulmonary conditions, it was found that only 32% of patients who met diagnostic criteria for depression and 9% who met criteria for anxiety actually had those diagnoses documented in their electronic medical records.[23] A screening tool could aid professionals to identify psychosocial problems—as well as lifestyle-related difficulties—that may be overlooked otherwise. Such a tool could also facilitate addressing those difficulties in consults and selecting patients who may benefit from specialized support strategies.[1,19] Recent studies suggest that online completion of questionnaires can make such a screening process more complete and efficient compared with paper-and-pencil completion.[24] Furthermore, patients evaluated online screening positively, for example, because it could contain direct visual feedback that provides them insights into their own health.[24,25]

An online modality may not only be a useful option for a screening tool, but also for specialized support strategies: When supporting patients with lifestyle-related chronic diseases in psychosocial and lifestyle adjustments, potential barriers for face-to-face support are, for instance, physical limitations that complicate traveling to therapy or perceived stigma related to mental support seeking.[16] To overcome such barriers and improve accessibility and acceptability of support, electronic health (eHealth) interventions, and specifically Internet-delivered cognitive-behavioral therapy (iCBT), may be a solution.[19] Additional advantages of eHealth and iCBT treatments are enhanced flexibility and tailoring to personal preferences, the accessibility of therapy from the privacy and comfort of one's home, and a relatively easy application of learned techniques in patients' own environments.[16,26] A recent systematic review showed a high feasibility of and satisfaction with eHealth interventions among patients with chronic kidney disease.[27] Furthermore, promising effects of iCBT have been shown by a growing body of evidence among patients with chronic diseases on physical and psychological outcomes as well as health-related quality of life, especially when interventions are guided by a therapist: Systematic reviews found moderate effects of therapist-guided iCBT on depression and anxiety, with effect sizes comparable to face-to-face CBT.[28,29] The largest effects have been found for interventions that are tailored to patients' individual complaints and needs.[29]

In conclusion, guided and tailored eHealth care pathways, that is, complex interventions that combine screening and integrated psychosocial and lifestyle support strategies, could aid patients with lifestyle-related chronic diseases. Therefore, the overall objective of this study was to develop such an eHealth care pathway, including (1) a screening tool with questionnaires to identify patients who experience psychosocial and lifestyle-related difficulties and to tailor the intervention, as well as personal profile charts to visualize screening outcomes, and (2) lifestyle treatment modules embedded within existing guided and tailored iCBT to treat psychological distress, diminish psychosocial barriers, and promote psychosocial facilitators for engagement in healthy and active lifestyle behaviors. In this paper, the systematic development per intervention component is described, as well as the final version of the tailored eHealth care pathway for application in patients with chronic kidney diseases.

Development

The eHealth care pathway was systematically developed by a research team of health psychologists working in academia and therapy practice (C.K.C., J.T., H.v.M., Y.C., A.W.M.E., and S.v.D.), as well as a clinical epidemiologist/medical decision-making scientist (J.K.S.), based on previous experiences in the development of (eHealth) interventions for patients with chronic diseases.[30,31] The eHealth care pathway was developed for different research projects among patients with lifestyle-related chronic diseases, including patients with chronic kidney disease (CKD; E-GOAL study. Netherlands Trial Registry, study number NL7338, medical ethics committee METC-LDD reference numbers P17.090 and P17.172), end-stage kidney disease (ESKD; E-HELD study. Netherlands Trial Registry, study number NL7160, METC-LDD reference number P18.013), and patients with lung, stomach, intestine, and liver diseases.[16] Some characteristics of the eHealth care pathway, such as specific questionnaires, may differ across research projects depending on the patient population. Here, the development of the version used in the E-GOAL study is presented. This study's version of the eHealth care pathway is developed for an effectiveness evaluation in a randomized controlled trial, conducted at the nephrology departments of four medical centers in the Netherlands.

For each component of the intervention, the development was conducted by: (1) Using scientific evidence and expertise from our research team to develop initial versions of the intervention components; (2) acquiring feedback from users (i.e., patients with lifestyle-related chronic diseases and health professionals) regarding usability and feasibility; and (3) revising and refining the intervention components. The second and third stage were conducted in several iterations if needed, to fully address users' needs and preferences. See Figure 1 for an overview.

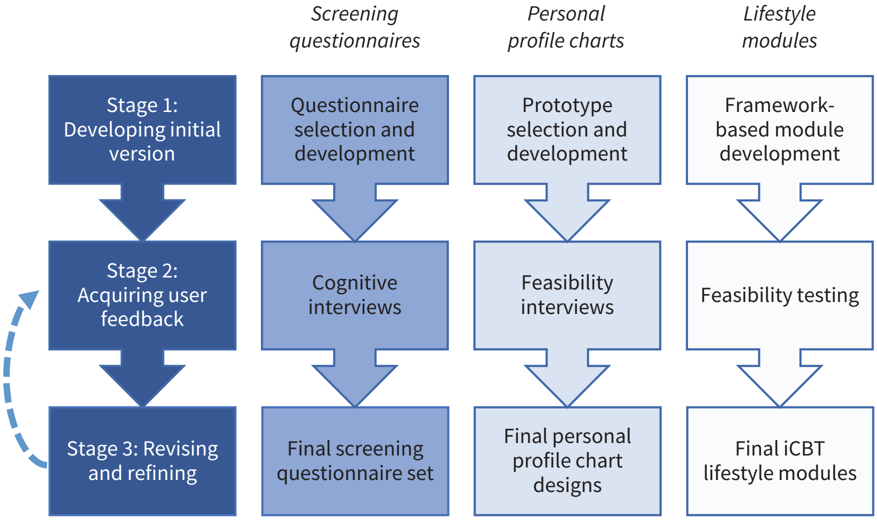


Figure 1. Stages of intervention development per intervention component. iCBT = Internet-delivered cognitive-behavioral therapy.

2.1. Screening Tool

The screening tool consists of (1) screening questionnaires to identify patients with an increased-risk profile—who experience psychosocial and lifestyle-related difficulties—as well as questionnaires to tailor the intervention, and (2) personal profile charts to visualize screening results. The screening tool was embedded in the online platform “PatientCoach”, an eHealth application to support patients with chronic somatic diseases, developed and hosted at Leiden University Medical Center (LUMC).[32]

2.2. Screening Questionnaires: Increased-Risk Profile and Intervention Tailoring

2.2.1. Development Screening Questionnaires Stage 1: Developing Initial Version

In order to limit the burden of filling out questionnaires, we decided to use a stepped approach in which the screening questionnaires are divided into two successive parts.

Part 1: Questionnaires for Increased-Risk Profile Identification. The first, brief part is used to select patients with an increased-risk profile, that is, patients who experience psychosocial and lifestyle-related difficulties, who are thus at increased risk of poor health outcomes. These patients are most likely to benefit from the iCBT treatment targeting psychosocial determinants of healthy lifestyle behaviors.[19] To screen for psychosocial difficulties that potentially form barriers for healthy lifestyle behaviors, we decided to measure depressive symptoms, anxiety symptoms, fatigue, and health-related quality of life. These domains have been prioritized for improvement and as barriers for lifestyle adherence by patients with lifestyle-related chronic diseases.[12,33] Furthermore, this set of psychological, social, and physical domains provides patients and health professionals a summarized overview of a patient’s mental and physical health status.[19] To screen for lifestyle-related difficulties, we included physical activity, body mass index (BMI), eating behaviors, smoking, and medication adherence. We selected questionnaires to measure these psychosocial and lifestyle variables, based on their validity and reliability in populations with chronic diseases, and their feasibility for users (i.e., low response burden and good comprehensibility). Detailed information regarding the selection of questionnaires can be found in Supplementary File 1.

Based on thorough discussion and previous experience of our research team, it was decided that patients were eligible for the iCBT treatment if they showed (1) at least mild psychological distress scores and (2) at least one suboptimal (i.e., unhealthy) lifestyle behavior or lifestyle-related outcome (i.e., BMI). To identify psychosocial difficulties, we used the original cut-off points of the psychological distress questionnaires to indicate at least mild depressive or anxiety symptoms. We based the cut-off points for suboptimal lifestyle behaviors on international recommendations for populations with lifestyle-related chronic diseases (e.g., <150 weekly minutes of physical activity, BMI ≥ 25). More detailed information regarding the cut-off points used can be found in Supplementary File 1.

Part 2: Questionnaires for Intervention-Tailoring. The second, complementary part of the screening questionnaires has to be filled out only by patients with an increased-risk profile who are eligible for the iCBT treatment, to gather more in-depth information for tailoring the iCBT treatment to their needs and priorities.[19] We included scales regarding different areas of behavioral, psychological, social, and physical functioning. Furthermore, we developed a short Personalized Priority and Progress Questionnaire (PPPQ) to measure patients' personal priorities for improvement as well as actual subjective improvements over time in different areas of functioning (seven items; e.g., "During the past 2 weeks, to what extent did you experience limitations regarding tiredness or sleeping problems?") and lifestyle behaviors (five items ; e.g., "During the past 2 weeks, to what extent did you manage to eat healthily?"). This questionnaire is based on validated goal setting instruments.[34-36] More information about the included scales can be found in Supplementary File 1.

2.2.2. Development Screening Questionnaires Stage 2: Acquiring User Feedback

Cognitive interviews took place to evaluate the comprehensibility of the PPPQ, and to determine whether the questions are consistently interpreted as intended among different patient groups.[37] We purposively recruited patients at the Department of Nephrology in a Dutch hospital in collaboration with health professionals. Eight individuals (5 male) of 18 years of age or older with a diagnosis of CKD (n = 4) or ESKD (n = 4) were invited to participate in a 30-minute session where they completed a paper-and-pencil questionnaire and were cognitively interviewed about the items. We held two rounds of cognitive interviews. In the first round, four patients were interviewed. The interview moderator (C.K.C. or J.T.) read each item out loud with the possibility for the participant to read along. Participants were first invited to think aloud to encourage an open-ended dialogue. After each response, the interview moderator used general and item-specific verbal probes to address specific items and issues regarding interpretation (e.g., "Without looking at the question again, could you explain in your own words what was asked?") and comprehension (e.g., "What does the term X mean to you?", "Did the question contain any difficult words?") of instructions, items, and response options. Additionally, the interviewer took notes and answered questions based on observation of the respondent (e.g., "Did the respondent seem to have any difficulty using the response options?").

The interview moderators documented a summary of each cognitive interview in a spreadsheet. This file contained difficulties in comprehension and interpretation (e.g., misunderstanding or uncertainty in the meaning of items), observations, and participants' suggestions for changes in difficult-to-understand items. After an interview round, the interview moderators discussed the problems encountered and how they could be corrected, and H.v.M. and S.v.D. reviewed the proposed modifications before the questionnaires were adapted. After this refinement, we repeated stages 2 and 3 of development, that is, C.K.C. and J.T. tested the adaptations in subsequent interviews with four other participants and repeated the analysis procedure.

2.2.3. Development Screening Questionnaires Stage 3: Revising and Refining

Regarding the PPPQ, most items functioned as intended. In the items assessing priorities for functioning, two out of seven items were revised to increase clarity and consistency of interpretation. An item about "fatigue and/or sleeping problems" caused confusion for a participant who did experience fatigue but did not suffer from sleeping problems. Therefore, "and/or" was replaced by "or". The item "To what degree do you experience limitations in your social environment (e.g., in communication with others or dependence on others)" was found too broad to answer and was inconsistently interpreted. To clarify its meaning, the examples were specified in more detail ("e.g., communication about your needs and wishes, asking or receiving support, or dependence on others"). Last, for some participants, it was unclear for which disease or condition they should answer the questions about their experienced limitations. For instance, for the item "To what degree do you experience limitations in the area of pain?", one participant was unsure whether to focus only on pain due to kidney disease, or also on pain due to an eye operation. To avoid this issue, "due to your [kidney] disease" (replaceable with other lifestyle-related diseases) was added to the instruction text. None of the items assessing priorities for lifestyle required revisions.

In the second interview round, no new issues with instructions, items, or response options were detected. The final version and validation of the PPPQ will be described in more detail in another manuscript by the research team (J.T., C.K.C., S.v.D., A.W.M.E., and H.v.M.), which is currently in preparation.

2.3. Personal Profile Charts to Visualize Screening Results

2.3.1. Development Personal Profile Charts Stage 1: Developing Initial Version

Our research team agreed that two types of charts would be needed: A chart showing an overview of scores in each domain of functioning and lifestyle to visualize a patient's current status (hereafter indicated as a profile chart), as well as a chart of measurements at different time points to monitor progress over time per domain (hereafter indicated as a monitor chart). We evaluated several prototypes for the profile chart and the monitor chart. For the profile chart, we selected two existing charts (a visual representation of scores in a wheel and in balloons) that were developed and investigated for other patient populations, respectively, within our research team (in collaboration with Netherlands Organisation for Applied Scientific Research) and by other researchers,[38] and we designed one chart (a visual representation of scores in thermometers) in collaboration with health professionals within our research team. To visualize the monitor charts, we designed a line chart and a bar chart. Supplementary File 2 contains the prototypes.

2.3.2. Development Personal Profile Charts Stage 2: Acquiring User Feedback

We conducted semi-structured interviews to evaluate the feasibility of each chart. Purposive recruitment took place of patients at the Departments of Gastroenterology ($n = 2$), Pulmonology ($n = 3$), and Nephrology ($n = 7$), in collaboration with health professionals. Nine of the 12 patients were male and their ages ranged from 40 to 82 years. Additionally, two nurse practitioners (both female) from the Department of Nephrology were interviewed. Participants had different levels of experience with online tools and patient portals. We held two rounds of feasibility interviews, with a total of 14 participants. In the first round, 10 patients and the two nurse practitioners were invited to participate in a feasibility interview with a duration of 15 to 30 min, in which the interview moderator (C.K.C. or Y.C.) showed respondents the charts on paper one by one. With each chart, the moderator asked questions about comprehension and interpretation (e.g., “What do you see?”). Then, they asked the participants to write down plus and minus symbols on the different parts of the chart to indicate their positive and negative impressions. Afterwards, the participants were invited to verbally elaborate on the pluses and minuses and the interviewer asked questions about feasibility (e.g., “What do you think of the design?”, “Does the information in the chart fit your needs?”, “What would you do differently?”). Last, participants were invited to choose their preferred design.

The interview moderators documented a summary of each feasibility interview in a spreadsheet. This file contained the first impression, positive remarks, improvement areas, suggested modifications, and preferred designs expressed by each participant. Subsequently, the researchers discussed the outcomes, selected the profile and monitor chart that received most votes, and adapted the designs by incorporating the respondents’ feedback. Since some major changes were made, we established another iteration, i.e., stages 2 and 3 of development were repeated: A second interview round took place among two patient members of the E-GOAL study group, one male and one female, both from the Department of Nephrology. In addition to the questions about comprehensibility and feasibility, they were asked what they would find the best way of showing the charts to users (e.g., online or on paper, with a health professional present or not). Afterwards, final refinements were made.

2.3.3. Development Personal Profile Charts Stage 3: Revising and Refining

In general, participants were rather positive about the use of personal profile charts as a tool in patient–provider communication, to gain insights into patient health and areas that need attention, and to set goals and action plans for improvement. For the profile chart, nine participants preferred the thermometers over the wheel (two votes) and balloons (one vote). For the monitor chart, 10 participants preferred the line charts over the bar charts (one vote; one participant did not have a specific preference). The designs of the thermometers and line charts were found clearest and most suitable for a hospital setting. The research group selected the profile and monitor charts that received most votes (see Figure 2).

Even though there was quite some consensus between participants about the preferred charts, they also provided feedback and suggestions for improvement. First, domain definitions were added to the profile chart, shown when users would position their mouse cursor on the domain. Regarding the profile chart, participants suggested a horizontal positioning of bars (instead of thermometers) and domain names, to diminish confusion and improve readability. Last, for both the profile and monitor chart, two participants found the different color tones, gradually changing from red to green, unclear. It was preferred to use three traffic light colors, which are easier to distinguish.

In the second interview round, only minor problems were detected and a final refinement took place. Both participants stated that it would be useful for patients to see their questionnaire results in personal profile charts directly after filling in the questionnaires, that is, without a health professional present, provided that there would be a possibility to contact a professional in case of any questions about the results. Furthermore, they stated that the personal profile charts should be presented both online and on paper, for people who find it difficult to navigate in online patient portals. This feedback was incorporated in the final eHealth care pathway. After developing the content of the screening tool (questionnaires with cut-off points for increased-risk profiles, as well as personal profile charts), it was built into the eHealth application PatientCoach[32] as introduced before. The tool was extensively tested before patients were invited for usage.

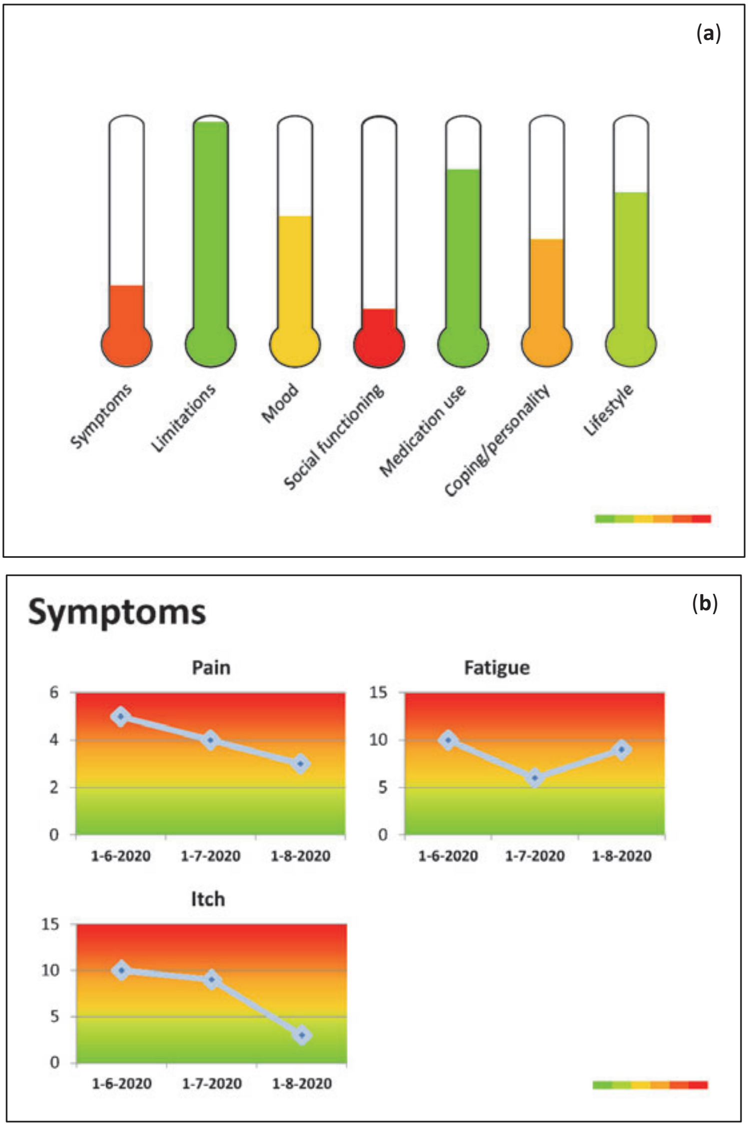


Figure 2. (**a**) Profile chart and (**b**) monitor chart preferred in the first user feedback round.

2.4. iCBT Treatment

For patients who were identified by the screening tool to have an increased-risk profile, and thus eligible for the iCBT treatment, our research team developed lifestyle self-management modules. These lifestyle modules were embedded within the existing generic guided and tailored iCBT intervention “E-coach”, which already contained modules to treat psychosocial difficulties related to chronic somatic disease. E-coach was developed by the research group of Prof. A.W.M. Evers (A.W.M.E.) at Leiden University and Radboud university medical center, based on evidence-based face-to-face CBT for patients with chronic somatic conditions.[30,31] The effectiveness of this iCBT was demonstrated in randomized controlled trials in different patient populations.[30,31]

2.5. Treatment: Lifestyle Modules

2.5.1. Development Treatment Stage 1: Developing Initial Version

To develop the initial version of the lifestyle modules, we used the Behavior Change Wheel (BCW) guide.[39] The BCW is a framework for designing interventions, which integrates 19 existing behavior change theories. It consists of eight steps to guide intervention design.[39] We broadly followed these steps (see Figure 3).

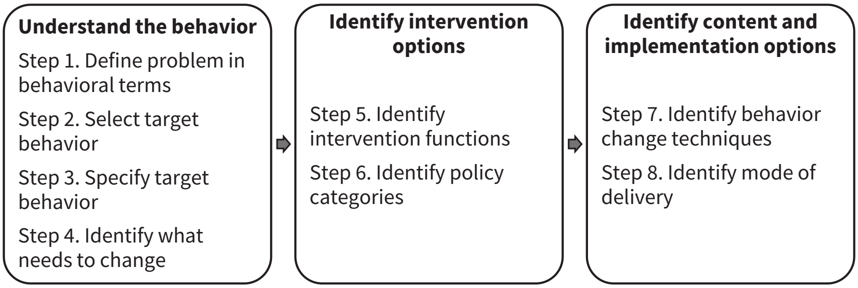


Figure 3. Eight steps of behavior change intervention design. Reproduced with permission from S. Michie, L. Atkins, and R. West, The behaviour change wheel: a guide to designing interventions; UK: Silverback Publishing, 2014.

In steps 1 to 3 of the BCW, researchers usually identify the specific behavior that needs to change by (1) defining the problem in behavioral terms, (2) selecting, and (3) specifying the target behavior by answering the following questions: What behavior needs to change, who needs to perform it, what do they need to do differently, when and where do they need to do it, how often, and with whom? As described before, the answers to most of these questions are quite well established in international guidelines and existing literature from various lifestyle-related chronic diseases.[1,4] We also took the likelihood of behavior change within an intervention into account (i.e., by exploring whether previous intervention studies have been successful in bringing about the desired lifestyle changes). Table 1 summarizes the target behaviors. Further specification of the target behaviors for an individual patient depends on the person and disease characteristics (e.g., physical activity should be compatible with a patient's health and tolerance). Thus, within the intervention, the target behavior should be further tailored to individual needs.

Table 1. Specification of the target behavior (Behavior Change Wheel steps 1 to 3). Table template adapted from S. Michie, L. Atkins, and R. West, The Behaviour Change Wheel: a guide to designing interventions; UK: Silverback Publishing, 2014.

Key Behavioral Problem	Unhealthy Lifestyle Behaviors (Leading to Poor Health Outcomes)
What (target behavior)	Physical activity: moderate-to-vigorous intensity ≥150 min per week in multiple sessions Healthy weight: BMI 18.5 to 24.9 Healthy diet: Adherence to dietary prescriptions (e.g., low sodium) Smoking: No tobacco smoking Medication: Adherence to medication prescriptions
Who (target group)	Individuals with lifestyle-related chronic diseases
When/where/how often	Regularly, i.e., on a weekly to daily basis, embedded in daily schedule
With whom	With support from health professionals and social environment

In step 4, we conducted eight focus groups among patients with non-dialysis-dependent chronic kidney disease (n = 24) and their health professionals (n = 23) to gain a deeper understanding of factors that may influence the target lifestyle behaviors. Barriers and facilitators for engagement in healthy lifestyle behaviors were explored, as well as intervention strategies needed to address those. Three researchers (C.K.C., S.v.D., and a physician researcher in nephrology) analyzed transcripts using thematic analysis. The codes from the inductive analysis were deductively mapped onto the domains of the Theoretical Domains Framework (TDF, e.g., knowledge, intentions, emotion) and structured onto three overarching components that are considered essential for behavior and behavior change to occur: Capability, Opportunity, and Motivation (the 'COM-B system'.[39] Table 2 includes an overview of the main barriers and facilitators for healthy lifestyle behaviors found in the focus group study, which has been reported in detail elsewhere.[12]

In step 5, C.K.C. listed all potentially relevant intervention functions, that is, methods by which an intervention may change behavior (e.g., education, training, environmental restructuring), by linking the TDF domains identified in step 4 to the intervention functions that are most likely to affect behavior change for each domain, as described in the BCW guide.[39] Then, C.K.C. and S.v.D. evaluated the relevant intervention functions using the affordability, practicability, effectiveness and cost-effectiveness, acceptability, side effects/safety, and equity (APEASE) criteria, to select the most appropriate intervention functions. Education (increasing knowledge and understanding to enhance patients'

Table 2. Matrix of links between COM-B system, TDF domains, selected intervention functions, and selected BCTs in the lifestyle modules (BCW steps 4, 5, and 7). Matrix template adapted from S. Michie, L. Atkins, and R. West, The behaviour change wheel: a guide to designing interventions; UK: Silverback Publishing, 2014.

COM-B Component (Step 4)	Main TDF Barriers and Facilitators (Step 4)	Selected Intervention Functions (Step 5)	Selected BCTs (Step 7)	Description of BCTs within the Intervention	Lifestyle iCBT Module (Based on Stages of Behavior Change)
Capability	Knowledge (How to engage in a healthy lifestyle)	Education, Persuasion	Instruction on how to perform the behavior; Information about antecedents; Information about health consequences; Feedback on behavior	Guidelines on what, how, and why to engage in healthy lifestyle behaviors; Instruction to keep a record of (unhealthy) behaviors and of events, emotions, and cognitions occurring prior to it; Information about advantages of healthy behaviors; Evaluative feedback on monitored behavior.	1: Goals Exploration (contemplation and decision)
Opportunity	Social influences (Support by professionals and social environment)	Enablement	Social support (unspecified); social support (practical); social support (emotional)	Exercise to discuss personal strengths with important others and how to implement them in behavior change; Exercise to think about ways in which social support is received and about emotional and practical support the person would (not) like to receive; Prompt to ask for support.	3: Goals Persistence (evaluation and maintenance)
	Environmental context and resources (Disease symptoms and material support tools)	Enablement	Restructuring the physical environment; Avoidance/changing exposure to cues for the behavior	Advice and prompt to think about how to avoid exposure to environmental cues for unhealthy behavior and to make adaptations to the environment that facilitate the wanted behavior.	2: Goals in Action (planning and action)
Motivation	Role and identity (Personality characteristics)	Persuasion	Valued self-identity	Exercise to list personal strengths.	3: Goals Persistence (evaluation and maintenance)
	Beliefs about capabilities (Self-efficacy, locus of control)	Persuasion	Focus on past success	Exercise to list previous successes in behavior change.	3: Goals Persistence (evaluation and maintenance)

COM-B Component (Step 4)	Main TDF Barriers and Facilitators (Step 4)	Selected Intervention Functions (Step 5)	Selected BCTs (Step 7)	Description of BCTs within the Intervention	Lifestyle iCBT Module (Based on Stages of Behavior Change)
	Optimism (Acceptance, focusing on possibilities vs. limitations)	Persuasion	Problem solving	Exercise to identify barriers for behavior change and explore ways to overcome them.	1: Goals Exploration (contemplation and decision)
	Emotion (Depression, stress, anxiety)	Education, Persuasion, Enablement	Education, Persuasion: Information on emotional consequences; Self-assessment of affective consequences Enablement: Reduce negative emotions	Information about emotional advantages of healthy lifestyle behaviors; Instruction to keep a record of feelings after performing unhealthy vs. healthy behaviors; Exercise to identify positive self-talk and images to promote positive emotions that facilitate maintenance of the wanted behavior; Exercise to identify ways to reduce negative and stressful emotions.	1: Goals Exploration (contemplation and decision) 3: Goals Persistence (evaluation and maintenance)
	Reinforcement (Noticeable effects of healthy behavior, rewards)	Incentivization	Self-reward, material reward	Prompt to use a personally relevant reward if there has been progress in the wanted behavior.	2: Goals in Action (planning and action)
	Intentions (Intrinsic motivation, joy, higher-order purposes)	Incentivization, Enablement	Pros and cons; Commitment	Exercise to identify and compare reasons for wanting and not wanting to change behavior; Exercise to link the wanted behavior to personally relevant higher-order values; Instruction to write down a decision statement indicating commitment to change behavior.	1: Goals Exploration (contemplation and decision)
	Goals (Concrete and feasible goals)	Enablement	Goal setting (outcome); Goal setting (behavior); Review of outcome goals; Review of behavior goals; Action planning	Exercise to set weekly goals; Instruction to create a daily action (implementation intentions); Prompt to reflect on behavior and correspondence with goals and action plans, leading to re-setting or adapting.	2: Goals in Action (planning and action) 3: Goals Persistence (evaluation and maintenance)
	Beliefs about Consequences (Beliefs about and experiences with consequences of behavior)	Enablement	Pros and cons	Exercise to identify and compare reasons for wanting and not wanting to change behavior.	1: Goals Exploration (contemplation and decision)

COM-B = Capability, Opportunity, Motivation—Behavior; TDF = Theoretical Domains Framework; BCT = Behavior Change Technique.

capability to change behavior), enablement (increasing means and reducing barriers to enhance patients' opportunity and motivation to change behavior), persuasion (inducing positive or negative feelings and stimulating action to enhance patients' motivation to change behavior), and incentivization (creating expectation or reward to enhance patients' motivation to change behavior) were selected as the intervention functions most relevant for the lifestyle modules in the iCBT treatment (see also Table 2). The remaining intervention functions were regarded as unfeasible to implement within a web-based intervention targeted at individual patients.

In step 6, as described in the BCW guide, for each intervention function identified in step 5, policy categories (e.g., service provision, guidelines, marketing) should be selected that are likely to be appropriate in supporting the intervention functions. However, since the lifestyle modules were intended to be built into the existing iCBT intervention E-coach,[30,31] the policy category service provision was predefined. Service provision is an adequate policy category to carry out the selected intervention functions.[39]

In step 7, the BCW guide describes a taxonomy of 93 behavior change techniques (BCTs, e.g., goal setting, social support, reframing), the "active ingredients" of behavior change. The BCW guide provides a list of potentially adequate BCTs (version 1, also indicated in the literature as BCTT v1) for every intervention function. Given the relevant intervention functions selected in step 5, C.K.C. created an initial longlist of potential BCTs per TDF domain. Then, C.K.C. and S.v.D. shortlisted the most appropriate BCTs, based on an evaluation against the APEASE criteria, the most commonly used and investigated BCTs that are likely to bring about the desired behavior changes, and the previous experiences of our research team.[39-41] Afterwards, in order to make the intervention more effective and tailored to a patient's lifestyle behavior change process, the BCTs were organized among three modules, representing different stages of behavior change, in accordance with stage theories:[42] Module 1: "Goals Exploration" (stages of contemplation and decision), Module 2: "Goals in Action" (stages of planning and action), and Module 3: "Goals Persistence" (stages of evaluation and maintenance). The selected BCTs and structure among the modules can be found in Table 2.

In the final step 8, the BCW guide recommends researchers to consider different modes of delivery for the intervention (e.g., face-to-face vs. web-based; individually vs. group). Since the lifestyle modules were embedded within the existing iCBT intervention E-coach,[30,31] the researchers only partly had to engage in this step. In E-coach, patients with chronic somatic diseases complete an online trajectory of one or more treatment modules (e.g., about mood, social functioning, or physical complaints) at home, and receive regular feedback from their therapist via text messages or by telephone. Treatments using E-coach start with a face-to-face intake session, can be online or blended (with additional face-to-face sessions), and are tailored to patients' personally relevant goals. For the newly developed lifestyle modules, we decided to employ the same online delivery mode, guided by a trained health psychologist. Experiences from our research team were used to decide on the duration of the intervention (i.e., 3–4 months) and on the inclusion of a possibility to offer additional sessions by telephone or face-to-face, in case a therapist would consider this beneficial for a patient.

2.5.2. Development Treatment Stage 2: Acquiring User Feedback

An initial version of the lifestyle modules was developed and its feasibility was tested among a patient with CKD (kidney–pancreas transplant recipient, male), a patient with osteoporosis and cured breast cancer (female), and a healthy control (female). The participants were invited to set a personally relevant goal related to their lifestyle, and to work through a paper-and-pencil workbook of the modules within 1–2 weeks (without guidance). They were asked to write down any feedback on comprehensibility, usability, and acceptability of each component (e.g., psychoeducational text or exercise) in the workbook. After finishing the modules, participants filled out a questionnaire with a few open questions per module, including "Which component did you find most/least useful and appealing?" and "What would you definitely change?" Finally, the first author (C.K.C.) conducted a 15–30 min interview with each participant to further discuss their experiences and ideas. Feedback was summarized and discussed within our research team (C.K.C., S.v.D., and A.W.M.E.) and adaptations were made.

2.5.3. Development Treatment Stage 3: Revising and Refining

In general, all three participants indicated that the modules were easy to comprehend, and written in a clear and positive language. Two participants stated that the option to get support or feedback, specifically when setting goals and creating action plans, is vital. They also positively evaluated the layout and structure of the modules and exercises: “It is well structured! A logical sequence of theory and exercises, and steps in the process [of behavior change] in which they [patients] will engage.” Regarding the content of the modules, two participants stressed the importance of the motivation-enhancing BCTs in the first module. They also found the exercise about strengths (BCT on valued self-identity) in the third module very appealing and valuable. Additionally, one participant found the examples and practical advices very motivating and feasible to put into practice. The same participant positively evaluated the diaries throughout the modules: “Good tools, clear and easy to use.”

All participants had some minor suggestions for improvement. Two participants reflected on the repetition of goal setting BCTs: “Goal setting appears in two exercises, with different explications and examples. This may be confusing.” Therefore, the two exercises were merged. Furthermore, with regard to the knowledge-enhancing BCTs, one participant suggested to refer to reliable sources (e.g., from the government) for additional practical and factual information about healthy lifestyle behaviors, and to encourage patients to consult a specialist (e.g., physiotherapist or dietician) for specific, personalized information on feasible lifestyle adaptations. Since these lifestyle modules are embedded in an iCBT intervention and thus mainly focused on behavior change from a psychosocial perspective, this suggestion was followed.

Since no major adaptations needed to be made, stages 2 and 3 of development were not repeated. That is, after refining the lifestyle modules based on the user feedback, the modules were built into the eHealth application E-coach,[30,31] as introduced before.

Results

The final version of the tailored eHealth care pathway for patients with lifestyle-related chronic diseases is depicted in Figure 4. First, patients receive an invitation by email with a link to a personal “to do list” in the eHealth application PatientCoach, where they can complete the screening questionnaires. All patients fill in the brief screening questionnaires, to identify whether they have an increased-risk profile, i.e., whether they are at increased risk of poor health outcomes due to psychosocial and lifestyle-related difficulties. All patients can review the results of the brief screening in their personal profile charts in PatientCoach (see Figure 5 for an example), and receive a paper version by mail.

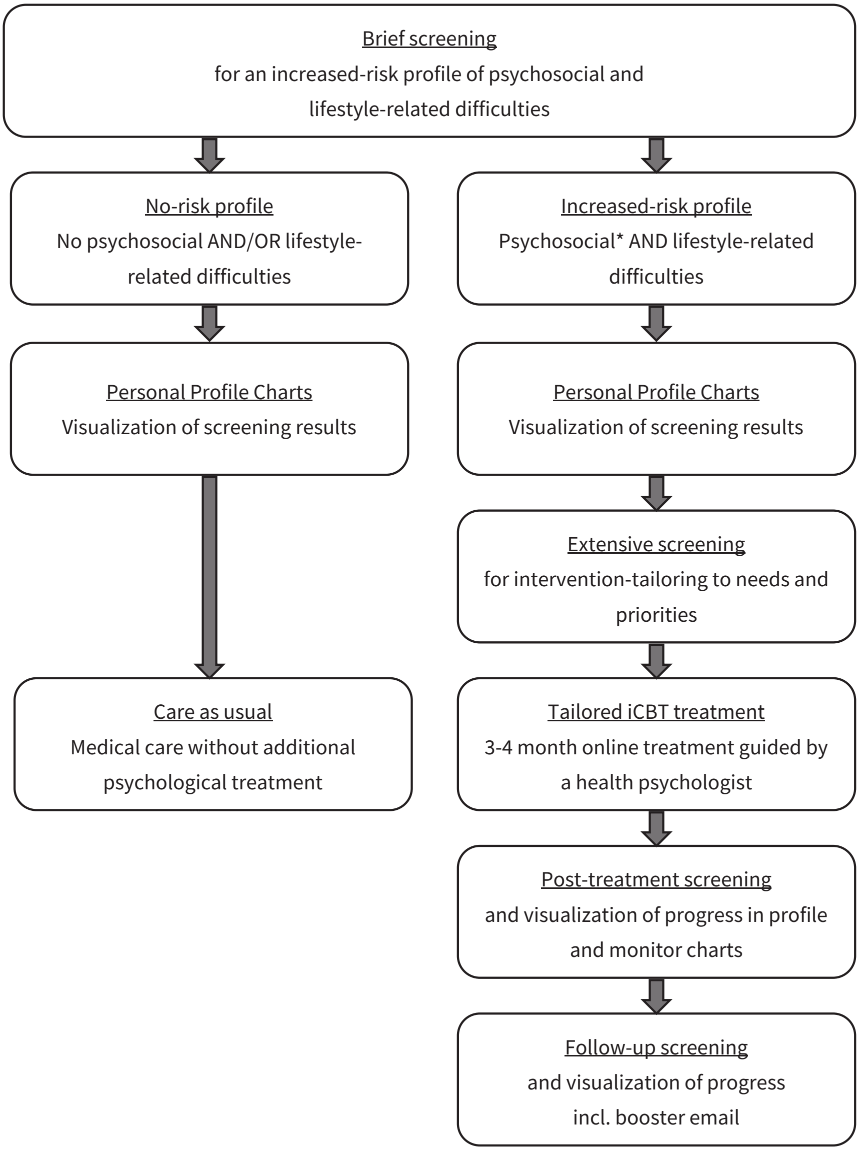


Figure 4. Tailored eHealth care pathway for patients with lifestyle-related chronic diseases. *Patients with severe psychological distress scores are advised to contact their GP for further evaluation and referral to specialized face-to-face mental healthcare.

The system automatically detects increased-risk profiles, by identifying patients who experience at least mild psychological distress and at least one suboptimal lifestyle behavior. For these patients, the complementary questionnaires—assessing specific areas of patients' behavioral, psychological, social, and physical functioning to tailor the intervention to personal needs and priorities—appear in their to do list directly after completing the brief screening questionnaires.

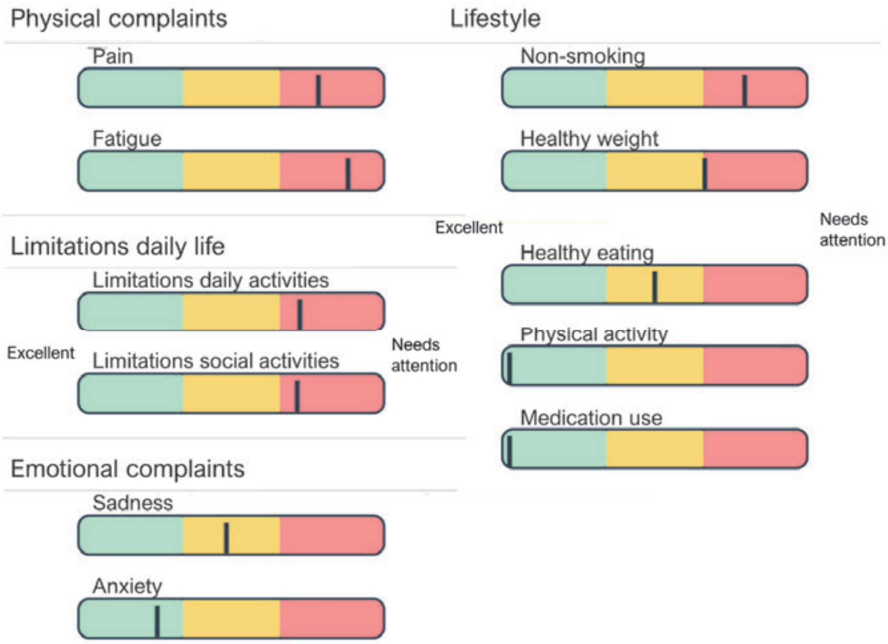
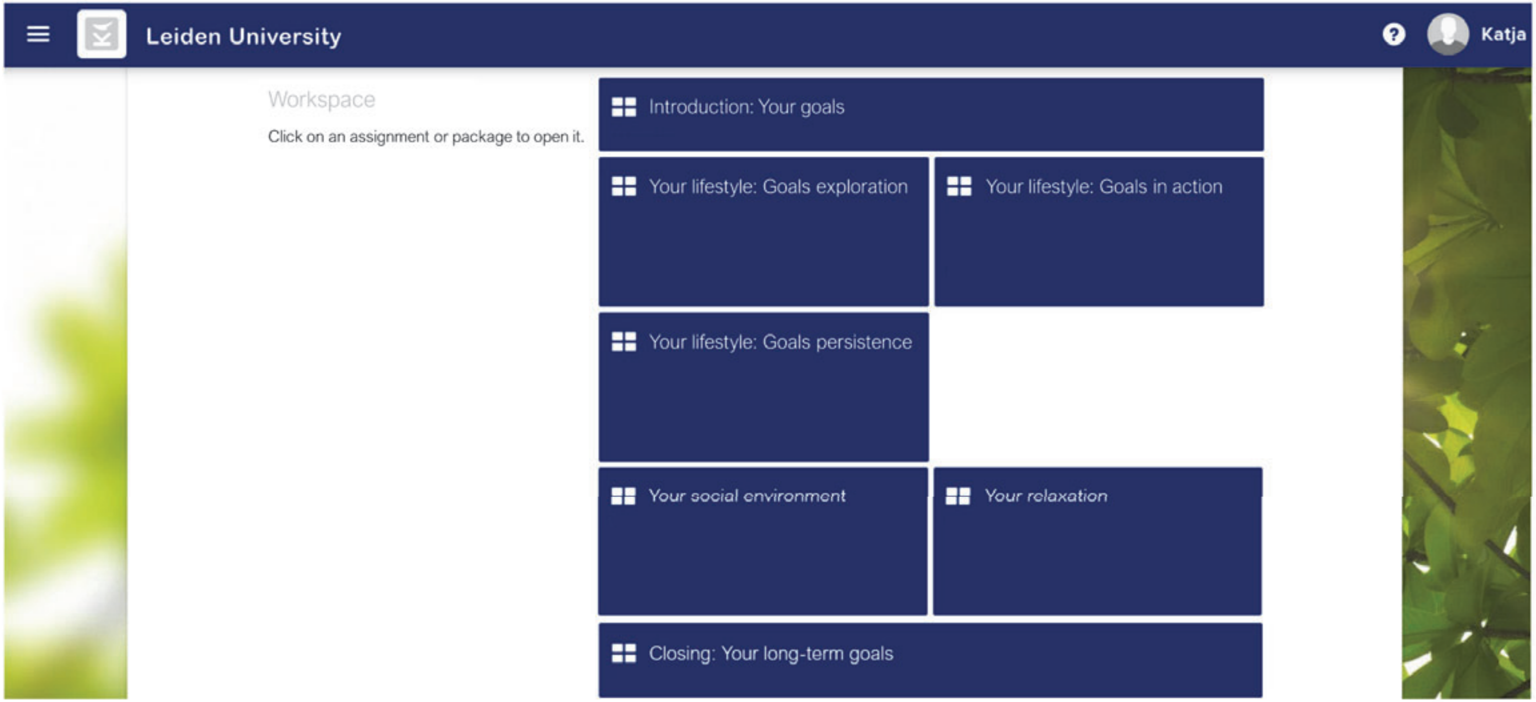


Figure 5. An example of personal profile charts. This patient shows an increased-risk profile with moderate depressive symptoms (which may be influenced by severe physical complaints and limitations in daily life), heavy smoking, obesity, and moderate adherence to dietary prescriptions.

Patients who show an increased-risk profile are invited by mail and telephone to receive tailored and guided blended CBT treatment using the eHealth application E-coach. This treatment starts with a face-to-face intake session of an individual patient with a therapist, that is, a trained health psychologist, which can take place in the patient's medical center. This initial session includes an assessment of a patient's physical, psychological, and social functioning and their interactions, guided by the personal profile charts and complementary screening results.[19] That is, by using clinical reasoning to combine and interpret the screening and intervention-tailoring questionnaires, the therapist obtains insights into the magnitude of psychosocial and lifestyle-related adjustment problems, relationships between co-occurring problems and symptoms, and their context (e.g., psychological aspects, personality characteristics, and social support). Combined, these insights indicate treatment priorities, a patient's vulnerabilities (e.g., neuroticism or pessimism) and resilience factors (e.g., high self-efficacy or motivation) to address in treatment.[19] With that information, the therapist and patient discuss which psychosocial difficulties form barriers for which lifestyle behaviors, explore a patient's resources that may facilitate change (e.g., based on questionnaires regarding personality characteristics and social support), and determine a patient's priorities for improvement (e.g., based on the PPPQ). With this information, the therapist aids the patient in formulating two to three personally relevant psychosocial and lifestyle goals, and introduces the eHealth application E-coach. Thereafter, during the next three to four months, patients in treatment systematically go through several treatment modules (e.g., regarding mood, social environment, fatigue, or lifestyle; see Figure 6 for an example) matching their personal goals. Modules include psychoeducational texts and exercises based on cognitive–behavioral BCTs. Patients work through the modules at home and receive regular (e.g., weekly or bi-weekly) personalized feedback from their therapist via a secured message box within E-coach. If needed, the treatment can be complemented with telephone or face-to-face appointments.

After completing the personalized modules, patients go through a final module about relapse prevention and long-term goals, to promote maintenance of the behavior changes after treatment. In this module, patients also write a letter to themselves regarding their achievements. Afterwards, they have a final telephone appointment with their therapist to evaluate the trajectory. The exact duration of a trajectory is tailored to the number of treatment goals and the adequate pace for the individual patient.



Workspace

Click on an assignment or package to open it.

Figure 6. An example of modules in eHealth application “E-coach”.

After finishing the treatment, patients complete the screening questionnaires again and receive profile and monitor charts (see Figure 7 for an example) to see treatment effects and progress. At follow-up (e.g., three months after finishing the treatment), this screening questionnaire completion is repeated and patients receive an email from their therapist including their own letter to themselves, as a reminder and booster to maintain their new healthy habits.

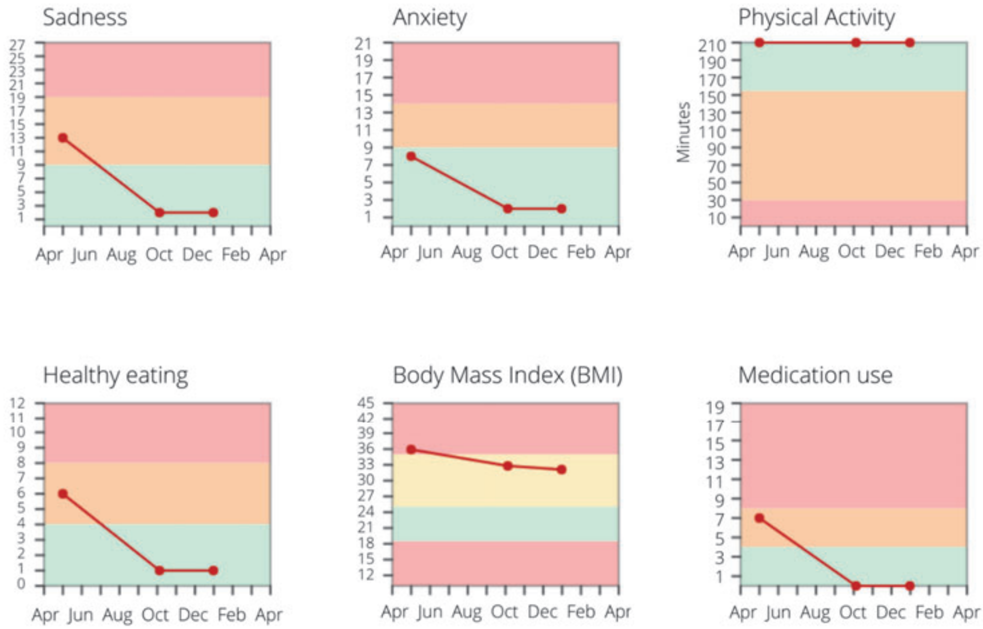


Figure 7. An example of monitor charts. Post-treatment, this patient shows major improvements in depressive and anxiety symptoms, as well as in dietary and medication adherence, which are maintained at follow-up.

Discussion

In the present paper, we described the systematic development of a generic eHealth care pathway, tailored to the needs of patients with lifestyle-related chronic diseases. The eHealth care pathway facilitates both psychosocial and lifestyle adjustments, which are important to reduce disease burden and risks of adverse health outcomes.[3,10] The eHealth care pathway comprises (a) a screening tool with questionnaires to identify patients who experience psychosocial and lifestyle-related difficulties and personal profile charts to visualize screening outcomes, as well as (b) tailored and guided lifestyle self-management modules alongside iCBT to treat psychological distress, diminish psychosocial barriers, and promote psychosocial facilitators for engaging in an active and healthy lifestyle. Each component was developed in three iterative stages of creating initial versions, acquiring user feedback, and further refinement. The creation of the initial versions was guided by scientific evidence and the BCW framework for intervention development. To acquire feedback from users (i.e., patients and health professionals), cognitive interviews, feasibility interviews, and focus groups took place.

In order to develop an eHealth care pathway that fits the priorities and preferences of its end users, we undertook a systematic and user-centered approach. Below, we elaborate on several characteristics of the intervention development, that is, on the advantages of using a theory-based framework and co-creation methods. First, although evidence for an association between theory use and increased intervention effectiveness compared to non-theory-based interventions is currently inconsistent, using theory-based frameworks is being promoted, since it is certainly beneficial to guide intervention design, evaluation, and optimization.[43] In the development of our eHealth care pathway, following the pre-determined steps of the BCW made it possible to systematically consider a wide range of options and BCTs for the intervention, to incorporate the ones that meet the needs of patients with lifestyle-related chronic diseases.[39] Second, multiple systematic reviews suggested that early involvement of patients, professionals, and other stakeholders in development processes is a prerequisite for successful and sustainable implementation of eHealth interventions within a medical organization.[27,44,45] We employed several co-creation methods that involved patients with different lifestyle-related chronic diseases (including kidney, lung, stomach, intestine, and liver diseases) and their health professionals, in order to develop an eHealth care pathway that is suitable for a broad range of potential end users.

A potential strength of the eHealth care pathway is its flexibility for usage in patient populations with different lifestyle-related chronic diseases.[19] Trial results indicate the feasibility and effectiveness of other versions of the screening tool and the iCBT treatment among individuals with asthma, psoriasis, and rheumatoid arthritis.[30-32] Furthermore, the iCBT intervention is already being applied in clinical practice, as part of regular CBT for individuals with a broad range of chronic diseases in the Netherlands (reimbursed by insurance companies), which is also a promising sign for the generalizability of the E-GOAL eHealth care pathway. Generic or transdiagnostic interventions that are applicable across various chronic diseases are becoming more relevant since multimorbidity (i.e., the co-occurrence of two or more chronic diseases in the same person) is an increasingly prevalent concern. This often results in challenges with regard to adequately tailored patient-centered care, for instance, due to fragmentation of healthcare provision.[46] A generic approach such as our eHealth care pathway goes beyond diagnoses and disease-specific support, and is therefore adequate for patients with different or multiple lifestyle-related chronic diseases. To assure that disease-specific concerns are taken into account, screening and treatment can be tailored by addressing specific symptoms (e.g., a module about itch may be relevant for a patient with ESKD, but may be left out for someone with CKD or lung complaints). Furthermore, as unhealthy lifestyle behaviors are interrelated and often occur together, the multifactorial approach in which multiple behaviors can be addressed at once could result in a greater reduction of health risks than a focus on a single lifestyle issue.[47,48] An additional advantage of our intervention is that it addresses (not necessarily disease-specific) psychosocial and lifestyle-related difficulties simultaneously. Recently, it has been recommended to implement treatments that synergistically target mental health needs and disease self-management of patients with chronic diseases,[49] and thus not only take into account physical, but also mental comorbidities. Given these recommendations, the eHealth care pathway may be a valuable innovation.

The eHealth care pathway has not only been tailored to general needs and preferences of different populations with lifestyle-related chronic diseases, but the online modality with combined screening and treatment also allows for various ways of tailoring on the individual patient's level. At the beginning of the intervention, screening for psychosocial and lifestyle-related difficulties enables a selection of patients that are most likely to benefit from the iCBT treatment.[19] Furthermore, visually represented feedback of screening results in personal profile charts gives both patients and their health professionals insights into individual health status and lifestyle, and into specific areas that may need attention.[19] As such, a screening tool with visualized feedback may form an easily implementable tool at a reasonable cost,[50] which in itself may already be helpful as a first step in behavior change and as a guide for referral to treatment that suits a patient's needs.[51,52] A screening tool should be as brief as possible for feasibility reasons. Although the questionnaire set that was composed in this research setting is rather extensive, it should be emphasized that it can be shortened to tailor the tool to clinical practice. Health professionals and patients can decide which instruments are most useful in specific patient populations. For example, if the PPPQ proves to be a valid and reliable instrument, it can be employed as a very brief tool with minimal burden for patients and health professionals, to detect and discuss an individual patient's functioning and priorities for improvement in a broad range of areas. Subsequently, within our iCBT treatment, individual tailoring is promoted when the patient and therapist collaborate in setting personally relevant treatment goals and selecting the treatment modules and exercises matching those goals.[19] Additionally, contact frequency, modality, and treatment duration can be adapted to optimize attainment of treatment goals.

Reviews of online psychological and self-management intervention studies among patients with chronic somatic diseases showed that guided eHealth interventions, in which therapist guidance aids in tailoring the intervention to an individual patient's needs, are most effective and best adhered to compared to self-help programs.[53,54] In sum, the combination of screening and treatment, provided in an online modality, may form a valuable opportunity to enhance individually tailored and patient-centered care.

In addition to its opportunities for individual tailoring, another main advantage of eHealth interventions is the improved accessibility of self-management support for most patients, including under-served groups.[55] Evidence supports the effectiveness of eHealth interventions in improving health, self-management, and psychosocial outcomes of under-served populations.[56] At the same time, some vulnerable populations may be disadvantaged by eHealth: Patients do need access to digital devices as well as general skills on a computer and Internet use,[45] and it has been found that, for instance, people who were unemployed or with low education benefited less from web-based interventions.[55] To optimize eHealth interventions' effectiveness and acceptability for individuals in under-served groups, it is recommended to incorporate specific tailoring strategies (e.g., to language, culture, and literacy) and technologies (e.g., simple features or no requirement for Internet access), and to include these populations in each stage of intervention development.[56] The latter is a limitation of the current study, as we did not pay special attention to sufficient involvement of members of under-served groups in the co-creation stages of the eHealth care pathway development. Therefore, our web-based care pathway may not be sufficiently accessible for people with limited eHealth literacy or who do not use electronic devices. Yet, we did develop alternative ways of support for people with limited eHealth literacy, such as paper-and-pencil versions of the screening questionnaires and the profile charts, as well as the possibility to add telephone or face-to-face sessions to the treatment. Regardless, involving more participants than we involved in this study is crucial in later stages of evaluation and continued development, including more diverse and under-served populations.

Conclusions

This paper outlines the evidence-based and systematic development of an eHealth care pathway for patients with lifestyle-related chronic diseases, to identify and treat psychosocial and lifestyle-related difficulties. The study describes the process of using the BCW framework combined with co-creation to design a screening tool and lifestyle self-management modules, tailored to the target population and to individual patient needs. Prior to implementing this eHealth care pathway in hospital care, studies are needed to evaluate its cost-effectiveness and effectiveness on psychosocial, lifestyle, and health-related outcomes, in populations with different lifestyle-related chronic diseases. Prospective assessment between groups would be useful, including a long-term follow-up assessment.[27,29] To this end, our research team is currently conducting randomized controlled trials among populations with chronic kidney disease and end-stage kidney disease (i.e., E-GOAL and E-HELD studies). Afterwards, to achieve successful implementation in regular healthcare, adaptations may be needed to integrate the eHealth care pathway within a specific medical organization or department.

To conclude, the development stages provided in this paper can help to use and refine existing knowledge and tools alongside newly designed intervention components, and merge this into a complex intervention. This systematic process can be applied to guide future intervention development and forms a fundament for further steps of an intervention's evaluation, continued development, and implementation.

Acknowledgments

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Supplementary File 1

Screening Questionnaire Selection and Development

Part 1: Questionnaires for Increased-Risk Profile Identification

First, to screen for psychological distress, we selected the nine-item Patient Health Questionnaire depression scale (PHQ-9)[1] and the seven-item Generalized Anxiety Disorder scale (GAD-7).[2] The scales measure depressive and anxiety symptoms, such as "Little interest or pleasure in doing things" or "Feeling nervous, anxious or on edge". Respondents are asked how much each symptom has bothered them over the past two weeks, with response options from 0 ("not at all") to 3 ("nearly every day"). The PHQ-9 and GAD-7 have been used in numerous studies and incorporated into a variety of clinical practice guidelines for medical and mental health care settings.[3] Second, health-related quality of life (HRQoL) and fatigue are associated with poor health outcomes[4] and may indicate an increased-risk profile of experiencing psychosocial barriers for a healthy lifestyle. Therefore, we included the Shortened Fatigue Questionnaire (SFQ)[5] and the RAND 36-item Short Form Health Survey (RAND SF-36)[6] in the first screening part. The SFQ assesses fatigue in four items (e.g. "I feel tired") with response options on a 7-point scale. The RAND SF-36 is a 36-item questionnaire assessing eight HRQoL dimensions. Physical HRQoL consists of the subscales physical functioning, role limitations due to physical health problems, pain, and general health perception. Mental HRQoL consists of the subscales vitality, social functioning, role limitations due to emotional health problems, and mental health.

Second, to determine which variables for lifestyle behaviors should be included, we consulted international guidelines for lifestyle-related diseases.[7,8] Such guidelines are based on scientific evidence, among other things regarding the potential benefits of the healthy lifestyle behaviors for physical and psychological health outcomes (e.g. by slowing down disease progression, diminishing complication risks, or improving quality of life). Key lifestyle variables are physical activity, BMI, eating behaviors, smoking, and medication adherence. To measure physical activity, we selected the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH),[9] in which respondents can indicate how many days per week, average minutes per day, and at which intensity they practice commuting activities, leisure time, household, and activities at work or school. To measure BMI, we included short questions on length (in cm) and weight (in kg). Measuring eating behaviors in a reliable way is challenging, since dietary prescriptions differ per disease and individual patient.[7,8] To avoid extensive questionnaires, we decided to measure adherence to a healthy diet perceived by the respondent, using two questions: "In the past week, how often have you kept a healthy diet?" with scores on a 5-point scale from "never" to "always", and "In the past week, how well do you believe you have kept a healthy diet?" on a 1-10 rating scale from "very badly" to "very well". For smoking, respondents can indicate whether they smoke, and if so, how many units per day. Last, for medication adherence, many validated questionnaires measure barriers and beliefs associated with adherence, whereas for the aim of screening and selecting patients that actually experience suboptimal adherence, it is more suitable to measure actual medication-taking behavior. Therefore, we found the Simplified Medication Adherence Questionnaire (SMAQ)[10] most adequate. This questionnaire consists of four dichotomous yes/no items (e.g. "Do you ever forget to take your medicine?") and two items to quantify omissions (e.g. "Thinking about last week, how often have you not taken your medicine?"). We translated the questionnaire from Spanish to Dutch with a back translation approach, with help from bilingual researchers.[11]

To detect an increased-risk profile, for psychological distress, the cut-off points of the original scales were used:[3] On the PHQ-9, cut-off points of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depressive symptom levels; On the GAD-7, cut-off points of 5, 10, and 15 represent mild, moderate, and severe anxiety symptom levels.[3] PHQ-9 and/or GAD-7 ≥ 5 thus were the cut-offs for psychological distress scores. Importantly, based the instruction manual of the scales and on previous experiences regarding suitability of web-based treatment for patients with severe psychological complaints,[12] the research team decided that patients with severe distress scores (PHQ-9 ≥ 20 or GAD-7 ≥ 15) should be advised to contact their general practitioner for further evaluation and referral to specialized face-to-face mental health care. For HRQoL, the Hays norm-based scoring algorithm was applied,[6] transforming raw RAND SF-36 scores into T-scores, and a standard deviation-derived cut-off score was used,[13] by subtracting 0.5 SD from the norm mean ($M=50\pm10$).[6] For the HRQoL subscales, scores ≤ 45 were thus used as cut-off points to determine an increased risk. For fatigue, the cut-off point of the original scale was used that indicates above-average fatigue, that is, SFQ scores ≥ 9.[5] For most lifestyle behaviors, the cut-off points for suboptimal behaviors were based on the recommendations in lifestyle-related chronic diseases,[7,8] that is, < 150 minutes per week of moderate-to-vigorous intensity physical activity, a BMI ≥ 25, and/or tobacco smoking ≥ 1 unit per day. The research team determined the cut-off point to detect an unhealthy diet as follows: Respondents who perceive their adherence to a healthy diet in the past week as "never", "seldom" or "half the time", with a rating of ≤ 6 on the 1-10 scale. For medication adherence, the authors of the original SMAQ consider a patient to be non-adherent when at least one of the four dichotomous items was answered non-adherent, or > two doses missed over the past week, or >2 days of total non-medication during the past three months.[10] However, this was found a very strict cut-off, which could lead to an inclusion of patients who do not need support to improve their adherence. Therefore, it was decided that at least two items instead of one should indicate non-adherence.

Part 2: Questionnaires for Intervention-Tailoring

Based on previous experiences in our research team regarding relevant information for intervention-tailoring,[14] we selected specific areas of behavioral, psychological, social, and physical functioning: chronic condition self-management (Partners in Health Scale),[15] sleep quality (Medical Outcomes Study Sleep Scale),[16] illness cognitions (Illness Cognition Questionnaire)[17] and perceptions (Brief Illness Perception Questionnaire),[18] perceived stress (Perceived Stress Scale),[19] worrying (Penn State Worry Questionnaire),[20] optimism (Life Orientation Test–Revised),[21] neuroticism (NEO NEO Personality Inventory–Revised Neuroticism),[22] and social support (Inventory for Social Reliance).[23] Furthermore, we developed a short Personalized Priority and Progress Questionnaire (PPPQ) to measure patients' personal priorities for improvement as well as actual subjective improvements over time in different areas of functioning (seven items) and lifestyle behaviors (five items). This questionnaire is based on validated goal setting measurements.[24-26] In the items assessing priorities for functioning, respondents are asked to what degree they experienced limitations in different areas of functioning over the past two weeks, such as fatigue, anxiety, or daily activities, with response options from 1 "not at all" to 5 "very much". In the items assessing priorities for lifestyle, respondents are asked to what degree they were able to keep a healthy lifestyle over the past two weeks, such as healthy eating and frequent physical activity, with response options from 1 "not at all" to 5 "very well". In both scales, respondents are asked to prioritize two areas they would prefer to improve. At subsequent time points (e.g. three and six months later), respondents are asked to indicate any worsening or improvement per area over time on a 7-point scale from -3 to +3, on which 0 indicates neither worsening nor improvement. The development and validation of the PPPQ will be described in more detail in another manuscript by the research team (J.T., C.C., S.D., A.E., and H.M.), which is currently in preparation. Last, to measure self-efficacy for disease management, we translated the Self-Efficacy for Managing Chronic Disease 6-item Scale[27] and the Manage Disease in General Scale (5-item subscale from the Stanford Chronic Disease Self-Efficacy Scales),[28] hereafter called Stanford scales, from English to Dutch with a back translation approach, with help from a bilingual researcher.[11] These two scales contain three overlapping items. Depending on the patient population, the most appropriate scale could be used (e.g. the 6-item scale contains items about fatigue and pain, which may be less relevant for populations with largely asymptomatic diseases).

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Supplementary File 2

Initial prototypes of personal profile charts and monitor charts

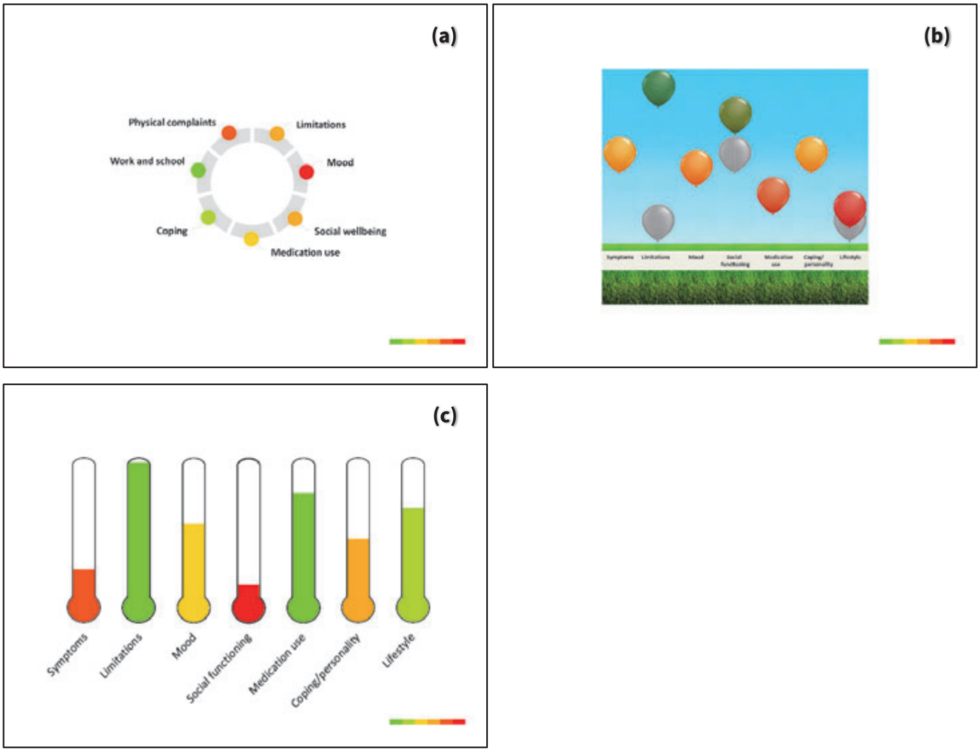

Figure B1. Prototypes of profile charts: (**a**) wheel, (**b**) balloons, and (**c**) thermometers. Balloon image is adapted with permission from A. H. M. Slok et al., Effectiveness of the Assessment of Burden of COPD (ABC) tool on health-related quality of life in patients with COPD: a cluster randomised controlled trial in primary and hospital care; published by NPJ Primary Care Respiratory Medicine, 2014.

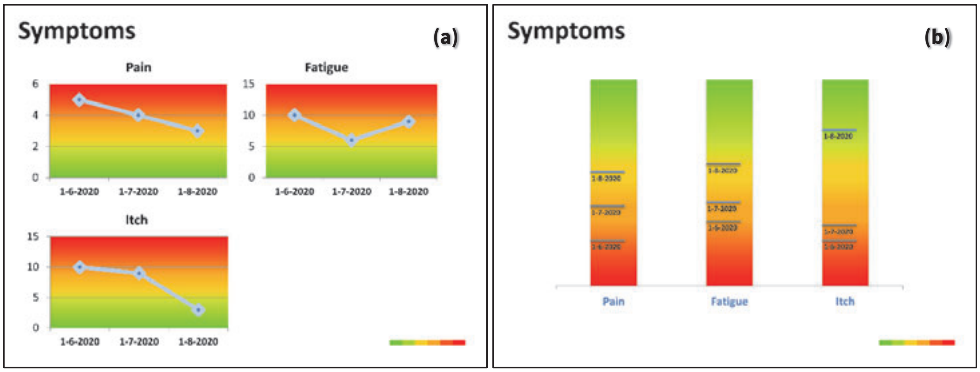

Figure B2. Prototypes of monitor charts: (**a**) line chart and (**b**) bar chart.

Chapter 4

Psychological distress and self-management among people with chronic kidney disease

Cinderella K. Cardol, Yvette Meuleman, Henriët van Middendorp,
Paul J.M. van der Boog, Luuk B. Hilbrands, Gerjan Navis,
Yvo W.J. Sijpkens, Jacob K. Sont, Andrea W.M. Evers,
and Sandra van Dijk, on behalf of the E-GOAL study group

Manuscript submitted for publication

Abstract

Background

Patients with chronic kidney disease (CKD) not receiving dialysis, including kidney transplant recipients, often experience difficulties regarding self-management. An important barrier for adherence to self-management recommendations may be the occurrence of psychological distress. We investigated relationships between psychological distress and adherence to self-management recommendations.

Methods

Patients completed online questionnaires as part of the E-GOAL study. We examined cross-sectional associations of psychological distress, including depressive and anxiety symptoms, with dietary adherence, physical activity, medication adherence, smoking, and body mass index (BMI), using adjusted multivariate regression analyses. To determine whether the number of suboptimal self-management behaviors increased proportionately to the severity of psychological distress symptoms, we used adjusted ordinal logistic regression analyses.

Results

In our sample (*N*=460), 27.2% of patients reported psychological distress and 69.8% were non-adherent to one or more recommendations. Higher psychological distress was significantly associated with poorer dietary adherence (β^{adj}=-0.13, 95%CI[-0.53,-0.09]), less physical activity (β^{adj}=-0.13, 95%CI[-0.32,-0.04]), and lower medication adherence (β^{adj}=-0.15, 95%CI[-0.04,-0.01]), but not with smoking and BMI. Findings were similar for depressive symptoms, whereas anxiety was only associated with poorer dietary and medication adherence. An increase in psychological distress was also associated with an increased likelihood of being non-adherent to a higher number of different recommendations (OR^{adj}=1.04, 95%CI[1.02,1.07]).

Conclusions

Many people with CKD experience psychological distress, of whom most have difficulties to self-manage their CKD. Given the relationships between psychological distress and adherence to CKD self-management recommendations, behavioral interventions are needed to identify and treat psychological distress as a potential barrier for CKD self-management.

Keywords Chronic kidney disease (CKD); Kidney transplantation; Psychological distress; Self-management; Lifestyle; Adherence

Introduction

With a prevalence of 13%, chronic kidney disease (CKD) is a global health concern.[1] CKD is often progressive, resulting in burdensome symptoms and treatments, such as dialysis, and increasing risks of cardiovascular events and related mortality.[2] Therefore, from diagnosis onward, patients are confronted with profound changes and challenges that require extensive emotional coping skills, such as coping with diagnosis, affected future perspective, physical symptoms, and social implications.[3] An additional burden is patients' challenge to decelerate disease progression and reduce risks of adverse health outcomes, by adhering to a set of disease self-management recommendations, including healthy lifestyle behaviors and medication regimens.[2] Thus, CKD is an impactful and demanding disease, both with regard to its emotional and behavioral management.

The behavioral management of CKD is important, as extensive literature shows that disease progression, kidney failure (including graft failure among kidney transplant recipients), cardiovascular complications, and mortality can be reduced when patients adhere to general and disease-specific dietary prescriptions (e.g., sodium restrictions),[4,5] undertake regular physical activity,[6] take their medication as prescribed (e.g., antihypertensive or immunosuppressive medication),[7,8] and avoid tobacco smoking.[9,10] Weight management is also included in CKD guidelines by using the proxy body mass index [BMI],[11] although risks of an unhealthy weight status are not entirely clear.[11] Despite the beneficial health outcomes of most self-management behaviors, non-adherence is common among patients with CKD not receiving dialysis. In recent studies, about 78% of patients had a suboptimal diet, 34–47% reported limited physical activity, 12–67% was non-adherent to medication prescriptions, and 13–17% were current smokers.[10,12,13]

The high non-adherence rates may be partly related to the emotional impact of CKD, which is reflected by the high prevalence of psychological distress, affecting 21–34% of patients.[14,15] Psychological distress is a negative emotional response to chronic disease stressors,[16,17] commonly assessed as symptoms of depression and anxiety in a composite measure or separately.[17-19] Importantly, psychological distress is associated with adverse health outcomes in CKD, including accelerated disease progression and mortality.[15,20] One of the explanations for these adverse outcomes among psychologically distressed patients is that distress can be a barrier for adhering to desirable self-management behavior.[15] Moreover, increasing levels of psychological distress may hinder an increasing amount of different non-adherent behaviors, which could lead to even worse health outcomes for patients who suffer from severe levels of distress.[12,21]

Relationships of psychological distress with self-management behaviors have been frequently examined in other chronically ill populations. For instance, patients with diabetes and psychological distress were more likely to report dietary non-adherence, physical inactivity, and tobacco smoking than patients without distress.[22,23] Whereas quite some literature exists regarding relationships between distress and self-management among patients with kidney failure who are treated with dialysis,[24] few studies addressed patients with CKD not receiving dialysis. Most published studies examined only one or few self-management factors, involved relatively small samples, or focused only on depression. Recently, Choi and colleagues found that a lack of physical activity and current smoking (but not alcohol use) were significantly associated with higher levels of psychological distress among patients with CKD. Their findings indicated that, compared to optimal self-management adherence, an increase in the number of non-adherent behaviors was linked to greater risks of more severe psychological distress. The authors stressed that the associations may also work the other way around with psychological distress being a barrier for optimal self-management.[12] Therefore, the first aim of our study was to assess relationships of psychological distress, and specifically depressive and anxiety symptoms, with adherence to self-management recommendations that are vital for individuals with CKD, namely: dietary adherence, physical activity, medication adherence, weight maintenance, and non-smoking.[2] The second aim of our study was to examine whether higher levels of psychological distress, and specifically depressive and anxiety symptoms, are proportionately related to non-adherence to a higher number of different self-management recommendations.

Methods

Study Design

Cross-sectional survey data were collected as a part of the E-health Guidance in identifying and Overcoming psychological barriers for Adopting a healthy Lifestyle among patients with chronic kidney disease study (E-GOAL; Netherlands Trial Registry: NL7338), a multicenter open randomized controlled trial to evaluate the effectiveness of a personalized electronic health (eHealth) care pathway. For the current study, we used baseline data from screening questionnaires completed by patients to examine their eligibility for trial participation. The study was approved for all participating centers by the Medical Research Ethics Committee Leiden The Hague Delft (P17.090), and complies with the 1964 Declaration of Helsinki. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement was used as a reference for reporting.[25]

Setting and Participants

Recruitment of participants and data collection took place from April 2018 to October 2020 at the nephrology departments of four university hospitals and one general hospital in The Netherlands: Leiden University Medical Center, University Medical Center Groningen, Radboud university medical center, and Haaglanden Medical Center. Patients ≥18 years with a kidney function (estimated Glomerular Filtration Rate [eGFR]) of 20–89 ml/min/1.73m^2 were eligible when they were treated by a nephrologist and Dutch speaking. Patients were not eligible if they had a rapid progression of kidney function loss (>10% loss of kidney function over the last year), were treated with dialysis or had an expected need for starting kidney replacement therapy during the study (<6 months), had kidney transplantation <1 year ago, had a systolic blood pressure <95 mmHg that did not react to cessation of antihypertensive medication, or had other (medical) problems that were considered likely to intervene with study participation (e.g., progressive cancer, recent cardiovascular event, severe psychiatric disorders, problems in understanding written communication, or pregnancy). Eligible patients received an invitation to participate via their nephrologist during regular hospital visits or by mail, containing written information regarding study purposes and procedures, together with an informed consent form. Upon receiving patients' written informed consent, patients were sent an email with a link to online screening questionnaires in the secured eHealth application "PatientCoach" (www.patientcoach.lumc.nl). Paper-and-pencil questionnaires were available for patients who had difficulties with online questionnaire completion. After completion (estimated duration 5–15 min.), participants could review a visual representation of their results (Personal Profile Charts, see Figure 1 for an example) in the eHealth application, and received a paper version by mail. Recruitment took place until the sample size needed for the trial was reached.[26]

Measurements

Demographic and Clinical Characteristics

In the screening questionnaires, demographic (age, sex, country of birth, marital status, parenthood, education level, and employment status), disease and treatment characteristics (comorbidities, treatment history for psychological and physical complaints) and physical and mental health-related quality of life (HRQoL) were assessed. The latter were measured with the RAND 36-item Short Form Health Survey (RAND SF-36):[27] Physical and mental HRQoL component summary scores are shown as *T*-scores (Hays norm-based scoring algorithm; mean=50, standard deviation [SD]=10 in the general population), with higher scores indicating better HRQoL.[27] The number of comorbidities was computed based on self-reported presence of diabetes mellitus, cardiovascular disease, cancer, pulmonary, rheumatic, liver, gastrointestinal or blood disease, and chronic fatigue syndrome. Additional medical data were extracted from hospital information systems (history of kidney transplantation or dialysis, eGFR, office systolic and diastolic blood pressure).

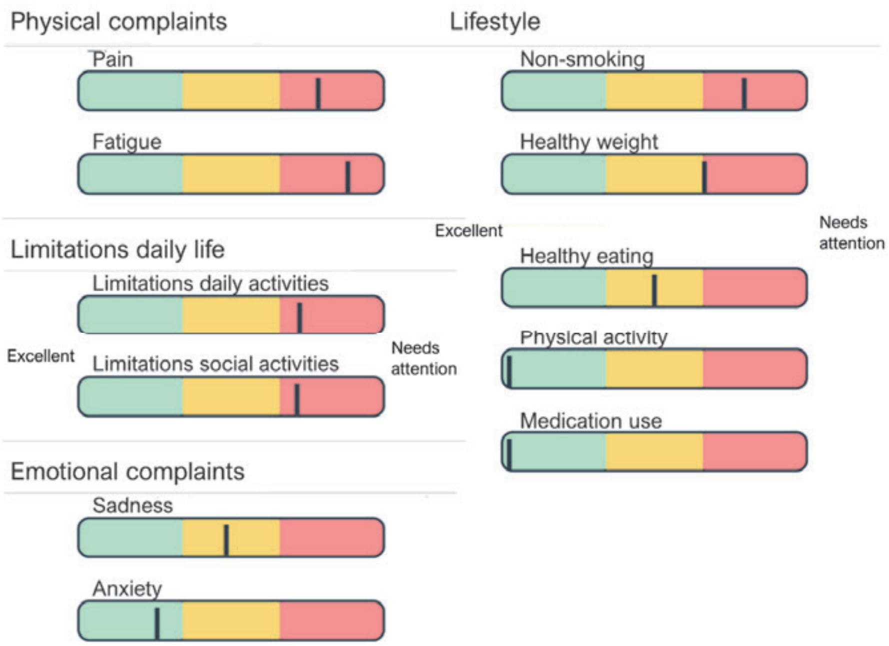

Figure 1. Example of Personal Profile Charts. Traffic light colors indicate current status on domains of functioning and self-management. Additional explanations are shown when hovering the mouse cursor over a domain. This patient shows moderate depressive symptoms (which may be influenced by severe physical complaints and limitations in daily life), heavy smoking, obesity, and moderate dietary adherence.

Psychological Distress

Psychological distress was measured with the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS),[18] a 16-item composite measure of depressive and anxiety symptoms. The scale consists of the 9-item Patient Health Questionnaire depression scale (PHQ-9)[28] and the 7-item Generalized Anxiety Disorder scale (GAD-7),[29] which both are well-validated and commonly used measures in research and clinical practice among chronic disease populations, including CKD.[18,30] Patients were asked to what degree a range of symptoms had bothered them over the past two weeks, with response options from 0 ("not at all") to 3 ("nearly every day"). Total scores of PHQ-ADS comprise the sum of PHQ-

9 (range 0–27) and GAD-7 (range 0–21) and thus range from 0 to 48, with higher scores indicating a higher level of psychological distress symptoms. Cut-off points of 10, 20, and 30 indicate mild, moderate, and severe levels of psychological distress, respectively (cut-off points are 5, 10, and 15 for the separate PHQ-9 and GAD-7). Scores below 10, indicating no or minimal psychological distress symptoms, are referred to as no presence of psychological distress. The PHQ-ADS proved to be reliable in this study with a Cronbach's alpha value of 0.91 (0.81 and 0.89 for the separate PHQ-9 and GAD-7, respectively).

CKD Self-Management

Dietary adherence, keeping a healthy diet in accordance with CKD guidelines or individual prescriptions as perceived by patients themselves, was assessed using two self-developed questions: "In the past week, how often have you kept a healthy diet? Think of a specific dietary regimen as prescribed by your healthcare provider. If you have not received dietary prescriptions, think of a healthy diet for people with chronic kidney disease in general, such as restricted salt consumption." with scores on a 5-point scale ranging from "never" to "always", and "In the past week, how well do you believe you have kept a healthy diet?" on a 1-10 rating scale ranging from "very badly" to "very well". A categorical or nonlinear principle components analysis was conducted to combine the two ordinal items and obtain a single summary variable (z-score) for dietary adherence.[31] The 1-dimension-solution had an eigenvalue exceeding Kaiser's criterion of 1, explained 85.75% of the variance, and showed a good internal consistency (Cronbach's α=0.83). To measure *physical activity*, the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH)[32] was used, in which respondents indicate how many days per week, average minutes per day, and at which intensity they practice commuting activities, leisure time, household, and work or school physical activities. Total scores were calculated of weekly medium-to-high intensity physical activity in minutes. *Medication adherence* was measured with the Simplified Medication Adherence Questionnaire (SMAQ)[33] consisting of four dichotomous yes/no items and two items to quantify omissions. In the original scale, participants were considered "non-adherent" when ≥ 1 item would indicate non-adherence. However, to facilitate interpretation, we used a pooled sum score, ranging from 0 to 6, with higher scores indicating better adherence: one point is given to each "adherent" response. For the quantitative items, ≤ 2 doses missed over the past week, and ≤ 2 days of non-adherence during the past three months are defined as adherent.[33] *Weight maintenance* was assessed by BMI,[34] measured with questions on respondents' weight and height. For *smoking behavior*, patients indicated whether they currently smoked or not, in dichotomous answer categories (yes/no). Last, we generated a *CKD self-management index* (CSI) by summing five binary indicators of adherence to the recommended self-management factors (adherent vs. non-adherent): 1) dietary adherence z-score >1 SD below the sample mean (i.e., perceived adherence to a healthy diet in the past week as “never”, “seldom” or “half the time”, with a rating of ≤6 on the 1–10 scale, as indicated on the separate dietary adherence items); 2) physical activity <150 minutes per week; 3) medication adherence score 0–4; 4) current smoker; and 5) BMI <18.5 or ≥25 kg/m^2. One point is assigned for each unhealthy or non-adherent behavior and summed (range 0–5) for each patient. The CSI is similar to the approach adopted to construct healthy lifestyle indices by previous studies.[9,35]

Statistical Analyses

Descriptive statistics were computed to describe sample characteristics, scores of psychological distress and of non-adherence to self-management recommendations, and summarized as mean±SD for normally distributed continuous variables, median (boundaries of interquartile range [IQR]) for skewed continuous variables, and as frequency (proportion) for categorical variables. Differences in demographic and clinical characteristics were examined between participants without and with (at least mild) psychological distress, between patients who were completely adherent and patients who were non-adherent to one or more self-management recommendations, and between complete cases and cases with missing data, using independent samples t-tests for continuous variables and χ^2-tests for categorical variables. Incomplete cases (7.4%) more often filled in paper-and-pencil questionnaires than complete cases. To avoid loss of power and biased results, missing data were imputed using multiple imputation (10 repetitions) under the “missing at random” assumption.[36]

To examine the hypotheses that psychological distress would be associated with less dietary adherence, physical activity, and medication adherence, univariate (crude) and multivariate (adjusted) regression analyses were carried out with the different CKD self-management factors as dependent variables. The association with weight maintenance was examined without predefined hypotheses, since BMI is not a behavior itself.[11] For the hypothesized association of psychological distress with the dichotomous dependent variable smoking, binomial logistic regression analyses were conducted. All multivariate models were adjusted for the potential confounders age, sex (male/female), marital status (single/partner), education level (lower/higher), eGFR, and physical comorbidities (0/1/2/≥3). To test the hypothesis that an increase in severity of psychological distress would be associated with an increase in the number of different non-adherent behaviors, we performed an ordinal logistic regression analysis with psychological distress as independent variable and the ordinal CSI as dependent variable. For the CSI, the highest categories were merged into non-adherent to 3–5 recommendations, since few participants had scores in those categories. All analyses were repeated for depressive and anxiety symptoms separately.

As sensitivity analysis, analyses were repeated without imputing missing data. Statistical analyses were performed using SPSS, version 25.0 (IBM), and *p* values <0.05 were considered statistically significant.

Results

Sample Characteristics

Table 1 shows the participant characteristics. The majority of participants were male (62.4%) and 68.9% had received a kidney transplant. Ages ranged from 19.0 to 88.0 years. The mean eGFR was 50.4±17.6 ml/min/1.73 m^2.

Table 2 shows prevalence rates and mean or median scores on the variables of interest for our study aims. The prevalence of (mild to severe) psychological distress symptoms was 27.2% (total score range 0–42); depressive symptoms were reported by 36.7% (score range 0–25) of the sample, anxiety symptoms by 23.3% (score range 0–19), and 18.7% reported both depressive and anxiety symptoms. Compared to participants without psychological distress, patients with distress were more often born outside The Netherlands, younger, had more comorbidities, lower physical and mental HRQoL, higher blood pressure, and more often had a treatment history for psychological complaints (see Table S1 in Supplementary File 1).

With regard to non-adherence to self-management recommendations, 17.4% of our patients reported having a suboptimal diet, 8.0% reported engaging less minutes than recommended in physical activity, 13.3% were not fully adherent to medication prescriptions, 54.1% did not have a healthy BMI (1.3% underweight, 36.3% overweight, 16.5% obese), and 7.8% were current smokers. In total, 321 patients (69.7%) were non-adherent to one or more self-management recommendations, of whom 208 participants were non-adherent to one recommendation, 88 to two recommendations, 21 to three, four to four, and none of the participants were non-adherent to all five recommendations. Participants who were non-adherent to one or more self-management recommendations had lower levels of education, more comorbidities, lower physical and mental HRQoL, higher blood pressure, and had received psychological treatment more often than participants who were completely adherent (see Table S2 in Supplementary File 1).

Table 1. Patient characteristics

Characteristic	*N*=460
Socio-demographic characteristics	
Age, y	58.5±12.5
Male sex, *n* (%)	287 (62.4)
Born in the Netherlands, *n* (%)	434 (94.3)
Married/partnered, *n* (%)	366 (79.6)
Having children, *n* (%)	330 (71.7)
Lower education[a,b], *n* (%)	228 (49.6)
Unemployed, *n* (%)	228 (49.6)
Disease and treatment characteristics	
Kidney transplant recipient, *n* (%)	317 (68.9)
Time since last kidney transplantation[c,d], y	9.6±8.2
History of dialysis, *n* (%)	175 (38.0)
Multimorbidity[d]	222 (48.4)
Diabetes mellitus[d], *n* (%)	70 (15.2)
Cardiovascular disease[d], *n* (%)	70 (15.2)
Hypertension[e], *n* (%)	145 (31.5)
eGFR, ml/min/1.73 m^2	50.4±17.6
Office SBP, mm Hg[f]	133.6±15.8
Office DBP, mm Hg[f]	77.9±9.7
Treatment history for psychological complaints[d], *n* (%)	125 (27.2)
Current treatment for psychological complaints[d], *n* (%)	22 (4.8)
Physical HRQoL[e]	43.2±10.8
Mental HRQoL[b]	48.3±10.8

Notes. Continuous variables are presented as mean±SD for normally distributed variables and as median[IQR] for skewed variables; DBP = diastolic blood pressure; eGFR=estimated glomerular filtration rate; HRQoL=health-related quality of life; SBP=systolic blood pressure. [a]Lower education includes primary, pre-vocational, and vocational education; Higher education includes advanced secondary and tertiary education; [b]3 unknown; [c]Only for kidney transplant recipients, *n*=316; [d]1 unknown; [e]2 unknown; [f]26 unknown.

Table 2. Prevalence and scores of psychological distress and self-management variables

Variable	*N*=460
Psychological distress	
Psychological distress symptoms	
Prevalence[a], *n* (%)	125 (27.2)
Mean, 0–48 score	7.0±7.2
Depressive symptoms	
Prevalence[a], *n* (%)	169 (36.7)
Mean, 0–27 score	4.2±4.1
Anxiety symptoms	
Prevalence[a], *n* (%)	107 (23.3)
Mean, 0–21 score	2.8±3.6
Self-management	
Dietary adherence	
Prevalence non-adherence (z-score >1 SD below sample mean)	80 (17.4)
Mean, 1–10 score[b]	7.4±1.9
Physical activity	
Prevalence non-adherence (<150 mins/week), *n* (%)[c]	37 (8.0)
Mean, hrs/week[b]	18.1±15.7
Medication adherence	
Prevalence non-adherence (score 0–4), *n* (%)	61 (13.3)
Mean, 0–6 score	5.5±0.9
Body mass index	
Prevalence non-adherence (<18.5 or ≥25), *n* (%)	249 (54.1)
Mean, kg/m^2	26.1±4.6
Smoking	
Prevalence non-adherence (current smoker), *n* (%)	36 (7.8)
Median, units/day	0 [0]
CKD self-management index (CSI)[c,d]	
0 (completely adherent)	137 (29.8)
1 (1*non-adherent)	208 (45.2)
2 (2*non-adherent)	88 (19.1)
3 (≥3*non-adherent)	25 (5.4)

Notes. Continuous variables are presented as mean±SD for normally distributed variables and as median[IQR] for skewed variables. [a] Prevalence of mild to severe symptoms, i.e., psychological distress scores ≥10, depressive and anxiety scores ≥5; [b]1 unknown; [c]2 unknown; [d]Calculated by summing five binary indicators of non-adherence to the recommended self-management factors.

Psychological Distress and CKD Self-Management

In Table 3, crude and adjusted linear regression analyses of psychological distress and CKD self-management are shown. Higher psychological distress was significantly associated with poorer dietary adherence (β^{adj}=-0.13, 95%Confidence Interval {CI}[-0.53,-0.09]), less physical activity (β^{adj}=-0.13, 95%CI[-0.32,-0.04]), and lower medication adherence (β^{adj}=-0.15, 95%CI[-0.04,-0.01]). Psychological distress was not significantly related to a higher BMI (β^{adj}=-0.09, 95%CI[-0.00,0.03]) or the likelihood that patients were current smokers (OR^{adj}=1.03, 95%CI[0.99,1.07]).

Table 3. Linear regression of psychological distress and CKD self-management

	Crude		Adjusted[a]	
	Coeff.[b] (95% CI)	*p*	Coeff.[b] (95% CI)	*p*
Dietary adherence	-0.19 (-0.65 to -0.23)	<0.001	-0.13 (-0.53 to -0.09)	0.006
Physical activity	-0.11 (-0.28 to -0.03)	0.019	-0.13 (-0.32 to -0.04)	0.011
Medication adherence	-0.19 (-0.05 to -0.02)	<0.001	-0.15 (-0.04 to -0.01)	0.002
Body mass index	0.11 (0.00 to 0.03)	0.015	0.09 (-0.00 to 0.03)	0.072
Smoking	1.03 (0.99 to 1.07)	0.198	1.04 (0.99 to 1.08)	0.131

Notes. CI=Confidence Interval; Coeff.=Regression Coefficient. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate); [b]Beta for continuous dependent variables, odds ratio for dichotomous variable.

Depressive and Anxiety Symptoms and CKD Self-Management

As shown in Tables 4 and 5, both higher levels of depressive and anxiety symptoms were significantly associated with poorer dietary adherence (β^{adj}=-0.14, 95%CI[-0.64,-0.12] and β^{adj}=-0.11, 95%CI[-0.53,-0.03], respectively) and medication adherence (β^{adj}=-0.15, 95%CI[-0.05,-0.01] and β=-0.13, 95%CI[-0.05,-0.01], respectively). Only reporting more depressive symptoms was associated with lower physical activity (β^{adj}=-0.15, 95%CI[-0.41,-0.09]), whereas no significant association between anxiety and physical activity was observed (β^{adj}=-0.07, 95%CI[-0.26,0.05]). No significant associations were found for either depressive or anxiety symptoms with BMI (β^{adj}=0.08, 95%CI[-0.00,0.04] and β^{adj}=0.05, 95%CI[-0.01,0.03], respectively) or smoking (OR^{adj}=1.07, 95%CI[1.00,1.16] and OR^{adj}=1.04, 95%CI[0.95,1.14], respectively).

Table 4. Linear regression of depressive symptoms and CKD self-management

	Crude		Adjusted[a]	
	Coeff.[b] (95% CI)	*p*	Coeff.[b] (95% CI)	*p*
Dietary adherence	-0.19 (-0.77 to -0.27)	<0.001	-0.14 (-0.64 to -0.12)	0.004
Physical activity	-0.14 (-0.38 to -0.08)	0.003	-0.15 (-0.41 to -0.09)	0.002
Medication adherence	-0.18 (-0.06 to -0.02)	<0.001	-0.15 (-0.05 to -0.01)	0.002
Body mass index	0.12 (0.01 to 0.04)	0.013	0.08 (-0.00 to 0.04)	0.092
Smoking	1.06 (0.99 to 1.14)	0.090	1.07 (1.00 to 1.16)	0.065

Notes. CI=Confidence Interval; Coeff.=Regression Coefficient. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate); [b]Beta for continuous dependent variables, odds ratio for dichotomous variable.

Table 5. Linear regression of anxiety symptoms and CKD self-management

	Crude		Adjusted[a]	
	Coeff.[b] (95% CI)	*p*	Coeff.[b] (95% CI)	*p*
Dietary adherence	-0.16 (-0.67 to -0.18)	0.001	-0.11 (-0.53 to -0.03)	0.026
Physical activity	-0.05 (-0.23 to 0.07)	0.282	-0.07 (-0.26 to 0.05)	0.185
Medication adherence	-0.17 (-0.06 to -0.02)	<0.001	-0.13 (-0.05 to -0.01)	0.009
Body mass index	0.06 (-0.01 to 0.03)	0.221	0.05 (-0.01 to 0.03)	0.346
Smoking	1.03 (0.94 to 1.12)	0.527	1.04 (0.95 to 1.14)	0.379

Notes. CI=Confidence Interval; Coeff.=Regression Coefficient. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate); [b]Beta for continuous dependent variables, odds ratio for dichotomous variable.

CKD Self-Management Index

Table 6 presents distributions of adherence to self-management recommendations per level of psychological distress. Taken together, 102 participants reported both (mild to severe) psychological distress and non-adherence to one or more self-management recommendations. Thus, 81.6% out of all participants who suffered from psychological distress also had problems with self-management; 31.8% out of all participants with problems in self-management also had heightened psychological distress. Complete adherence to all five self-management recommendations was most common among patients without psychological distress (34.0%) and least common among those with moderate to severe distress (11.8%). Inversely, non-adherence to three or more recommendations least common in the no distress group (3.9%) and most common in the moderate to severe distress group (14.7%). Distribution patterns of adherence to self-management recommendations were very similar when group assignment was based on no, mild, and moderate to severe depressive or anxiety symptoms separately.

Table 6. Adherence to self-management recommendations by psychological distress, depressive, and anxiety symptoms, *n* (%)

Psychological distress	No (*n*=335)	Mild (*n*=91)	Moderate to severe (*n*=34)
CSI[a]			
0 (completely adherent)	114 (34.0)	19 (20.9)	4 (11.8)
1 (1*non-adherent)	150 (44.8)	41 (45.1)	17 (50.0)
2 (2*non-adherent)	56 (16.7)	24 (26.4)	8 (23.5)
3 (≥3*non-adherent)	13 (3.9)	7 (7.7)	5 (14.7)
Depressive symptoms	No (*n*=291)	Mild (*n*=120)	Moderate to severe (*n*=49)
CSI[a]			
0 (completely adherent)	100 (34.4)	32 (26.7)	5 (10.2)
1 (1*non-adherent)	128 (44.0)	56 (46.7)	24 (49.0)
2 (2*non-adherent)	51 (17.5)	24 (20.0)	13 (26.5)
3 (≥3*non-adherent)	11 (3.8)	7 (5.8)	7 (14.3)
Anxiety symptoms	No (*n*=353)	Mild (*n*=81)	Moderate to severe (*n*=26)
CSI[a]			
0 (completely adherent)	115 (32.6)	18 (22.2)	4 (15.4)
1 (1*non-adherent)	156 (44.2)	39 (48.1)	13 (50.0)
2 (2*non-adherent)	64 (18.1)	17 (21.0)	7 (26.9)
3 (≥3*non-adherent)	16 (4.5)	7 (8.6)	2 (7.7)

Notes. BMI=Body Mass Index; CSI=CKD self-management index. [a]2 unknown.

These observed accumulation patterns were confirmed by significant ordinal logistic regression analyses of the CSI by psychological distress: every one-point increase in the level of psychological distress was associated with a 1.04 times increase in the likelihood of being non-adherent to a higher amount of self-management recommendations (OR^{crude}=1.05, 95%CI[1.03,1.08]; OR^{adj}=1.04, 95%CI[1.02,1.07]). Similar results were found for depressive symptoms (OR^{crude}=1.11, 95%CI[1.06,1.15]; OR^{adj}=1.09, 95%CI[1.04,1.14]) and anxiety symptoms (OR^{crude}=1.08, 95%CI[1.03,1.13]; OR^{adj}=1.06, 95%CI[1.01,1.11]) separately.

Sensitivity Analyses

Supplementary File 2 contains the results of all sensitivity analyses repeated on the original dataset without multiple imputation. The outcomes of all regression analyses remained stable as compared to those conducted in the multiple imputation dataset.

Discussion

This study shows that over a quarter of patients with CKD not receiving dialysis report psychological distress. Psychological complaints are associated with poor health outcomes, including disease progression, diminished HRQoL, and even an increased mortality risk.[15,20,37] Our findings provide support for a potential explanation of the relationship between psychological distress and poor outcomes. Higher psychological distress, as well as its underlying symptoms of depression and anxiety, are associated with a lower rate of adherence to several health-enhancing self-management recommendations. Moreover, patients with higher levels of distress have a higher likelihood to be unsuccessful in multiple areas of self-management compared to patients with lower levels of distress. Psychological distress could thus form a barrier for adequate CKD management.

The linear associations of psychological distress with a lack of physical activity and medication non-adherence observed in our study are similar to those described in recent literature.[12,38] In addition, our results show that higher psychological distress is related to poorer dietary adherence. To our knowledge, the association between distress and adherence to CKD-specific dietary recommendations has not been studied before. We did not find a significant association between psychological distress and smoking, whereas a recent study among patients with CKD of Choi and colleagues (2019) did. Their study had more participants, of whom 17.3% were current smokers,[12] compared to 7.8% in our sample. As the odds ratios in our study are in the hypothesized direction, we may have had insufficient power to detect statistical significance.

The findings of depressive and anxiety symptoms separately are similar to psychological distress as a composite: associations of psychological distress with dietary and medication adherence can be explained by both depressive and anxiety symptoms, while only having more depressive symptoms is related to lower physical activity levels. Main effects are slightly larger for depressive symptoms compared to anxiety symptoms. These findings suggest that depressive symptoms have a more important role in self-management than anxiety. A possible explanation may be that typical depressive symptoms are pessimistic perceptions and underestimations of one's capabilities to engage in self-management behaviors, which could have a discouraging effect. Alternatively, effects of anxiety may work in two ways due to different coping styles, i.e., avoidant or approach coping:[39] anxiety could have a paralyzing effect on health behavior, but it may also activate and motivate patients to live healthily and to be adherent.[40] Although we did not find indications that higher anxiety would be associated with better adherence either, such contrasting responses could have been present within the sample and may have somewhat diluted the associations.

Another explanation for the relatively small linear associations in general may be that self-management is not severely hampered if patients only experience mild levels of psychological distress. Our findings suggest that the number of suboptimal self-management behaviors increases proportionally to the severity of distress symptoms. For instance, patients who suffer from moderate to severe distress are relatively more often non-adherent to three or more recommendations compared to patients with no or mild distress symptoms. The findings are alarming, since detrimental effects of non-adherence to multiple self-management recommendations may be additive.[9,41]

This study has some limitations. First, data are cross-sectional, which makes it impossible to determine the directionality of the relationships found. Plausibly, associations between psychological distress and self-management are bi-directional.[16,21,35] On the one hand, psychological distress may entail negative or catastrophic cognitions and expectations, an excessive focus on somatic symptoms, problems in motivation, energy, self-efficacy, concentration, or social withdrawal, which may all hinder patients' ability to engage in healthy self-management behaviors; on the other hand, unhealthy behaviors may hamper psychological wellbeing through various mechanisms, for instance due to diminished social or physical activity, decreased physical fitness, or a lack of self-esteem due to the inability to succeed in adherence.[16,21,42] Future research with a longitudinal design should investigate the exact working mechanisms and directions of the associations. Second, we adjusted for multiple potential confounders, including kidney function and multimorbidity. However, possible residual confounding from unmeasured variables should be considered.[43] Third, self-management behaviors were measured by self-report, which could have over or underestimated true adherence.[44,45] Strengths of this study are the large sample size and relatively low percentage of missing data, which were handled carefully.[36] Also, the high degree of multimorbidity of diabetes and cardiovascular diseases in our sample promotes generalizability of the findings to other patient populations.

The high prevalence rates of psychological and self-management difficulties reported in this study and their interrelatedness emphasize a need for detection and treatment of both psychological distress and non-adherence to self-management recommendations in clinical practice. First, psychological distress and its constituents depression and anxiety are burdensome and important priorities for patients with CKD.[3,46] However, psychological symptoms often remain unnoticed, since patients and healthcare professionals may be hesitant to talk about these aspects of disease and no regular assessments take place.[3,46] Recognition is especially important since psychological distress could come along with behavioral self-management problems, as shown in this study by the finding that over four out of five patients with psychological distress also reported non-adherence. Routine screening procedures comprising short questionnaires, such as the CKD self-management index that was developed in this study, may identify patients at risk of distress and inadequate self-management.[47,48]

Second, as psychological distress and self-management are associated, treating one could potentially improve the other. Indeed, intervention studies in other populations have shown that interventions focused at physical exercise and dietary improvements also reduced distress,[49,50] and vice versa, psychological interventions enhanced treatment adherence and reduced smoking.[51] In terms of self-management models, such as the stress-coping models:[39,52] when a patient faces disease-related stressors, strategies that enhance both problem-focused coping (facilitating self-management behaviors) and emotion-focused coping (regulating psychological distress) should lead to the most beneficial outcomes.[17] This implies that the effectiveness of current personalized self-management interventions for patient with CKD[52,53] could be further augmented by integrating cognitive-behavioral treatment of psychological distress.

Conclusions

To conclude, in the current study, we found that higher psychological distress is associated with poorer dietary and medication adherence as well as lower physical activity among patients with CKD not receiving dialysis. Furthermore, increased psychological distress severity is associated with an enhanced risk of non-adherence to an accumulating number of self-management recommendations. These results suggest that psychological distress is a potential barrier for self-management. Tailored interventions to screen for and treat both psychological and self-management difficulties in parallel may be effective in improving physical as well as psychological outcomes.[21,23,35] Future research should provide more insights in causality mechanisms in the relationships of psychological distress, depressive, and anxiety symptoms with separate and concurrent self-management behaviors.

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Supplementary File 1

Patient Characteristics by Subgroups

Table S1. Patient characteristics by subgroups without and with psychological distress

Characteristic	No psychological distress (*n*=335)	≥Mild psychological distress (*n*=125)
Socio-demographic characteristics		
Age, y	59.7±12.3	55.4±12.6
Male sex, *n* (%)	217 (64.8)	70 (56.0)
Born in the Netherlands, *n* (%)	322 (96.1)	112 (89.6)
Married/partnered, *n* (%)	274 (81.8)	92 (73.6)
Having children, *n* (%)	243 (72.5)	87 (69.6)
Lower education[a,b], *n* (%)	162 (48.4)	66 (52.8)
Unemployed, *n* (%)	166 (49.6)	66 (52.8)
Disease and treatment characteristics		
Kidney transplant recipient, *n* (%)	230 (68.7)	87 (69.6)
Time since last kidney transplantation[c,d], y	10.0±8.7	8.4±6.3
History of dialysis, *n* (%)	127 (37.9)	48 (38.4)
Multimorbidity[d]	153 (45.9)	69 (55.2)
Diabetes mellitus[d], *n* (%)	46 (13.7)	24 (19.2)
Cardiovascular disease[d], *n* (%)	46 (13.7)	24 (19.2)
Hypertension[e], *n* (%)	98 (29.3)	47 (37.6)
eGFR, ml/min/1.73 m^2	50.8±17.6	49.2±17.6
Office SBP, mm Hg[f]	132.1±15.5	137.5±15.8
Office DBP, mm Hg[f]	77.0±9.6	80.1±9.5
Treatment history for psychological complaints[d], *n* (%)	65 (19.4)	60 (48.0)
Current treatment for psychological complaints[d], *n* (%)	6 (1.8)	16 (12.8)
Physical HRQoL[e]	46.4±9.6	34.6±9.0
Mental HRQoL[b]	53.1±7.3	35.8±8.3

Notes. Continuous variables are presented as mean±SD for normally distributed variables and as median[IQR] for skewed variables; DBP = diastolic blood pressure; eGFR=estimated glomerular filtration rate; HRQoL=health-related quality of life; SBP=systolic blood pressure. [a]Lower education includes primary, pre-vocational, and vocational education; Higher education includes advanced secondary and tertiary education; [b]3 unknown; [c]Only for kidney transplant recipients, *n*=316; [d]1 unknown; [e]2 unknown; [f]26 unknown.

Table S2. Patient characteristics by subgroups of adherence and non-adherence to self-management recommendations

Characteristic	Completely adherent (*n*=137)	≥1*Non-adherent (*n*=321)[a]
Socio-demographic characteristics		
Age, y	59.4±11.9	58.2±12.6
Male sex, *n* (%)	84 (61.3)	202 (62.9)
Born in the Netherlands, *n* (%)	132 (96.4)	300 (93.5)
Married/partnered, *n* (%)	116 (84.7)	248 (77.3)
Having children, *n* (%)	94 (68.6)	235 (73.2)
Lower education[b,c], *n* (%)	57 (41.6)	169 (52.6)
Unemployed, *n* (%)	69 (50.4)	162 (50.5)
Disease and treatment characteristics		
Kidney transplant recipient, *n* (%)	99 (72.3)	216 (67.3)
Time since last kidney transplantation[d,e], y	10.0±7.9	9.3±8.3
History of dialysis, *n* (%)	50 (36.5)	125 (38.0)
Multimorbidity[e]	59 (43.1)	163 (50.8)
Diabetes mellitus[e], *n* (%)	17 (12.4)	53 (16.5)
Cardiovascular disease[e], *n* (%)	21 (15.3)	49 (15.3)
Hypertension[a], *n* (%)	33 (24.1)	111 (34.6)
eGFR, mL/min/1.73 m2	52.5±16.5	49.3±18.0
Office SBP, mm Hg[f]	131.3±15.8	134.6±15.7
Office DBP, mm Hg[f]	76.0±9.6	78.7±9.6
Treatment history for psychological complaints[e], *n* (%)	30 (21.9)	96 (29.9)
Current treatment for psychological complaints[e], *n* (%)	2 (1.5)	20 (6.2)
Physical HRQoL[a]	46.0±9.7	42.0±11.0
Mental HRQoL[c]	51.1±9.8	37.1±11.1

Notes. Continuous variables are presented as mean±SD for normally distributed variables and as median[IQR] for skewed variables; DBP = diastolic blood pressure; eGFR=estimated glomerular filtration rate; HRQoL=health-related quality of life; SBP=systolic blood pressure. [a]2 unknown; [b]Lower education includes primary, pre-vocational, and vocational education; Higher education includes advanced secondary and tertiary education; [c]3 unknown; [d]Only for kidney transplant recipients, *n*=316; [e]1 unknown; [f]26 unknown.

Supplementary File 2

Sensitivity Analyses

Below, the results of the analyses can be found, repeated on the original dataset without multiple imputation.

Table S3. Linear regression of psychological distress and CKD self-management

	Crude		Adjusted[a]	
	Coeff.[b] (95% CI)	*p*	Coeff.[b] (95% CI)	*p*
Dietary adherence	-0.19 (-0.67 to -0.24)	<0.001	-0.14 (-0.56 to -0.12)	0.003
Physical activity	-0.10 (-0.26 to -0.01)	0.032	-0.12 (-0.30 to -0.02)	0.022
Medication adherence	-0.19 (-0.05 to -0.02)	<0.001	-0.14 (-0.04 to -0.01)	0.004
Body mass index	0.11 (0.00 to 0.03)	0.014	0.09 (-0.00 to 0.03)	0.066
Smoking	1.03 (0.99 to 1.07)	0.194	1.04 (0.99 to 1.08)	0.134

Notes. CI=Confidence Interval; Coeff.=Regression Coefficient. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate); [b]Beta for continuous dependent variables, odds ratio for dichotomous variable.

Table S4. Linear regression of depressive symptoms and CKD self-management

	Crude		Adjusted[a]	
	Coeff.[b] (95% CI)	*p*	Coeff.[b] (95% CI)	*p*
Dietary adherence	-0.20 (-0.78 to -0.29)	<0.001	-0.15 (-0.66 to -0.14)	0.003
Physical activity	-0.13 (-0.35 to -0.06)	0.007	-0.14 (-0.38 to -0.07)	0.005
Medication adherence	-0.18 (-0.06 to -0.02)	<0.001	-0.14 (-0.05 to -0.01)	0.003
Body mass index	0.12 (0.01 to 0.04)	0.012	0.09 (-0.00 to 0.04)	0.082
Smoking	1.06 (0.99 to 1.14)	0.088	1.07 (1.00 to 1.16)	0.066

Notes. CI=Confidence Interval; Coeff.=Regression Coefficient. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate); [b]Beta for continuous dependent variables, odds ratio for dichotomous variable.

Table S5. Linear regression of anxiety symptoms and CKD self-management

	Crude		Adjusted[a]	
	Coeff.[b] (95% CI)	*p*	Coeff.[b] (95% CI)	*p*
Dietary adherence	-0.17 (-0.68 to -0.20)	<0.001	-0.12 (-0.57 to -0.07)	0.014
Physical activity	-0.05 (-0.22 to 0.07)	0.327	-0.07 (-0.24 to 0.06)	0.241
Medication adherence	-0.17 (-0.06 to -0.02)	<0.001	-0.12 (-0.04 to -0.01)	0.015
Body mass index	0.06 (-0.01 to 0.03)	0.207	0.05 (-0.01 to 0.03)	0.328
Smoking	1.03 (0.94 to 1.12)	0.522	1.04 (0.95 to 1.14)	0.387

Notes. CI=Confidence Interval; Coeff.=Regression Coefficient. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate); [b]Beta for continuous dependent variables, odds ratio for dichotomous variable.

Table S6. Ordinal logistic regression of CKD self-management index (CSI) by psychological distress, depressive, and anxiety symptoms

CSI	Crude		Adjusted[a]	
	OR[b] (95% CI)	*p*	OR[b] (95% CI)	*p*
Psychological distress	1.05 (1.03 to 1.08)	<0.001	1.04 (1.02 to 1.07)	0.001
Depressive symptoms	1.11 (1.06 to 1.16)	<0.001	1.09 (1.04 to 1.14)	<0.001
Anxiety symptoms	1.08 (1.03 to 1.13)	0.001	1.06 (1.01 to 1.11)	0.018

Notes. OR=Odds Ratio; CI=Confidence Interval. [a]Adjusted for age, sex, education level, marital status, comorbidities, and kidney function (estimated glomerular filtration rate).

Chapter 5

The Personalized Priority and Progress Questionnaire (PPPQ): A personalized instrument for quality of life and self-management for use in clinical trials and practice

Judith Tommel*, Cinderella K. Cardol*, Andrea W.M. Evers,
Rianne Stuivenberg, Sandra van Dijk, and Henriët van Middendorp

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*Shared first authorship

Abstract

Background

The aim of this study was to develop and validate a brief personalized instrument that (1) defines patients' priorities for improvement, (2) measures progress in prioritized quality of life (QoL) and self-management outcomes, and (3) is applicable in both clinical practice and clinical trials.

Methods

The instrument was developed based on literature on personalized assessment and patient priorities, feedback by clinicians, and six cognitive interviews with patients with chronic kidney disease. The resulting questionnaire, the Personalized Priority and Progress Questionnaire (PPPQ), contains a baseline and follow-op measurement. The baseline measurement assesses functioning on QoL (eight items) and self-management (five items). The final item evaluates patients' priorities for improvement. The follow-up measurement assesses progress in QoL and self-management. A personalized progress score can be calculated indicating the amount of progress on the QoL or self-management domain that is prioritized by the individual patient. Psychometric properties of the PPPQ were evaluated among patients with chronic kidney disease (*n*=121) and patients with kidney failure treated with dialysis (*n*=22).

Results

The PPPQ showed to be a feasible instrument that is easy and quick to complete. With regard to the construct validity, small to large correlations were found between the items and existing validated questionnaires measuring related constructs.

Conclusions

The PPPQ proved to be a feasible and valid instrument. The PPPQ could be a useful tool both in clinical practice (e.g., to identify priorities and tailor treatment) and clinical trials (e.g., to evaluate the effectiveness of personalized interventions).

Keywords Personalized outcome; Patient-centered care; Patient priorities; Quality of life; Self-management; Chronic disease

Introduction

Every patient is unique. Patients do not only vary in functioning, but also in preferences, goals, and values and all have unique personal situations.[1,2] Therefore, it is argued that intervention research should not only focus on mean levels of biological and clinical functioning, but should incorporate these individual differences and priorities.[3,4] As found by several studies on patients with chronic kidney disease (CKD), patients expressed a clear need for such a holistic approach to care that includes all aspects of a person's health and wellbeing, including quality of life (QoL) and the self-management behaviors they need to adopt (e.g., engage in physical activity, dietary changes, taking medication, stopping with smoking).[2,5] Moving away from a 'mechanistic' focus on laboratory results and focusing on patients' actual wellbeing instead, is thought to be key for patient-centered care (PCC).[5] PCC is defined as providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions.[6] Several studies found positive associations of PCC with enhanced QoL, wellbeing, patient satisfaction, perceived quality of care, and self-management.[7-9] PCC was also shown to relate to improved clinical outcomes, for example reductions in pain, blood pressure, complications, and hospitalization.[8] Qualitative research showed that patients highly value the principles of PCC: patients want to be taken seriously and treated by competent and empathic clinicians who consider each patient's unique situation, needs, and wishes.[10]

This implies that instead of evaluating one-size-fits-all interventions to find an effect in "the average patient", the focus should be on identifying and offering the best intervention for *every individual patient*.[11] Conform the PCC principles, this calls for (1) personalized interventions and (2) personalized outcome variables in order to properly evaluate the effectiveness of personalized interventions while doing justice to the individual patient's unique treatment trajectory.[3,4,11]

As personalized interventions imply individual differences in the focus of treatment, using only standard generic outcome measures to evaluate their effectiveness will not suffice. Multiple questionnaires would be necessary to evaluate the different treatment goals, which could significantly harm the power of these studies since only the data of subgroups that worked on similar treatment goals can be used.[4] Moreover, standard generic measures will invalidate the personalized character of the intervention by clouding patients' results with scores on health domains that may be unimportant to them and that were not the focus of their treatment.[3,4,11,12] Adding personalized assessments, however, enables researchers to evaluate whether the invention is not only clinically, but also personally relevant to patients (i.e., personal utility).[13] Such personalized assessment would allow for general conclusions on the effectiveness of a treatment, while taking each patient's unique treatment trajectory into account. This feature makes personalized outcome measures highly valuable in research settings.

Next to research settings, personalized assessment can be of great value in clinical practice. Since personalized assessments help to clarify patients' needs and priorities, they would be a valuable asset in shared decision-making.[12] In shared decision-making, patients have an active role in selecting treatment and care plans that match their preferences, which is a crucial element of PCC. Another application of personalized assessments is that they could help to define personally-relevant treatment goals, which form the basis of personalized treatment.[12] Subsequently, personalized outcomes can be used to monitor patient functioning over time.[12] Although incorporating patient priorities in decision-making and interventions is highly valued,[6] patient priorities are usually not routinely assessed or recorded in medical records, making them not explicitly visible and thereby unlikely to be discussed.[14] A personalized instrument or tool that assesses priorities would be helpful to make patient priorities explicitly visible in clinical practice.

However, adequate practical tools for use in either clinical practice or clinical trials are sparse. A review focusing on patients with multiple comorbid conditions found several studies on tools that measure priorities or preferences, but all tools lacked an assessment of the effect on health outcomes that are prioritized by patients themselves.[14] Other than these tools, the McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)[15] does offer the possibility to assess change in areas of functioning that actually matter to patients. This questionnaire, however, requires trained interviewers and has complex scoring, which limits its feasibility in clinical care and clinical trials.[16] Similarly, scales with a focus on goal setting such as Goal Attainment Scaling (GAS),[17] the Patient Goal Priority Questionnaire (PGPQ),[18] and Self-Identified Goal Assessment (SIGA)[19] can be highly valuable as a way to help patients prioritize their needs for improvement, but have the same limitation of being time-consuming and requiring a trained interviewer or therapist to help patients in setting realistic goals.[20]

The aim of the current study is to develop and validate a brief personalized instrument that (1) defines patients' top priorities for improvement, (2) measures changes in patient functioning on QoL and self-management outcomes that are prioritized by the patient, and (3) is applicable in both clinical practice and clinical trials. This newly developed instrument includes a variety of QoL areas (e.g., physical health, mental health, social functioning, and daily activities) and self-management behaviors, and is a generic and easily adjustable questionnaire that is applicable to diverse populations of patients with (chronic) somatic conditions. To illustrate this, this study evaluates the psychometric properties of the instrument in two different chronic kidney disease (CKD) samples. If this instrument proves to be a feasible and valid instrument, this brief, personalized tool can be used to easily identify, prioritize, and monitor individual problems and progress over time.

Methods

Study Population

Questionnaire Development

In the developmental phase of the questionnaire, cognitive interviews were conducted to evaluate the feasibility, comprehensibility, readability, and relevance of the items. Using purposeful sampling, four patients with CKD not on dialysis and two patients with kidney failure treated with dialysis were recruited from the Leiden University Medical Center. The interviews were conducted in March 2018.

Questionnaire Evaluation

To evaluate the psychometric properties of the questionnaire, datasets of two multicenter randomized controlled trials (RCT) were used. Both trials evaluated the effectiveness of a personalized e-health intervention in chronic somatic populations, with one trial focusing on patients with CKD not on dialysis (the E-GOAL study)[21] and the other focusing on patients with kidney failure treated with dialysis (the E-HELD study).[22]

Recruitment of patients with CKD for the E-GOAL study took place from April 2018 through March 2020. Patients were recruited from academic hospitals (Leiden University Medical Center, Leiden; Radboud university medical center, Nijmegen; University Medical Center Groningen, Groningen) and a non-academic hospital (Haaglanden Medical Center, The Hague) in the Netherlands. To determine eligibility for participating in the RCT, patients completed screening questionnaires on depressive and anxiety symptoms as well as problems with adherence to self-management recommendations. Adult patients with CKD with an eGFR of 20-89 ml/min/1.73 m^2 under treatment by an internist-nephrologist were invited to participate when their screening questionnaire results showed that they had at least mild depressive or anxiety symptoms and that they failed to meet at least one of the nephrology guidelines for self-management.[23]

Recruitment of patients on dialysis for the E-HELD study took place from February 2019 through October 2021. Patients were recruited from academic hospitals (Radboud university medical center, Nijmegen; Leiden University Medical Center, Leiden), non-academic hospitals (VieCuri Medical Centre, Venlo; Bernhoven Hospital, Uden), and dialysis centers (Ravenstein Dialysis Centre, Ravenstein; Dialysis Center Groningen, Groningen) in the Netherlands. To determine eligibility, patients completed a screening questionnaire on adjustment problems including questionnaires on QoL, fatigue, itch, depression, and anxiety. Adult patients with an eGFR <15 ml/min/1.73 m^2 that were treated with hemodialysis or peritoneal dialysis for at least three months were invited to participate when they presented adjustment problems as shown by the screening questionnaire (i.e., low QoL or symptoms of fatigue, itch, depression, or anxiety). Since this intervention did not focus on self-management, adherence to self-management recommendations was not assessed.

Exclusion criteria for both studies were: having an age of <18 years; having >10% renal function loss over the last year, serious comorbid physical (life expectancy <12 months) or psychiatric conditions, recent major stressful life events unrelated to CKD or kidney failure, cognitive problems that would interfere with participating in the study, receiving psychological treatment, having received a kidney transplant <1 year ago or a scheduled kidney transplant within the upcoming 12 months, not being fluent in Dutch language, pregnancy, and not having access to a computer or internet. Additionally, the E-GOAL study excluded patients who had an anticipated need for dialysis work-up within the time frame of the study and patients who had a systolic blood pressure <95 mmHg not responding to withdrawal or antihypertensives.

Ethical approval was obtained from the Medical Ethical Committee Leiden-Den Haag-Delft, with reference numbers P17.172 (E-GOAL) and P18.013 (E-HELD). The procedures used in both studies were in line with the principles of the Declaration of Helsinki.

Item Generation

The topics assessed by the questionnaire items were based on expertise within the research team and literature on frequently reported symptoms and patient priorities in the CKD and dialysis population.[2,24-27] The structure of the questionnaire, including the items in which patients are asked to prioritize individual problems, is based on relevant elements from existing personalized measurements and questionnaires on goal setting.[15-19] The resulting items were judged on comprehensibility and relevance by medical psychologists and nephrologists and were revised accordingly.

Cognitive Interviews

Subsequently, six cognitive interviews were conducted with patients with CKD and kidney failure to evaluate the feasibility, comprehensibility, readability, and relevance of the items according to patients. The interviewers, JT and CKC, made use of the *think-aloud* approach and *verbal probing techniques* to gain insight in the response process of patients answering the questionnaire.[28] In the think-aloud approach, the interviewees are asked to vocalize their thoughts while answering the items on the questionnaire. Verbal probing techniques that were used included comprehension/interpretation probes (e.g., explaining terms in own words), paraphrasing (e.g., repeating the question in own words), recall probes (e.g., remembering QoL three months ago), specific probes (e.g., 'What do you think this questionnaire aims to measure?'), and general probes (e.g., 'How did you arrive at that answer?'; 'Was that easy or hard to answer?').[28] Based on the results of the cognitive interviews, minor textual revisions were made and the questionnaire was finalized.

Personalized Priority and Progress Questionnaire (PPPQ)

The resulting questionnaire, called the Personalized Priority and Progress Questionnaire (PPPQ), consists of a baseline and follow-up measurement:

Baseline measurement. The goal of the baseline measurement is to assess personal priorities for improvement, both in QoL areas and self-management behaviors.

- QoL: The baseline measurement starts by assessing whether patients experience limitations in several QoL areas in the past two weeks using eight items (fatigue, pain, itch, anxiety, depression, social environment, daily activities, and dependency), with the possibility to omit any item that may not be relevant in a particular population. Items are scored on a 5-point Likert scale (1 = not at all, 5 = extremely). An example item is "To what extent have you experienced limitations in the area of fatigue or sleep problems?".
- Self-management: Self-management behaviors are assessed by five items (medication adherence, healthy diet, physical activity, weight maintenance, and non-smoking) using 5-point Likert scales (1 = not at all, 5 = extremely well). An example item is "To what extent have you managed to always take your medication as prescribed?".
- Prioritize: Patients are asked to select the areas of QoL they prioritize for improvement and would actively commit to over the coming period by making a top 2. Also with regard to self-management, patients select the areas they prioritize for improvement and would actively commit to in the upcoming period by making a top 2.

Progress measurement. The goal of the follow-up measurement is to assess the amount of progress in QoL or self-management behavior compared to the baseline measurement, especially progress on the areas selected as personal priorities at baseline.

- QoL: Patients are asked to indicate whether they feel that their experienced limitations in the QoL areas changed (worsened, remained the same, or improved) since the baseline measurement. The items are answered using a 7-point Likert scale (-3 = many more, 0 = remained the same, +3 = much fewer). Higher scores indicate less limitations and, thus, improved functioning. An example item is: "Compared to the last time I completed this questionnaire, I now experience more/fewer limitations in the area of fatigue or sleep problems".
- Self-management: Patients are asked to indicate whether they feel that their self-management behaviors changed (worsened, remained the same, or improved) since the baseline measurement. The items are answered using a 7-point Likert scale (-3 = much less well, 0 = equally well, +3 = much better), with higher scores indicating improved self-management behavior. An example item is: "Compared to the last time I completed this questionnaire, I have managed less well/better to always take my medication as prescribed".
- Prioritize: Patients are asked to indicate if they tried to improve anything in any of these QoL or self-management areas over the recent period. Patients can select a maximum of two QoL areas and two self-management behaviors. If they worked on another area, they can select the option 'other'. If they did not work on any of the QoL areas or self-management behaviors, they can select the option 'not applicable'.

Progress score. The progress score indicates the amount of progress (i.e., change) on the QoL or self-management domain that is prioritized by the individual patient. This score consists of the isolated scores on the progress items that represent the areas that were selected as priorities at baseline. For example, when fatigue was selected as priority at baseline, the score on the progress item on fatigue will be used for the calculation. Ultimately, this will result in one single score that includes all personally meaningful changes.

The original Dutch version of the PPPQ was translated in English using the forward-backward method.[29] This multistep approach included the following steps: (1) the original Dutch version was translated into English by a professional translator, bilingual in English and Dutch; (2) the English version was translated back to Dutch by a native Dutch speaker; (3) the translations were reviewed by the developers of the questionnaire; and (4) the developers and the translators reached consensus and decided upon the final English version. The complete, English version of the PPPQ is enclosed in Supplementary File 1: PPPQ_EN. The Dutch version is enclosed in Supplementary File 2: PPPQ_NL.

Measures

Patient Characteristics

Information on socio-demographic and clinical characteristics (age, sex, education level, marital status, and comorbidity) was collected using self-administered questionnaires.

In addition to the PPPQ, several existing validated measures were administered in order to evaluate the construct validity of the PPPQ.

Areas of QoL

Fatigue and sleep. The Shortened Fatigue Questionnaire (SFQ)[30] was used to assess fatigue. The SFQ is a 4-item shortened version of the Checklist Individual Strength.[30] Higher scores indicate more fatigue. To assess sleeping problems, the 9-item Sleep Problem Index of the Medical Outcomes Study (MOS) Sleep Scale[31] was used, with higher scores indicating more sleeping problems. Energy was measured by the subscale energy of the RAND Short Form-36 Health Status Inventory (RAND SF-36).[32] This subscale consists of four items, with higher scores indicating more energy. Scores on the RAND SF-36 are shown as T-scores (Hays norm-based scoring algorithm; $M = 50$, $SD = 10$ in the general population).[32]

Pain. The subscale pain of the RAND SF-36[32] was used to assess pain. This subscale contains two items, with higher scores indicating less pain.

Itch. A subscale of the Impact of Chronic Skin Disease on Daily Life (ISDL)[33] was used to measure itch. This scale contains four items. Higher scores indicate more itch.

Anxiety symptoms and worrying. The Generalized Anxiety Disorder 7-item Scale (GAD-7)[34] was used to assess anxiety symptoms, with higher scores indicating a higher level of anxiety symptoms. The Penn State Worry Questionnaire (PSWQ)[35] was used to measure worrying. The PSWQ contains 16 items, with higher scores indicating a stronger tendency to worry.

Depressive symptoms. The Patient Health Questionnaire depression scale (PHQ-9)[36] was used to measure depressive symptoms. Higher scores indicate a higher level of depressive symptoms.

Social environment. The 2-item subscale social functioning of the RAND SF-36[32] was used to assess social functioning, with higher scores indicating better social functioning. Additionally, the subscales perceived support (five items), actual support (three items), and mutual visiting (two items) of the Inventory for Social Reliance (ISR)[37] were administered. Higher scores on the ISR indicate better social functioning.

Daily activities. To measure limitations in daily activities, the subscale role limitations due to physical problems of the RAND SF-36[32] was administered. This subscale contains four items, with higher scores indicating fewer limitations.

Self-Management Behavior

Self-management. The Partners in Health Scale (PiH)[38] was used to assess chronic condition self-management knowledge and behaviors. The PiH consists of 12 items. Higher scores indicate better self-management.

Medication adherence. To assess medication adherence the Simplified Medication Adherence Questionnaire (SMAQ)[39] was used. The SMAQ contains six items, with higher scores indicating better medication adherence.

Dietary adherence. Dietary adherence was operationalized as keeping a healthy diet in accordance with the CKD guidelines or individual prescriptions as perceived by patients themselves. It was assessed using two questions: "In the past week, how often have you kept a healthy diet?" with scores on a 5-point scale from "never" to "always", and "In the past week, how well do you believe you have kept a healthy diet?" on a 1-10 rating scale from "very badly" to "very well". A categorical or nonlinear principal components analysis[40] was done to combine the two ordinal items, in order to obtain a single summary variable (z-score) for dietary adherence. Higher scores indicate better dietary adherence.

Physical activity. The Short Questionnaire to Assess Health-enhancing physical activity (SQUASH)[41] was used to assess physical activity. In the SQUASH, respondents indicate how many days per week, average minutes per day, and at which intensity they practice commuting, leisure time, and household activities, and activities at work or school. Total scores were calculated of weekly moderate-to-high intensity physical activity in minutes. Higher scores indicate more physical activity.

Smoking behavior. Patients could indicate whether they currently smoke (on a daily or nondaily basis) or not, in dichotomous answer categories (yes/no). Subsequently, patients could indicate how much tobacco they smoke on a daily basis. Higher scores indicate more tobacco use.

Weight maintenance. Weight maintenance was assessed by body mass index (BMI),[42] by calculating the ratio of body weight (kg) and the square of height (m). Scores <18.5 indicate underweight, scores of 18.5-24.9 indicate normal weight, and scores ≥ 25 indicate overweight with scores ≥ 30 indicating obesity.[42]

Statistical Analyses

It is important to note that the PPPQ does not intend to measure a single underlying concept—the PPPQ measures different QoL areas and self-management behaviors—and, therefore, homogeneity of the items is not assumed. Consequently, no factor analysis was performed; we did examine the internal consistency of the functioning and self-management items of the PPPQ to explore possible associations between the individual items.[43,44]

Descriptives were calculated of the patient characteristics, the PPPQ, and related constructs as measured by existing validated measurements. We calculated the means and standard deviations (*SD*s) of the baseline and progress measurement and of all the individual items of the PPPQ. The means and *SD*s were separately calculated for the QoL items and the self-management items. The internal consistency was calculated for the PPPQ QoL and self-management items and the measurements of related constructs, with Cronbach's alphas between .70 and .95 as an indicator of good internal consistency.[43] Additionally, exploratory intercorrelations between the PPPQ items were calculated to detect possible associations between the individual items.

In order to examine item characteristics of the PPPQ items, the presence of floor and ceiling effects was evaluated using the descriptives of the PPPQ items. Floor or ceiling effects were considered to be present if more than 15% of the patients achieved the lowest or highest possible score.[43]

To examine the construct validity of the PPPQ, correlations were calculated between the PPPQ items and existing validated measurements assessing similar constructs. The baseline items of the PPPQ were correlated with their related constructs as assessed at baseline. Since the follow-up measurement assesses progress (i.e., change) in QoL or self-management behavior, we calculated change scores of the measurements (mean score at follow-up subtracted by mean score at baseline) and used these in the correlation analyses with the PPPQ progress items to ensure a proper comparison. As result of the heterogeneity of the PPPQ items, all correlational analyses were performed on item level. For example, the PPPQ item on fatigue was correlated with fatigue scales (e.g., SFQ) and the PPPQ item on patients' social environment was correlated with social functioning scales (e.g., ISR). Due to the small number of patients in the dialysis sample (E-HELD study), the magnitude of the association was deemed more informative than its statistical significance (*p*-values), with correlation coefficients above .10, .30, and .50 being interpreted as small, moderate, and large.[45]

For the calculations focusing on the QoL items we used both the CKD and dialysis sample. For calculations focusing on the self-management items we only used the CKD sample: The trial that included patients treated with dialysis did not focus on self-management and, therefore, the PPPQ self-management items and other measures focusing on self-management behavior were not administered. The item on dependency was not added in the CKD sample, since the trial that included CKD patients did not focus on dependency.

Results

Questionnaire Development

Feasibility PPPQ

Six patients completed the PPPQ as part of the cognitive interviews and gave feedback on the answering process. None of the patients reported difficulties with comprehending or answering the questionnaire. The questions on limitations in QoL and on self-management behavior were clear and easy to understand. The item on depression, for example, was explained as “Feeling down, don’t feel like doing anything, lying on the couch’’ and the item on medication adherence as “Taking medication as told: when, at what time, how many, and at how many times during the day”. The areas that were listed under limitations in QoL and self-management were thought to be relevant for patients with a kidney disease. Additionally, patients had no trouble selecting areas as personal priorities: “Select what keeps you occupied, what is the thing you would most like to get rid of what comes with your disease”; “What are the most important areas to me, what keeps me busy, what I would like to improve”. Patients completed the questionnaire quickly, in 2-4 minutes.

Questionnaire Evaluation

Patient Characteristics

Of the 2240 eligible patients with CKD not on dialysis, 460 patients completed screening questionnaires (20.5%). Based on the screening results, 146 patients were eligible for randomization based on the presence of at least mild depressive or anxiety symptoms and failing to meet at least one of the nephrology guidelines for self-management outcomes. Of these patients, 121 (82.9%) were included in the trial.

Of the 195 eligible patients with kidney failure treated with dialysis, 59 completed the screening questionnaires (30.3%). Based on the screening results, 46 were eligible for randomization based on the presence of adjustment problems. Of these patients, 35 (76.1%) were included in the trial. Twenty-two of them completed the assessments that are needed for the current study's analyses (NB these analyses are not the focus of the main research questions of the E-HELD study). Patient characteristics are shown in Table 1.

Table 1. Patient characteristics

		CKD patients (*N* = 121)	Dialysis patients (*N* = 22)
Age,	Mean (*SD*)	55.95 (13.87)	65.50 (11.68)
	Median	57.31	67.00
	Range	25.77–81.59	46.00–83.00
Male sex		56.7%	54.5%
Education level,	Lower	52.9%	45.5%
	Higher	46.3%	54.5%
	Unknown	0.8%	-
Marital status, with partner		73.6%	95.5%
Comorbidity		69.4%	86.4%
	Hypertension	39.7%	50.0%
	Heart disease	19.0%	40.9%
	Diabetes	16.5%	31.8%
	Gastrointestinal disease	9.1%	27.3%
	Lung disease	6.6%	18.2%
	Cancer	5.8%	9.1%
Physical quality of life (PCS, RAND SF-36)		35.97 (8.64)	34.18 (7.14)
Mental quality of life (MCS, RAND SF-36)		39.81 (8.68)	44.18 (9.22)

Notes: Lower education includes primary, pre-vocational, and vocational education; higher education includes advanced secondary and tertiary education. Abbreviations: CKD, chronic kidney disease; SD, standard deviation; PCS, physical component summary; RAND SF-36, RAND Short Form-36 Health Status Inventory; MCS, mental component summary.

Descriptives PPPQ and Other Measurements

Descriptives of the sum scores of the PPPQ baseline and progress items and the measurements of related constructs as measured at baseline and follow-up can be found in Table 2. The internal consistency of the QoL items was $\alpha = .74$ (CKD sample) and $\alpha = .60$ (dialysis sample) at baseline. The progress items showed an internal consistency of $\alpha = .88$ (CKD sample) and $\alpha = .80$ (dialysis sample). In the CKD sample, the self-management items showed an internal consistency of $\alpha = .42$ (baseline items) and $\alpha = .69$ (progress items). Results of exploratory intercorrelations between the PPPQ items can be found in Supplementary File 3: Intercorrelations.

Table 2. Descriptives of the Personalized Priority and Progress Questionnaire (PPPQ) and measures of related constructs

	CKD patients (*N* = 121)				Dialysis patients (*N* = 22)			
	Baseline		Follow-up[a]		Baseline		Follow-up[b]	
	Mean (*SD*)	α	Mean (*SD*)	α	Mean (*SD*)	α	Mean (*SD*)	α
PPPQ QoL items[c]	2.15 (0.63)	.74	0.42 (0.91)	.88	1.94 (0.43)	.60	0.27 (0.82)	.80
PPPQ self-management items[c]	3.56 (0.58)	.42	0.28 (0.74)	.69	-	-	-	-
Fatigue (SFQ)	18.98 (5.16)	.85	17.10 (5.94)	.89	20.59 (5.47)	.87	19.54 (5.75)	.86
Sleeping problems (Sleep Problem Index II, MOS Sleep scale)	40.63 (15.89)	.81	36.16 (15.90)	.81	-	-	-	-
Energy (Energy scale, RAND SF-36)	42.29 (6.41)	.63	44.31 (7.70)	.76	44.77 (8.92)	.82	41.91 (7.19)	.67
Pain (subscale RAND SF-36)	44.26 (9.60)	.73	46.33 (9.82)	.74	47.64 (11.17)	.76	47.23 (10.16)	.66
Itch (ISDL)	-	-	-	-	7.05 (2.89)	.88	6.87 (2.44)	.80
Anxiety (GAD-7)	5.49 (3.78)	.81	3.95 (3.16)	.81	2.36 (1.92)	.68	2.55 (2.44)	.72
Worrying (PSWQ)	44.79 (10.94)	.91	42.01 (11.33)	.91	-	-	-	-
Depression (PHQ-9)	7.91 (3.33)	.54	5.76 (3.78)	.74	5.73 (3.67)	.77	7.14 (4.39)	.79
Social functioning (subscale RAND SF-36)	39.07 (9.67)	.68	42.24 (10.50)	.79	39.68 (9.78)	.56	35.68 (10.47)	.78
Perceived emotional support (ISR)	14.47 (3.52)	.82	14.89 (3.47)	.82	15.68 (3.71)	.81	15.82 (3.58)	.88
Actual emotional support (ISR)	7.25 (2.00)	.77	7.22 (1.84)	.72	6.36 (2.24)	.81	6.05 (2.01)	.80
Mutual visiting (ISR)	5.35 (1.42)	.74	5.35 (1.26)	.64	5.18 (1.53)	.84	4.81 (1.62)	.53
Role limitations due to physical problems (subscale RAND SF-36)	36.18 (11.44)	.82	40.77 (11.80)	.81	30.73 (9.40)	.88	33.05 (10.40)	.84
Self-management (PiH)	80.04 (9.63)	.78	82.74 (9.27)	.81	-	-	-	-
Medication adherence (SMAQ)	5.16 (1.05)	n/a	5.25 (0.95)	n/a	-	-	-	-
Dietary adherence	0.00 (0.93)	n/a	0.35 (0.76)	n/a	-	-	-	-
Physical activity, hrs. per week (SQUASH)	17.10 (16.04)	n/a	15.54 (15.52)	n/a	-	-	-	-
BMI	27.38 (5.33)	n/a	27.16 (5.35)	n/a	-	-	-	-
Smoking, %	9.1	n/a	8.3	n/a	-	-	-	-
Amount of tobacco per day, units	0.80 (3.31)	n/a	0.50 (2.75)	n/a	-	-	-	-

Notes: Mean and standard deviations shown as mean (*SD*); internal consistency: Cronbach's α; Follow-up[a]: 3-months follow-up; Follow-up[b]: 6-months follow-up; PPPQ QoL/self-management items[c]: average sum scores, the items differ per assessment point, i.e. the baseline measurement assessed the baseline items and the follow-up measurement assessed the progress items. Abbreviations: CKD, chronic kidney disease; SD, standard deviation; QoL, quality of life; SFQ, Shortened Fatigue Questionnaire (SFQ); MOS Sleep Scale, Medical Outcomes Study Sleep Scale; RAND SF-36, RAND Short Form-36 Health Status Inventory; ISDL, Impact of Chronic Skin Disease on Daily Life; GAD-7, Generalized Anxiety Disorder 7-item Scale; PSWQ, Penn State Worry Questionnaire; PHQ-9, Patient Health Questionnaire depression scale; ISR, Inventory for Social Reliance; PiH, Partners in Health Scale; SMAQ, Simplified Medication Adherence Questionnaire; SQUASH, Short Questionnaire to Assess Health-enhancing physical activity; BMI, body mass index.

Item Characteristics PPPQ and Floor or Ceiling Effects

QoL items. Item characteristics of the PPPQ QoL items as measured in the CKD and dialysis sample are shown in Table 3. Regarding the baseline items, mean item scores ranged from 1.61 (itch) to 3.15 (fatigue) in the CKD sample. All items covered the full range from 1 to 5, except for the item on depression, where none of the patients selected the option "very much". Floor effects were found for the items on pain, itch, anxiety, depression, social environment, and daily activities. No ceiling effects were detected. In the dialysis sample, the mean of the baseline items ranged from 1.55 (anxiety and depression) to 2.86 (fatigue). The item on fatigue was the only one covering the full range from 1 to 5. The items on itch, social environment, daily activities, and dependency ranged from 1 to 4; the items on pain and depression ranged from 1 to 3; and the item on anxiety ranged from 1 to 2. Floor effects were found for all items except for the item on fatigue. No ceiling effects were detected.

Regarding the progress items, mean item scores ranged from 0.21 (fatigue) to 0.62 (depression) in the CKD sample. All items covered the full range from -3 to 3, except for the itch item that ranged from -2 to 3, indicating that none of the patients selected the option "much worse". No floor or ceiling effects were detected. In the dialysis sample, the mean of the progress items ranged from -0.45 (fatigue) to 0.59 (anxiety and depression). The item on dependency was the only one covering the full scale from -3 to 3. The fatigue item ranged from -3 to 2, indicating that none of the patients selected the option "much better"; the items on pain, anxiety, depression, and the social environment ranged from -2 to 3; and the item on itch ranged from -1 to 3. No floor effects were found. Ceiling effects were detected for anxiety and depression.

Self-management items. Item characteristics of the PPPQ self-management items as measured in the CKD sample are shown in Table 3. Regarding the baseline items, mean item scores ranged from 2.64 (weight maintenance) to 4.52 (non-smoking). All items covered the full range from 1 to 5, except for the medication adherence item that ranged from 2 to 5, indicating that none of the patients selected the option 'not at all'. A floor effect was found for the item on weight maintenance. Ceiling effects were found for the items on medication adherence and non-smoking.

Concerning the progress items, mean scores ranged from 0.17 (weight maintenance) to 0.45 (non-smoking). The healthy diet and non-smoking item covered the full range from -3 to 3. The items on medication adherence, physical activity, and weight maintenance ranged from -2 to 3, indicating that none of the patients selected the option "much worse". No floor or ceiling effects were detected.

Table 3. Characteristics of the Personalized Priority and Progress Questionnaire (PPPQ) items

	Baseline								Follow-up							
	CKD patients (*N* = 121)				Dialysis patients (*N* = 22)				CKD patients (*N* = 121)				Dialysis patients (*N* = 22)			
Item	Mean (*SD*)	Floor (%)	Ceiling (%)	Range	Mean (*SD*)	Floor (%)	Ceiling (%)	Range	Mean (*SD*)	Floor (%)	Ceiling (%)	Range	Mean (*SD*)	Floor (%)	Ceiling (%)	Range
QoL																
Fatigue	3.15 (1.12)	5.0	13.2	1 – 5	2.86 (1.04)	4.5	9.1	1 – 5	0.21 (1.14)	0.8	2.5	-3 – 3	-0.45 (1.18)	4.5	0	-3 – 2
Pain	2.08 (1.05)	36.4	0.8	1 – 5	1.82 (0.85)	45.5	0	1 – 3	0.32 (1.21)	1.7	8.3	-3 – 3	0.27 (1.07)	0	4.5	-2 – 3
Itch	1.61 (0.93)	62.0	0.8	1 – 5	2.05 (0.72)	18.2	0	1 – 4	0.56 (1.25)	0	13.2	-2 – 3	0.45 (1.10)	0	4.5	-1 – 3
Anxiety	2.02 (0.91)	30.6	0.8	1 – 5	1.55 (0.51)	45.5	0	1 – 2	0.57 (1.25)	0.8	8.3	-3 – 3	0.59 (1.44)	0	18.2	-2 – 3
Depression	1.79 (0.87)	43.8	0	1 – 4	1.55 (0.60)	50.0	0	1 – 3	0.62 (1.29)	0.8	9.9	-3 – 3	0.59 (1.47)	0	18.2	-2 – 3
Social environment	1.90 (0.96)	39.7	3.3	1 – 5	1.59 (0.96)	63.6	0	1 – 4	0.33 (1.15)	0.8	5.8	-3 – 3	0.41 (1.30)	0	13.6	-2 – 3
Daily activities	2.50 (1.14)	19.8	5.8	1 – 5	2.27 (0.99)	18.2	0	1 – 4	0.32 (1.14)	1.7	5.0	-3 – 3	0.36 (1.09)	0	4.5	-1 – 3
Dependency	-	-	-	-	1.86 (0.89)	40.9	0	1 – 4	-	-	-	-	-0.09 (1.34)	4.5	4.5	-3 – 3
Self-management																
Medication adherence	4.45 (0.77)	0	58.7	2 – 5	-	-	-	-	0.23 (0.78)	0	4.1	-2 – 3	-	-	-	-
Healthy diet	3.39 (0.90)	1.7	8.3	1 – 5	-	-	-	-	0.29 (1.04)	0.8	3.3	-3 – 3	-	-	-	-
Physical activity	2.82 (1.04)	9.9	4.1	1 – 5	-	-	-	-	0.29 (1.21)	0	5.8	-2 – 3	-	-	-	-
Weight maintenance	2.64 (1.23)	20.7	7.4	1 – 5	-	-	-	-	0.17 (1.16)	0	4.1	-2 – 3	-	-	-	-
Non-smoking	4.52 (1.24)	9.9	85.1	1 – 5	-	-	-	-	0.45 (1.29)	2.5	14.9	-3 – 3	-	-	-	-

Notes: Follow-up measures for the CKD and dialysis population took place at, respectively, 3- and 6-months follow-up. Abbreviations: CKD, chronic kidney disease; SD, standard deviation; QoL, quality of life.

Construct Validity PPPQ

QoL items. The results regarding the construct validity of the baseline QoL items of the PPPQ can be found in Table 4. In the CKD sample, all baseline items correlated at least moderately with validated questionnaires measuring related constructs, with correlations varying from $r = .38$ to $r = .68$, except for the social environment item that did not show a meaningful correlation with perceived and actual emotional support and mutual visiting (ISR; r-values $\leq$ -.10). In the dialysis sample, insignificant or small correlations were found between the social environment item and actual emotional support and mutual visiting (ISR); between the daily activities item and role limitations due to physical problems (RAND SF-36); and between the dependency item and perceived and emotional support and mutual visiting (ISR; r-values $\leq$ -.22). All other baseline items correlated at least moderately with their related constructs, with correlations varying from $r = -.31$ to $r = .70$.

The results regarding the construct validity of the QoL progress items of the PPPQ can be found in Table 5. In the CKD sample, insignificant or small correlations were found between the items pain, anxiety, social environment, and daily activities and change in their related construct as measured by validated questionnaires(r-values $\leq .21$). All other progress items showed at least moderate correlations with questionnaires measuring related constructs, with correlations varying from $r = .30$ to $r = .36$. In the dialysis sample, insignificant or small correlations were found between the PPPQ progress item on pain and change in pain (RAND SF-36); between the anxiety item and change in anxiety (GAD-7); between the depression item and change in depression (PHQ-9); between the social environment item and change in social functioning (RAND SF-36), actual emotional support (ISR), and mutual visiting (ISR); between the daily activities item and change in role limitations due to physical problems (RAND SF-36); and between the dependency item and change in perceived emotional support (ISR), with r-values $\leq .27$. All other PPPQ progress items showed moderate correlations with their related constructs as measured by validated questionnaires, with correlations varying from $r = .30$ to $r = -.43$.

Self-management items. The results regarding the construct validity of the baseline self-management items of the PPPQ can be found in Table 6. In the CKD sample, all baseline items showed at least moderate correlations with questionnaires measuring related constructs, with correlations varying from $r = .43$ to $r = -.66$, except for the physical activity item that only showed a small correlation with hours of physical activity per week ($r = .23$). Additionally, small correlations between the PPPQ self-management items and self-management were found (r-values $\leq .27$).

Table 4. Construct validity of baseline quality of life items of the Personalized Priority and Progress Questionnaire (PPPQ) and related constructs (Pearson correlations)

		Fatigue	Pain	Itch	Anxiety	Depression	Social environment	Daily activities	Dependency
Fatigue (SFQ)	CKD:	.47**	-	-	-	-	-	-	-
	Dialysis:	.41							
Sleeping problems (Sleep Problem Index II, MOS Sleep scale)	CKD:	.42**	-	-	-	-	-	-	-
	Dialysis:	-							
Energy (subscale, RAND SF-36)	CKD:	-.42**	-	-	-	-	-	-	-
	Dialysis:	-.43*							
Pain (subscale RAND SF-36)	CKD:	-	-.68**	-	-	-	-	-	-
	Dialysis:		-.70*						
Itch (ISDL)	CKD:	-	-	-	-	-	-	-	-
	Dialysis:			.68**					
Anxiety (GAD-7)	CKD:	-	-	-	.67**	-	-	-	-
	Dialysis:				.32				
Worrying (PSWQ)	CKD:	-	-	-	.55**	-	-	-	-
	Dialysis:				-				
Depression (PHQ-9)	CKD:	-	-	-	-	.46**	-	-	-
	Dialysis:					.70**			
Social functioning (subscale RAND SF-36)	CKD:	-	-	-	-	-	-.38**	-	-
	Dialysis:						-.44**		-.35
Perceived emotional support (ISR)	CKD:	-	-	-	-	-	-.09	-	-
	Dialysis:						-.31		.13
Actual emotional support (ISR)	CKD:	-	-	-	-	-	-.02	-	-
	Dialysis:						-.22		.002
Mutual visiting (ISR)	CKD:	-	-	-	-	-	-.10	-	-
	Dialysis:						-.21		-.16
Role limitations due to physical problems (subscale RAND SF-36)	CKD:	-	-	-	-	-	-	-.42**	-
	Dialysis:							-.003	

*$p<.05$; **$p<.01$; CKD patients ($N = 121$); Dialysis patients ($N = 22$). Abbreviations: CKD, chronic kidney disease; SFQ, Shortened Fatigue Questionnaire; MOS Sleep Scale, Medical Outcomes Study Sleep Scale; RAND SF-36, RAND Short Form-36 Health Status Inventory; ISDL, Impact of Chronic Skin Disease on Daily Life; GAD-7, Generalized Anxiety Disorder 7-item Scale; PSWQ, Penn State Worry Questionnaire; PHQ-9, Patient Health Questionnaire depression scale; ISR, Inventory for Social Reliance.

Table 5. Construct validity of quality of life items of the Personalized Priority and Progress Questionnaire (PPPQ) and change scores (Pearson correlations)

		Fatigue	Pain	Itch	Anxiety	Depression	Social environment	Daily activities	Dependency
Fatigue (SFQ)	CKD:	-.36**	-	-	-	-	-	-	-
	Dialysis:	-.39							
Sleeping problems (Sleep Problem Index II, MOS Sleep scale)	CKD:	-.30**	-	-	-	-	-	-	-
	Dialysis:	-							
Energy (subscale, RAND SF-36)	CKD:	.36**	-	-	-	-	-	-	-
	Dialysis:	.39							
Pain (subscale RAND SF-36)	CKD:	-	.14	-	-	-	-	-	-
	Dialysis:		.05						
Itch (IHDL)	CKD:	-	-	-	-	-	-	-	-
	Dialysis:			-.43*					
Anxiety (GAD-7)	CKD:	-	-	-	-.21*	-	-	-	-
	Dialysis:				-.15				
Worrying (PSWQ)	CKD:	-	-	-	-.11	-	-	-	-
	Dialysis:				-				
Depression (PHQ-9)	CKD:	-	-	-	-	-.35**	-	-	-
	Dialysis:					-.04			
Social functioning (subscale RAND SF-36)	CKD:	-	-	-	-	-	.14	-	-
	Dialysis:						.13		.30
Perceived emotional support (ISR)	CKD:	-	-	-	-	-	.03	-	-
	Dialysis:						-.41		.27
Actual emotional support (ISR)	CKD:	-	-	-	-	-	-.03	-	-
	Dialysis:						-.20		-.32
Mutual visiting (ISR)	CKD:	-	-	-	-	-	.004	-	-
	Dialysis:						.20		-.30
Role limitations due to physical problems (subscale RAND SF-36)	CKD:	-	-	-	-	-	-	.21*	-
	Dialysis:							-.06	

**p*<.05; ***p*<.01; CKD patients (*N* = 121); Dialysis patients (*N* = 22). Abbreviations: CKD, chronic kidney disease; SFQ, Shortened Fatigue Questionnaire; MOS Sleep Scale, Medical Outcomes Study Sleep Scale; RAND SF-36, RAND Short Form-36 Health Status Inventory; ISDL, Impact of Chronic Skin Disease on Daily Life; GAD-7, Generalized Anxiety Disorder 7-item Scale; PSWQ, Penn State Worry Questionnaire; PHQ-9, Patient Health Questionnaire depression scale; ISR, Inventory for Social Reliance.

Table 6. Construct validity of the baseline self-management items of the Personalized Priority and Progress Questionnaire (PPPQ) (Pearson correlation) in a CKD sample (Pearson correlation)

	Medication adherence	Healthy diet	Physical activity	Weight maintenance	Non-smoking
Self-management (PiH)	.19*	.27**	.23*	.22*	.25**
Medication adherence (SMAQ)	.44**	-	-	-	-
Dietary adherence	-	.61**	-	-	-
Physical activity, hrs per week (SQUASH)	-	-	.23*	-	-
Physical activity, days per week minimally 30 mins			.43**		
BMI	-	-	-	-.63**	-
Amount of tobacco per day					-.66**

**p*<.05; ***p*<.01, *N* = 121, CKD patients. Abbreviations: CKD, chronic kidney disease; PiH, Partners in Health Scale; SMAQ, Simplified Medication Adherence Questionnaire; SQUASH, Short Questionnaire to Assess Health-enhancing physical activity; BMI, body mass index.

The results regarding the construct validity of the self-management progress items of the PPPQ can be found in Table 7. The progress in physical activity ($r = .40$) and weight maintenance items ($r = .31$) showed moderate correlations with change in self-management. The other progress items showed small correlations with their related constructs and change in self-management (r-values $\leq .29$).

Table 7. Construct validity of self-management progress items of the Personalized Priority and Progress Questionnaire (PPPQ) and change scores of measurements assessing similar constructs (Pearson correlations) in a CKD sample

	Medication adherence	Healthy diet	Physical activity	Weight maintenance	Non-smoking
Self-management (PiH)	.09	.26**	.40**	.31**	-.02
Medication adherence (SMAQ)	.15	-	-	-	-
Dietary adherence	-	.29**	-	-	-
Physical activity, hrs per week (SQUASH)	-	-	-.12	-	-
Physical activity, days per week minimally 30 mins			.18		
BMI	-	-	-	-.18	-
Amount of tobacco per day					-.25**

***p*<.01, *N* = 121, CKD patients. Change scores of the measurements assessing similar constructs were calculated by subtracting the mean score at baseline from the mean score at follow-up. Abbreviations: CKD, chronic kidney disease; PiH, Partners in Health Scale; SMAQ, Simplified Medication Adherence Questionnaire; SQUASH, Short Questionnaire to Assess Health-enhancing physical activity; BMI, body mass index.

Discussion

The aim of this study was to develop a brief personalized instrument that (1) defines patients' priorities for improvement, (2) measures change in functioning on QoL and self-management outcomes that are prioritized by the individual patient, and (3) is applicable in both clinical practice and clinical trials. The resulting questionnaire, the PPPQ, includes a baseline and a follow-up measurement. The baseline measurement assesses personal priorities for improvement, both in QoL and self-management. The follow-up measurement assesses the amount of self-perceived progress in QoL or self-management compared to the baseline measurement. Based on these results, a progress score can be calculated indicating the amount of progress on the area of QoL or self-management that is prioritized by the individual patient. The PPPQ was completed in two samples–a sample of patients with CKD and a sample of patients with kidney failure treated with dialysis–and subsequently evaluated on its psychometric properties. The PPPQ showed to be a valid and feasible instrument that is easy and quick to complete. This indicates that the PPPQ could be a valuable tool to easily identify, prioritize, and monitor individual QoL and self-management problems over time, both in clinical practice and clinical trials.

The PPPQ showed to have good construct validity. With regard to the baseline items, moderate to large correlations were found between all items and validated questionnaires measuring related constructs. Only the scales measuring emotional support and mutual visiting did not show significant correlations with the PPPQ items on social functioning and dependency. Possibly, this social support questionnaire (ISR) was not a good choice to determine the construct validity of these items. Social support is, after all, a different construct that is not necessarily related to social functioning and dependency.[46,47]

The correlations between the progress items and questionnaires measuring related constructs were somewhat smaller than the correlations of the baseline items. Possibly, this is the result of different ways of determining progress (i.e., change). In the PPPQ progress items, patients make their own comparison of their current versus their previous functioning, while for the measurements of related constructs we calculated change by subtracting the baseline score from the follow-up score. Possibly, patients' self-perceived comparison of their current and previous functioning is influenced by 'response shift'. This phenomenon involves changing internal standards, values and the conceptualization of QoL as part of adaptation to disease.[48] In both samples, no associations were found between the progress items on pain and daily activities and their related constructs. Additionally, in the CKD sample, no correlations were found between the social environment item and scales on social functioning or social support. In the dialysis sample, no correlations were found between the progress items on anxiety and depression and the anxiety and depression scales. The latter could have been the result of the fact that almost none of the dialysis patients reported symptoms of anxiety or depression, which diminishes potential changes in these areas that could be picked up by the progress part of the PPPQ (i.e., floor effect).[43] Due to differences in the eligibility screening, all CKD patients reported at least mild symptoms of anxiety or depression. In this sample, we did find significant associations between the progress anxiety and depression items and their related constructs. Based on these results, the construct validity of the baseline measurement was positively evaluated. Regarding the progress items, the correlations were slightly too small.

Since the PPPQ includes items on several domains of QoL and self-management—instead of measuring one single concept—we did not necessarily expect high Cronbach's alpha's of the QoL and self-management items.[43,44] Nevertheless, the internal consistency of the QoL items was surprisingly good. The self-management items showed lower Cronbach's alphas, possibly because they are less related in terms of content. Weight maintenance, for example, is not necessarily related to medication adherence.

Several floor and ceiling effects were detected for the baseline items. Particularly in the dialysis sample, several items did not cover the full range, which probably results from the small sample size. Beyond that, floor and ceiling effects are dependent upon the population.[49] The fact that, for example, 85% answered "very well" on the question "To what extent do you succeed in stopping with smoking?" demonstrates that not all areas are experienced as problematic in this sample. Normally, floor and ceiling effects would decrease the responsiveness of a questionnaire: they make it difficult to detect an intervention effect in participants who score on the lower levels of the scale before the start of an intervention.[49] Since the PPPQ is a personalized scale that specifically addresses changes in the areas patients do find important, this will not be a problem. Besides, the progress score is based on the scores of the progress items and these items rarely showed any floor or ceiling effects.

Strengths and Limitations

It is increasingly recognized that a one-size-fits all approach to health care falls short to the complexity and diversity of individual patients. Shifting to a personalized approach (i.e., PCC) helps to better understand individual patient needs.[7-9,50] For PCC to succeed, adequate tools that promote personalization are required.[4] We believe the specific functionalities of the PPPQ, of isolating personally meaningful areas and using these scores as an outcome measure (i.e., progress score), could make this instrument a valuable tool in PCC. While there are instruments that assess patient priorities, it is precisely the effect on QoL and self-management outcomes that are valued by patients themselves that is lacking in current instruments.[14] An additional strength is the high flexibility in which the PPPQ items can be adapted to match diverse populations. It is, for example, possible to only administer the QoL items—as illustrated by the dialysis sample in this study—or only the self-management items. The possibility of adding or omitting items is illustrated by the dependency item that was added only in the dialysis sample since patients have indicated dependency on others to be a major problem in this specific population.[2] Another strength is the ease and speed in which this questionnaire can be completed by patients without needing assistance, as shown by the cognitive interviews. This low burden is a great advantage compared to existing personalized instruments that are usually time-consuming and require trained interviewers or therapists.[16]

A limitation of this study is the relatively small sample size, especially regarding the dialysis sample. Therefore, when interpreting the results in this sample, we decided to focus more on the magnitude than on the significance of the associations. For a more robust examination of the validity of the PPPQ, larger samples of patients with diverse medical conditions would be advised. Another limitation is the lack of a gold standard that measures personalized health outcomes that are prioritized by patients.[20] Consequently, instead of using a similar personalized instrument to compare the PPPQ to, we had to select different questionnaires for each item to evaluate the construct validity.

Implications

The PPPQ could be of use in both clinical and research settings. See Box 1. for an overview of the applicability of the PPPQ. In clinical settings, the PPPQ could be used as a brief tool to evaluate patients' priorities and to keep track of patients' functioning. In this sense, the PPPQ could be used to evaluate patients' functioning in general–similar to QOL questionnaires–but also to specifically zoom in on the areas of QoL and self-management that patients themselves find important. The PPPQ could be completed on a routine basis and the results can be discussed during consultations between clinicians and patients. In this way, the PPPQ results can form the starting point of a discussion on patient priorities and shared decision-making to decide on a personalized treatment plan. Patients usually find it difficult to discuss their priorities, especially if this is not explicitly asked by clinicians,[51,52] and clinicians may find it difficult to know what to ask for to each patient and lack the time to discuss all potential QoL areas or self-management behaviors. The PPPQ could lower this threshold by making it easier for patients to discuss their particular difficulties and needs. Thereby, patient-clinician communication can be facilitated.[53,54]

Box 1. Implications of the Personalized Priority and Progress Questionnaire (PPPQ) in clinical and research settings

Clinical settings	Research settings
- Identify patient priorities	- Evaluate personalized interventions by using the progress score
- Use as conversation starter for a talk on patient priorities and patient needs	- Add or remove items to match the specific needs of the study population
- Use to support shared decision-making and tailor treatment based on results	- Use both the QoL and self-management items or only the QoL or self-management items to match the specific research questions
- Monitor patients' QoL and adherence to self-management behaviors	- All implications listed under clinical settings are applicable in intervention studies as well

Abbreviations: QoL, quality of life.

In research settings, the PPPQ is an ideal tool to evaluate the effectiveness of personalized interventions. In personalized interventions, treatment goals vary per participant. Some participants may work on improving their coping skills with regard to fatigue, while others work on improving their social relationships. When evaluating personalized treatments using general health outcomes, the outcome will be clouded by scores on areas that may be unimportant to patients and, therefore, the personalized character will be lost.[3,4,11,12] Additionally, multiple questionnaires would be necessary to evaluate the different treatment goals (e.g., questionnaires on fatigue and social relationships), with the consequence of decreased power, since only part of the participants worked on fatigue or social relationships.[4] Ideally, researchers would have one overall score that justifies the personalized character of the intervention. We believe the progress score of the PPPQ could be that score. By using the progress score, scores on personally meaningful areas will be isolated and this will result in one single score that researchers can use in their analyses. When determining this progress score, researchers can use the priorities as selected at baseline or the areas patients indicated to have actively worked on at follow-up. The latter option can be useful if there is indication of switched treatment goals over the course of the study. Additionally, this option can be used as a check question to find out whether patients in the control condition spontaneously worked on their health. For trials with waiting list or care as usual control conditions, we advise to use the priorities as selected at baseline. This strategy is in line with existing personalized measurements such as the MACTAR and the GAS[15,16] that advice patients to set goals prior to randomization which enables researchers to apply the same calculations to both the control and the intervention condition.[15,16,55]

Conclusions

To identify and monitor patient priorities over time, the PPPQ was developed. The PPPQ can be used in both clinical and research settings and proved to be a valid questionnaire that patients can easily complete without needing assistance. The PPPQ is a personalized scale that specifically addresses changes in the areas prioritized by patients themselves. Using the results of the PPPQ, a progress score can be calculated. This score is based on the isolated areas that are personally meaningful to the individual patient and thus not blurred by areas that may be unimportant to them. This great benefit makes the PPPQ a suitable instrument to evaluate personalized interventions in which patients work on different treatment goals. In clinical settings, the PPPQ could be used as a quick and easy tool to evaluate patients' priorities and to monitor their functioning. With these characteristics, the PPPQ could aid in delivering high-quality care that is tailored to the unique needs and priorities of every individual patient.

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Supplementary File 1

Personalized Priority and Progress Questionnaire (PPPQ) - English

Quality of life

1. **Baseline: Score for current functioning – general**

The following questions are about limitations that people may experience **due to their kidney disease**. Think about the past 2 weeks. Please indicate to what extent you have experienced **limitations in the following areas**.

GENERAL

	To what extent have you experienced limitations in the area of…	*Not at all*	*Slightly*	*Moderately*	*Considerably*	*Extremely*
a.	...fatigue or sleep problems?	1	2	3	4	5
b.	...pain?	1	2	3	4	5
c.	...itching?	1	2	3	4	5
d.	...tension, anxiety, or worrying?	1	2	3	44	55
e.	...low mood or feeling down?	1	2	3	4	5
f.	...your social environment (e.g., communication about your needs or wishes, asking for or receiving support)?	1	2	3	4	5
g.	...daily activities (e.g., work, hobbies, or social activities)?	1	2	3	4	5
h.	...dependence on others?	1	2	3	4	5

2. **Baseline: Setting priorities - general**

Choose the top two areas related to your perceived limitations that you would **most like** to improve, and that you plan to work on actively over the coming period. Rank these in order of relevance, where priority 1 is the most relevant, and priority 2 the next most relevant.

Limitations in the area of...

1. fatigue or sleep problems
2. pain
3. itching
4. tension, anxiety, or worrying
5. low mood or feeling down
6. social environment
7. daily activities
8. dependence
9. other (please state):

Priority 1: ____________________

Priority 2: ____________________

3. Follow-up measurement: Score for self-perceived progress – general

The following questions are about limitations that people may experience **due to their kidney disease**. For the statements below, please indicate whether, compared to the last time you completed these questionnaires, you now experience more or fewer **limitations**, or whether your situation has remained the same. It is not a problem if you do not remember exactly what you entered the last time: a rough estimate will do.

GENERAL Compared to the last time I completed this questionnaire, I now experience more/fewer limitations in the area of...	*Many more*	*More*	*Slightly more*	*Remained the same*	*Slightly fewer*	*Fewer*	*Much fewer*
a. fatigue or sleep problems.	-3	-2	-1	0	1	2	3
b. pain.	-3	-2	-1	0	1	2	3
c. itching.	-3	-2	-1	0	1	2	3
d. tension, anxiety, or worrying.	-3	-2	-1	0	1	2	3
e. low mood or feeling down.	-3	-2	-1	0	1	2	3
f. social environment (e.g., communication about your needs or wishes, asking for or receiving support).	-3	-2	-1	0	1	2	3
g. daily activities (e.g., work, hobbies, or social activities).	-3	-2	-1	0	1	2	3
h. dependence on others.	-3	-2	-1	0	1	2	3

4. Follow-up measurement: Areas actively worked on – general

Have you tried to improve anything in any of these areas over the recent period?
If so, please choose up to two areas below that you have actively tried to improve recently. Rank these two areas, where number 1 is the area you have worked on most, and number 2 the area you have worked on slightly less.
If you have not actively worked on any of these areas, choose "not applicable".

Limitations relating to..

1. fatigue or sleep problems
2. pain
3. itching
4. tension, anxiety, or worrying
5. low mood or feeling down
6. social environment
7. daily activities
8. dependence
9. other (please state):
10. not applicable

Area 1: I worked on limitations in the area of ____________________
Area 2: I worked on limitations in the area of ____________________

Self-management

1. **Baseline: Score for current functioning - self-management**

The following questions are about self-management. Think about the past 2 weeks. Please indicate to what extent you have successfully managed to maintain a healthy lifestyle in the following areas.

SELF-MANAGEMENT To what extent have you managed...	*Not at all*	*Slightly*	*Reasonably well*	*Well*	*Extremely well*
a. ...to always take your medication as prescribed?	1	2	3	4	5
b. ...to eat healthily?	1	2	3	4	5
c. ...to engage in enough physical activity?	1	2	3	4	5
d. ...to maintain a healthy body weight?	1	2	3	4	5
e. ...to not smoke?	1	2	3	4	5

2. **Baseline: Setting priorities - self-management**

Choose the top two areas related to your current self-management that you would **most like** to improve, and that you plan to work on actively over the coming period? Rank these in order of relevance, where priority 1 is the most relevant, and priority 2 the next most relevant.

Self-management in the area of...

1. taking medication
2. healthy eating
3. sufficient physical activity
4. healthy body weight
5. not smoking
6. other (please state):

Priority 1: ____________________
Priority 2: ____________________

3. <u>Follow-up measurement: Score for self-perceived progress - self-management</u>

For the following statements about your current self-management, please indicate whether you have managed more or less successfully than the last time to carry out or maintain the behavior in question, or whether your situation has remained the same. It is not a problem if you do not remember exactly what you entered the last time: a rough estimate will do.

SELF-MANAGEMENT Compared to the last time I completed this questionnaire, I have managed less well / better ...	*Much less well*	*Less well*	*Slightly less well*	*Equally well*	*Slightly better*	*Better*	*Much better*
1. to always take my medication as prescribed.	-3	-2	-1	0	1	2	3
2. to eat healthily.	-3	-2	-1	0	1	2	3
3. to engage in enough physical activity.	-3	-2	-1	0	1	2	3
4. to maintain a healthy body weight.	-3	-2	-1	0	1	2	3
5. to not smoke.	-3	-2	-1	0	1	2	3

4. <u>Posttest measurement: Areas actively worked on - self-management</u>

Have you tried to improve anything in any of these areas over the recent period?
If so, please choose up to two areas below that you have actively tried to improve recently. Rank these two areas, where number 1 is the area you have worked on most, and number 2 the area you have worked on slightly less.

If you have not actively worked on any of these areas, choose "not applicable".

Self-management in the area of...

1. taking medication
2. healthy eating
3. sufficient physical activity
4. healthy body weight
5. not smoking
6. other (please state):
7. not applicable

Area 1: I worked on my self-management in the area of ____________________
Area 2: I worked on my self-management in the area of ____________________

Supplementary File 2

Personalized Priority and Progress Questionnaire (PPPQ) - Dutch

Kwaliteit van leven

1. **<u>Baseline: Scoren huidig functioneren – algemeen</u>**

Onderstaande vragen gaan over beperkingen die mensen **door hun nieraandoening** kunnen ervaren. Denk aan de afgelopen 2 weken. Geef aan in hoeverre u **beperkingen ervaart op de volgende gebieden**.

ALGEMEEN

	In welke mate ervaart u beperkingen op het gebied van…	*Helemaal niet*	*Enigszins*	*Nogal*	*Veel*	*Heel erg veel*
a.	…vermoeidheid of slaapproblemen?	1	2	3	4	5
b.	…pijn?	1	2	3	4	5
c.	…jeuk?	1	2	3	4	5
d.	…spanning, angst of bezorgdheid?	1 1	2 2	3	4	5
e.	…een sombere of neerslachtige stemming?	1	2	3	4	5
f.	…uw sociale omgeving (bijv. communicatie over uw behoeften of wensen, het vragen of ontvangen van steun)?	1	2	3	4	5
g.	…dagelijkse activiteiten (bijv. bij werk, hobby's of sociale activiteiten)?	1	2	3	4	5
h.	…afhankelijkheid van anderen?	1	2	3	4	5

2. **<u>Baseline: Prioriteiten stellen – algemeen</u>**

Maak een top 2 van gebieden die te maken hebben met uw ervaren beperkingen, die u het **liefst** zou willen verbeteren en waarop u zich actief wilt inzetten de komende tijd. Hierbij vindt u prioriteit 1 het meest relevant en prioriteit 2 iets minder relevant van de twee gebieden die u kiest.

Beperkingen op het gebied van…

1. vermoeidheid of slaapproblemen
2. pijn
3. jeuk
4. spanning, angst of bezorgdheid
5. sombere of neerslachtige stemming
6. sociale omgeving
7. dagelijkse activiteiten
8. afhankelijkheid
9. anders, namelijk …

Prioriteit 1: ____________________

Prioriteit 2: ____________________

3. **Nameting: Scoren zelfwaargenomen verandering – algemeen**

Onderstaande vragen gaan over beperkingen die mensen **door hun nieraandoening** kunnen ervaren. Geef voor onderstaande stellingen aan of u ten opzichte van de vorige keer dat u deze vragenlijsten invulde meer of minder **beperkingen** ervaart, of dat uw situatie gelijk gebleven is. Het is niet erg als u niet meer precies weet wat u toen heeft ingevuld, een globale inschatting is voldoende.

ALGEMEEN

In vergelijking met de vorige keer dat ik deze vragenlijst invulde ervaar ik meer/minder beperkingen op het gebied van…	*Veel meer*	*Meer*	*Een beetje meer*	*Gelijk gebleven*	*Een beetje minder*	*Minder*	*Veel minder*
a. vermoeidheid of slaapproblemen.	-3	-2	-1	0	1	2	3
b. pijn.	-3	-2	-1	0	1	2	3
c. jeuk.	-3	-2	-1	0	1	2	3
d. spanning, angst of bezorgdheid.	-3	-2	-1	0	1	2	3
e. een sombere of neerslachtige stemming.	-3	-2	-1	0	1	2	3
f. mijn sociale omgeving (bijv. communicatie over mijn behoeften of wensen, het vragen of ontvangen van steun).	-3	-2	-1	0	1	2	3
g. dagelijkse activiteiten (bijv. bij werk, hobby's of sociale activiteiten).	-3	-2	-1	0	1	2	3
h. afhankelijkheid van anderen.	-3	-2	-1	0	1	2	3

4. **Nameting: Gebieden waar actief aan gewerkt is – algemeen**

Heeft u in de afgelopen periode geprobeerd om iets te verbeteren in een van deze gebieden?
Zo ja, kies hieronder maximaal twee gebieden die u de afgelopen tijd actief hebt proberen te verbeteren.
Maak een top 2, waarbij u het meest bezig bent geweest met nummer 1 en iets minder met nummer 2 van de twee gebieden die u kiest.
Als u aan geen van deze gebieden actief hebt gewerkt, kunt u de optie "niet van toepassing" invullen.
Beperkingen op het gebied van…

1. vermoeidheid of slaapproblemen
2. pijn
3. jeuk
4. spanning, angst of bezorgdheid
5. sombere of neerslachtige stemming
6. mijn sociale omgeving
7. dagelijkse activiteiten
8. afhankelijkheid
9. anders, namelijk …
10. niet van toepassing

Gebied 1: Ik heb gewerkt aan beperkingen op het gebied van ____________________
Gebied 2: Ik heb gewerkt aan beperkingen op het gebied van ____________________

Zelfmanagement

1. **Baseline: Scoren huidig functioneren – zelfmanagement**

   Onderstaande vragen gaan over zelfmanagement. Denk aan de afgelopen 2 weken. Geef aan in hoeverre het u lukt om gezond te leven op de volgende gebieden.

ZELFMANAGEMENT In welke mate lukt het u…	*Helemaal niet*	*Enigszins*	*Redelijk goed*	*Goed*	*Heel erg goed*
a. …om uw medicijnen altijd volgens voorschrift te nemen?	1	2	3	4	5
b. …om gezond te eten?	1	2	3	4	5
c. …om voldoende te bewegen?	1	2	3	4	5
d. …om een gezond lichaamsgewicht aan te houden?	1	2	3	4	5
e. …om niet te roken?	1	2	3	4	5

2. **Baseline: Prioriteiten stellen – zelfmanagement**

   Maak een top 2 van gebieden die te maken hebben met uw huidige zelfmanagement, die u het **liefst** zou willen verbeteren en waarop u zich actief wilt inzetten de komende tijd. Hierbij vindt u prioriteit 1 het meest relevant en prioriteit 2 iets minder relevant van de twee gebieden die u kiest.

   Zelfmanagement op het gebied van…

   1. medicijnen nemen
   2. gezond eten
   3. voldoende bewegen
   4. gezond lichaamsgewicht
   5. niet roken
   6. anders, namelijk …

Prioriteit 1: ____________________
Prioriteit 2: ____________________

3. Nameting: Scoren zelfwaargenomen verandering – zelfmanagement

Geef voor onderstaande stellingen over uw huidige zelfmanagement aan of het uitvoeren of volhouden ervan u ten opzichte van de vorige keer minder goed of beter lukt, of dat uw situatie gelijk gebleven is. Het is niet erg als u niet meer precies weet wat u toen heeft ingevuld, een globale inschatting is voldoende.

ZELFMANAGEMENT In vergelijking met de vorige keer dat ik deze vragenlijst invulde lukt het mij minder goed/beter om…	*Veel minder goed*	*Minder goed*	*Een beetje minder goed*	*Even goed*	*Een beetje beter*	*Beter*	*Veel beter*
6. mijn medicijnen altijd volgens voorschrift te nemen.	-3	-2	-1	0	1	2	3
7. gezond te eten.	-3	-2	-1	0	1	2	3
8. voldoende te bewegen.	-3	-2	-1	0	1	2	3
9. een gezond lichaamsgewicht aan te houden.	-3	-2	-1	0	1	2	3
10. niet te roken.	-3	-2	-1	0	1	2	3

4. Nameting: Gebieden waar actief aan gewerkt is – zelfmanagement

Heeft u in de afgelopen periode geprobeerd om iets te verbeteren in een van deze gebieden?
Zo ja, kies hieronder maximaal twee gebieden die u de afgelopen tijd actief hebt proberen te verbeteren.
Maak een top 2, waarbij u het meest bezig bent geweest met nummer 1 en iets minder met nummer 2 van de twee gebieden die u kiest.

Als u aan geen van deze gebieden actief hebt gewerkt, kunt u de optie ‘niet van toepassing’ invullen.

Zelfmanagement op het gebied van…

8. medicijnen nemen
9. gezond eten
10. voldoende bewegen
11. gezond lichaamsgewicht
12. niet roken
13. anders, namelijk …
14. niet van toepassing

Gebied 1: Ik heb gewerkt aan mijn zelfmanagement op het gebied van ____________________
Gebied 2: Ik heb gewerkt aan mijn zelfmanagement op het gebied van ____________________

Supplementary File 3

Intercorrelations

QoL items

The results of the exploratory intercorrelation analyses between the PPPQ QoL items as measured in the CKD and dialysis sample are shown in Table S1. Regarding the baseline items as measured in the CKD sample, moderate to large correlations were found between the fatigue item and the items on pain, itch, depression, and daily activities; between the pain and daily activities items; between the anxiety item and the items on depression, social environment, and daily activities; between the depression and social environment items; and between the social environment and daily activities items; with correlations varying from *r* = .32 (fatigue and depression) to *r* = .65 (anxiety and depression). Thus, these correlations indicated that experienced limitations in these QoL areas were associated with limitations in other QoL areas. Between the other items, insignificant or small correlations were found (*r*-values ≤ .27). In the dialysis sample, moderate to large correlations were found between the fatigue item and the items on anxiety, depression, social environment, and dependency; between the itch and the social environment items; and between the depression item and the items on social environment and daily activities; with correlations varying from *r* = .30 (itch and social environment) to *r* = .71 (fatigue and social environment). Between the other baseline items, insignificant to small correlations were found (*r*-values ≤ .29).

Regarding the progress items as measured in the CKD sample, moderate to large correlations were found between all of the progress items of the PPPQ, with correlations varying from *r* = .38 (fatigue and itch) to *r* = .78 (social environment and daily activities). Thus, these correlations indicated that progress in one QoL area is generally associated with progress in other QoL areas. In the dialysis sample, moderate to large correlations were found between the fatigue item and the items on pain, anxiety, depression, daily activities, and dependency; between the pain item and the items on itch and daily activities; between the itch and daily activities items; between the anxiety item and the items on depression, social environment, daily activities, and dependency; between the depression item and the items on daily activities and dependency; and between the social environment and daily activities items; with correlations varying from *r* = .30 (anxiety and social environment) to *r* = .98 (anxiety and depression). Between the other progress items, non-existent or small correlations were found (*r*-values ≤ .29).

Table S1. Intercorrelations between the Quality of Life items of the Personalized Priority and Progress Questionnaire (PPPQ)

	CKD patients (*N* = 121)							Dialysis patients (*N* = 22)							
Baseline items	1.	2.	3.	4.	5.	6.	7.	1.	2.	3.	4.	5.	6.	7.	8.
1. Fatigue	-							-							
2. Pain	.37**	-						.08	-						
3. Itch	.32**	.17	-					.009	.17	-					
4. Anxiety	.27**	.12	.15	-				.51*	.13	-.07	-				
5. Depression	.33**	.07	.10	.65**	-			.43*	.11	.27	.23	-			
6. Social environment	.22*	.23*	.26**	.57**	.37**	-		.71*	.25	.30	.09	.49*	-		
7. Daily activities	.45**	.34**	.16	.33**	.26**	.43**	-	.18	.29	.05	-.22	.38	.17	-	
8. Dependency	-	-	-	-	-	-	-	-.33	.15	.16	-.25	-.03	.10	.10	-
Progress items															
1. Fatigue	-							-							
2. Pain	.48**	-						.32	-						
3. Itch	.38**	.46**	-					.13	.61**	-					
4. Anxiety	.56**	.49**	.59**	-				.64**	.11	.18	-				
5. Depression	.43**	.50**	.60**	.79**	-			.65**	.10	.24	.98**	-			
6. Social environment	.49**	.40**	.41**	.53**	.51**	-		.19	.09	.13	.30	.27	-		
7. Daily activities	.54**	.43**	.42**	.40**	.45**	.78**	-	.32	.60**	.41	.31	.31	.36	-	
8. Dependency	-	-	-	-	-	-	-	.42	.28	.29	.45*	.44*	.10	.12	-

*$p<.05$; **$p<.01$. Abbreviations: CKD, chronic kidney disease.

Self-management items

The results of the exploratory intercorrelation analyses between the PPPQ self-management items as measured in the CKD sample are shown in Table S2. Regarding the baseline items, moderate correlations were found between the healthy diet and weight maintenance items (*r* = .45) and between the physical activity and weight maintenance items (*r* = .46). Between the other baseline items insignificant or small correlations were found (*r*-values ≤ .28). With regard to the progress items, large correlations were found between the healthy diet item and the items on physical activity (*r* = .64) and weight maintenance (*r* = .65) and between the physical activity and weight maintenance items (*r* = .61). A moderate correlation was found between the medication adherence and non-smoking items (*r* = .42) Between the other progress items insignificant or small correlations were found (*r*-values ≤ .28).

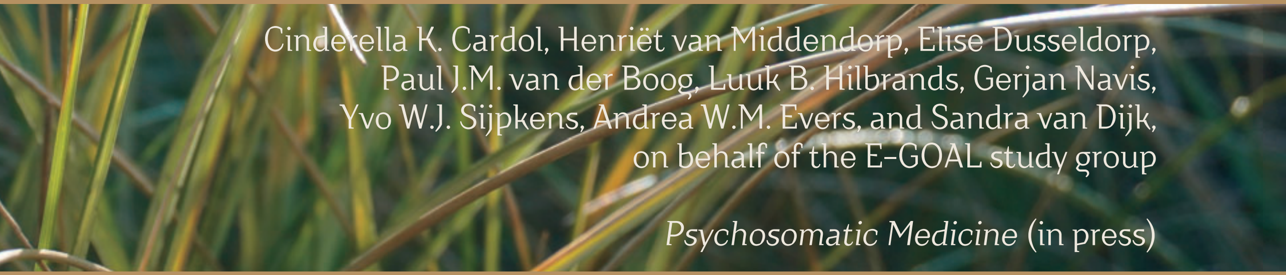
Table S2. Intercorrelations between self-management items of the Personalized Priority and Progress Questionnaire (PPPQ) in a CKD sample (*N* = 121)

Baseline items	1.	2.	3.	4.	5.
1. Medication adherence	-				
2. Healthy diet	.26**	-			
3. Physical activity	-.01	.29**	-		
4. Weight maintenance	-.12	.45**	.46**	-	
5. Non-smoking	.28**	-.08	-.09	-.03	-
Progress items					
1. Medication adherence	-				
2. Healthy diet	.28**	-			
3. Physical activity	.20*	.64**	-		
4. Weight maintenance	.21*	.65**	.61**	-	
5. Non-smoking	.42**	.09	.04	.06	-

*p<.05; **p<.01. Abbreviation: CKD, chronic kidney disease.

Chapter 6

eHealth to improve psychological functioning and self-management of people with chronic kidney disease: a randomized controlled trial



Cinderella K. Cardol, Henriët van Middendorp, Elise Dusseldorp,
Paul J.M. van der Boog, Luuk B. Hilbrands, Gerjan Navis,
Yvo W.J. Sijpkens, Andrea W.M. Evers, and Sandra van Dijk,
on behalf of the E-GOAL study group

Psychosomatic Medicine (in press)

Abstract

Background

Psychological distress is common among patients with chronic kidney disease (CKD), and can interfere with disease self-management. We assessed the effectiveness of the personalized E-GOAL eHealth care pathway with screening and cognitive-behavioral therapy including self-management support, aimed to treat psychological distress and facilitate self-management among people with CKD not on dialysis (*N*=121).

Methods

Primary outcome of the open two-arm parallel randomized controlled trial in four Dutch hospitals was psychological distress after the 3-month intervention and at 6-month follow-up. Secondary outcomes were physical and mental health-related quality of life (HRQoL), self-efficacy, chronic disease self-management, and personalized outcomes, i.e., perceived progress compared to the previous time point on functioning (e.g., mood or social functioning) and self-management (e.g., dietary or medication adherence) outcomes that were prioritized by each individual.

Results

Linear mixed-effects analyses showed no significant time-by-group interaction effects for psychological distress, HRQoL, and self-efficacy, whereas the improvement in self-management between baseline and 3-months was significantly larger in the intervention group than for controls, *b*=-0.09, 95%CI[-0.17, -0.01], with Cohen's *d* of 0.22 (small effect). ANCOVAs showed significantly more perceived progress in the intervention group at 3-months on personally prioritized areas of functioning, *b*=0.46, 95%CI[0.07, 0.85], and self-management, *b*=0.55, 95%CI[0.16, 0.95], with Cohen’s *d*s of 0.46 and 0.54 (medium effects), respectively. Effects on personalized outcomes were maintained at 6-months.

Conclusions

Compared to regular care only, the eHealth intervention did not reduce psychological distress, whereas self-management and personalized outcomes did improve significantly post-intervention. Future studies could consider personalized outcomes that reflect individually relevant areas and treatment goals, matching person-tailored treatments.

Keywords Chronic kidney disease (CKD); Randomized controlled trial; Psychological distress; Self-management; eHealth; Patient-tailored care

Introduction

Adhering to disease self-management recommendations is essential for patients with chronic kidney disease (CKD) not receiving dialysis, including kidney transplant recipients.[1] However, many do not succeed in achieving recommended behavioral goals for non-smoking, physical activity, weight maintenance, and adherence to medication prescriptions or dietary recommendations:[2,3] About 50% of individuals with CKD show suboptimal adherence.[4]

Evidence on intervention effectiveness in enhancing self-management in this population is promising but limited.[5] For instance, in two recent trials that evaluated dietary interventions, patients were able to successfully reduce their sodium excretion, but effects diminished over time.[6,7] A possible explanation for the lack of sustained effects may be that interventions only address self-management behaviors directly, with limited attention for psychological complaints that may hinder behavior change.[8] Psychological distress, often assessed as depressive or anxiety symptoms, may come along with problems in motivation, lack of energy and self-efficacy, pessimistic cognitions, and social withdrawal, which could all form barriers to self-management.[8-10] Vice versa, suboptimal self-management may induce psychological distress, for instance by diminished physical and social activity, reduced physical fitness, or negative perceptions toward oneself regarding non-adherent behaviors.[8-10] Accordingly, psychological distress has been associated with suboptimal self-management among patients with CKD.[11] These mechanisms are alarming as both factors have been related to adverse health outcomes, including disease progression, accelerated initiation of dialysis, and mortality.[3,12]

Therefore, the psychological distress symptom prevalence of 13 to 34% among patients with CKD not on dialysis is concerning for patients' psychological and physical health.[12,13] Intervening advocates multicomponent approaches, focused on bi-directional improvements in psychological functioning and self-management. Literature suggests that such combined interventions could be more effective than one-sided treatments in improving health outcomes.[9,14] To our knowledge, no literature exists regarding interventions that synergistically target both psychological distress and CKD self-management among patients not on dialysis.

Next to incorporating treatment of psychological distress in self-management interventions, the importance of patient-tailoring is also increasingly being emphasized.[15,16] Person-centered care—tailored to individual needs, wishes, and goals—has been associated with enhanced patient satisfaction, quality of life, psychological and physical outcomes, and self-management skills.[17] In the E-GOAL study, we designed a 3-month personalized and blended electronic health (eHealth) care pathway.[18] Personalization was deployed in three ways: First, a screening tool with personalized feedback was used to identify patients with psychological distress and suboptimal self-management, in order to offer treatment only to people who needed it, and to determine patients' personal priorities for intervention.[16] Second, in guided Internet-delivered cognitive-behavioral therapy (iCBT) with self-management support, patients could choose their preferred goals, eHealth modules, delivery modes, and time investment, making the intervention personally relevant, feasible, and acceptable.[19] Last, since patients focused on distinct, personally meaningful goals, they likely improved on different outcomes. Therefore, we included personalized outcome measures.[20]

The primary aim of this multicenter randomized controlled trial (RCT) was to investigate the effectiveness of the E-GOAL personalized iCBT intervention in reducing psychological distress directly after the 3-month intervention and at 6-month follow-up among patients with CKD not on dialysis compared with a care as usual control condition. We hypothesized larger improvements in the intervention group than in the control group on psychological distress, and on secondary outcomes physical and mental health-related quality of life (HRQoL), self-efficacy for disease management, chronic condition self-management (i.e., engaging in health-promoting behaviors, managing symptoms, coping with impacts on functioning, and adhering to treatment),[21] and perceived progress on personally prioritized areas of functioning (PPP-functioning) and self-management (PPP-self-management).[20] after the 3-month intervention that would be sustained till 6-months. For the latter, personalized outcomes, we expected no worsening within-group at 6-months, which would indicate that possible intervention effects remained stable. Last, to better understand the effectiveness of the intervention on the composite psychological distress, we explored effects on its separate components depressive and anxiety symptoms.

Methods

Trial Design

E-GOAL was an open RCT with two parallel groups (allocation ratio 1:1), conducted from April 2018 to October 2020. The study was approved by the Medical Ethics Committee of Leiden University Medical Center (P17.172), is registered at the Netherlands Trial Register (NL7338), and complies with the 1964 Declaration of Helsinki. The Consolidated Standards of Reporting Trials (CONSORT) statement and the Template for Intervention Description and Replication (TIDieR) checklist were used for reporting.[22,23]

Participants

Box 1. Inclusion and exclusion criteria

Criteria screening phase

Inclusion criteria

- Under medical treatment by an internist-nephrologist
- Chronic kidney disease with an estimated glomerular filtration rate (eGFR) 20-89 mL/min/1.73 m^2
- ≥18 years old
- Sufficient command of the Dutch language
- Able to give informed consent
- Access to a computer or tablet with internet

Exclusion criteria

- Rapidly progressive renal function loss (>10% renal function loss over the last year)
- Anticipated need for dialysis work-up within the time frame of the study
- Systolic blood pressure <95 mmHg not responding to withdrawal of antihypertensive medication
- Medical conditions that are likely to interfere with study completion (e.g., progressive malignancy, recent cardiovascular event, severe psychiatric disorders) at the discretion of the nephrologist
- Kidney transplantation <1 year ago
- Difficulties in (written) communication (e.g., due to analphabetism)
- Pregnancy

Criteria randomization phase

Inclusion criteria (increased-risk profile)

- At least mild depressive or anxiety symptoms (PHQ-9 ≥5 or GAD-7 ≥5)[31,32] AND
- At least one suboptimal self-management outcome (<150 minutes per week of moderate-to-vigorous intensity physical activity,[a] a body mass index ≥25 kg/m^2,[b] tobacco smoking ≥1 unit per day,[c] dietary or medication non-adherence based on questionnaire cut-off points)[d,e,1]

Exclusion criteria

- Severe depressive or anxiety symptoms (PHQ-9 ≥20 or GAD-7 ≥15)[27]
- Ongoing psychological treatment elsewhere

Notes. PHQ-9=Patient Health Questionnaire depression scale; GAD-7=Generalized Anxiety Disorder scale; [a]Short Questionnaire to Assess Health-enhancing physical activity (SQUASH).[60]; [b]Ratio of body weight (kg) and square of height (m); [c]"Do you smoke?" and "How much do you smoke on average per day?"; [d]"In the past week, how often have you kept a healthy diet?" with scores on a 1-5 scale from "never" to "always" (cut-off for inclusion ≤3) or "In the past week, how well do you believe you have kept a healthy diet?" on a 1-10 scale from "very badly" to "very well" (cut-off for inclusion ≤6); [e]Simplified Medication Adherence Questionnaire (SMAQ, cut-off for inclusion ≥2 items indicating non-adherence).[61]

Recruitment and data collection took place at nephrology departments of three university hospitals and one general hospital in the Netherlands: Leiden University Medical Center, University Medical Center Groningen, Radboud university medical center, and Haaglanden Medical Center. Patients with CKD not receiving dialysis were recruited in two phases: In the screening phase, patients were invited to complete screening questionnaires regarding psychological distress and self-management. In the randomization phase, only patients whose screening results indicated that they could benefit from the intervention were invited to participate in the RCT (Box 1 depicts all inclusion and exclusion criteria by phase).

Potentially eligible patients were invited to participate in the screening phase via their nephrologist. They received verbal and written information regarding study purposes and procedures, with informed consent forms. Upon obtaining written consent, we sent patients emails with a link to online screening questionnaires in the secured eHealth application "PatientCoach".[24] Paper-and-pencil questionnaires were available for patients who had difficulties with online completion. With a brief screening, patients with increased-risk profiles—who experienced at least mild depressive or anxiety symptoms and at least one suboptimal self-management behavior—were automatically detected. These patients were invited to complete complementary questionnaires, assessing specific areas of behavioral, psychological, social, and physical functioning as baseline measurements and to tailor the intervention to personal needs in case they would be randomized to the intervention group. All participants could instantly review digital Personal Profile Charts: visual representations of their questionnaire results (see Figure 1 for an example). They also received paper versions by mail, including a letter to inform patients whether they were eligible for randomization: Patients with increased-risk profiles received study information and a second informed consent form.[16] Patients without increased-risk profiles were informed that they were not eligible for the RCT. Additionally, patients with severe psychological distress were not eligible either. They were contacted by phone and advised to approach their general practitioner for further evaluation.

Intervention

All patients received Personal Profile Charts in addition to care as usual in line with common practice in patients' medical center. After randomization, participants in the intervention group additionally received tailored and therapist-guided iCBT including self-management support. The intervention was adapted for patients with lifestyle-related chronic diseases including CKD[18] from an existing iCBT for coping with chronic somatic disease, which is developed from evidence-based face-to-face CBT and has been evaluated among different patient populations.[25,26] The intervention had the aims to treat psychological distress, diminish psychosocial barriers and promote facilitators for adherence to self-management recommendations, and to support patients in adopting and maintaining healthy and adherent behaviors. Treatment was guided by therapists, i.e., health psychologists who received training specific to this trial and attended weekly meetings with a skilled CBT supervisor and registered clinical psychologist.

At the start of treatment, a therapist conducted a face-to-face intake session (± 90–120 minutes) with an individual patient, which took place in the patient's medical center—one video call took place due to COVID-19 measures. The initial session included an assessment of a patient's physical, psychological, and social functioning, guided by the Personal Profile Charts and screening results.[16] Therapist and patient discussed which psychosocial difficulties hindered relevant self-management behaviors, explored patient's resources that could facilitate change, and determined priorities for improvement. With this information, the therapist aided the patient in formulating two to three personally relevant goals, of which at least one was related to improving psychosocial functioning and one to improving self-management. Also, eHealth application "E-coach" was introduced.[26,27] See Figure 2 for an example of modules in E-coach and Supplementary File 1 for an overview of all modules.

During the next three to four months, each patient in the intervention condition systematically went through a personalized selection of E-coach modules, which entailed an introduction module and several treatment modules matching personal goals (e.g., modules regarding mood improvement, social functioning, coping with fatigue, and self-management behavior change). Modules included psychoeducational information and exercises based on cognitive-behavioral (e.g., thought record, activity scheduling)[28] and behavior change techniques (e.g., pros and cons, action planning).[29] Each patient worked through modules at home and received weekly or bi-weekly feedback from their therapist via a secured message box within E-coach (± 6–16 therapist messages). If needed, treatment was complemented with telephone or face-to-face appointments. After completing personalized modules, the patient went through a final module about relapse prevention and long-term goals. In this module, among other things, each patient wrote a letter to themselves regarding their achievements. Afterwards, they had a final telephone appointment (± 15–30 minutes) with their therapist to evaluate treatment. Three months later they received an email from their therapist with their letter to themselves, to maintain goal behaviors. The exact duration of a trajectory was tailored to treatment goals and adequate pace for each individual. Precise details of the development and content of the eHealth care pathway has been published elsewhere.[18]

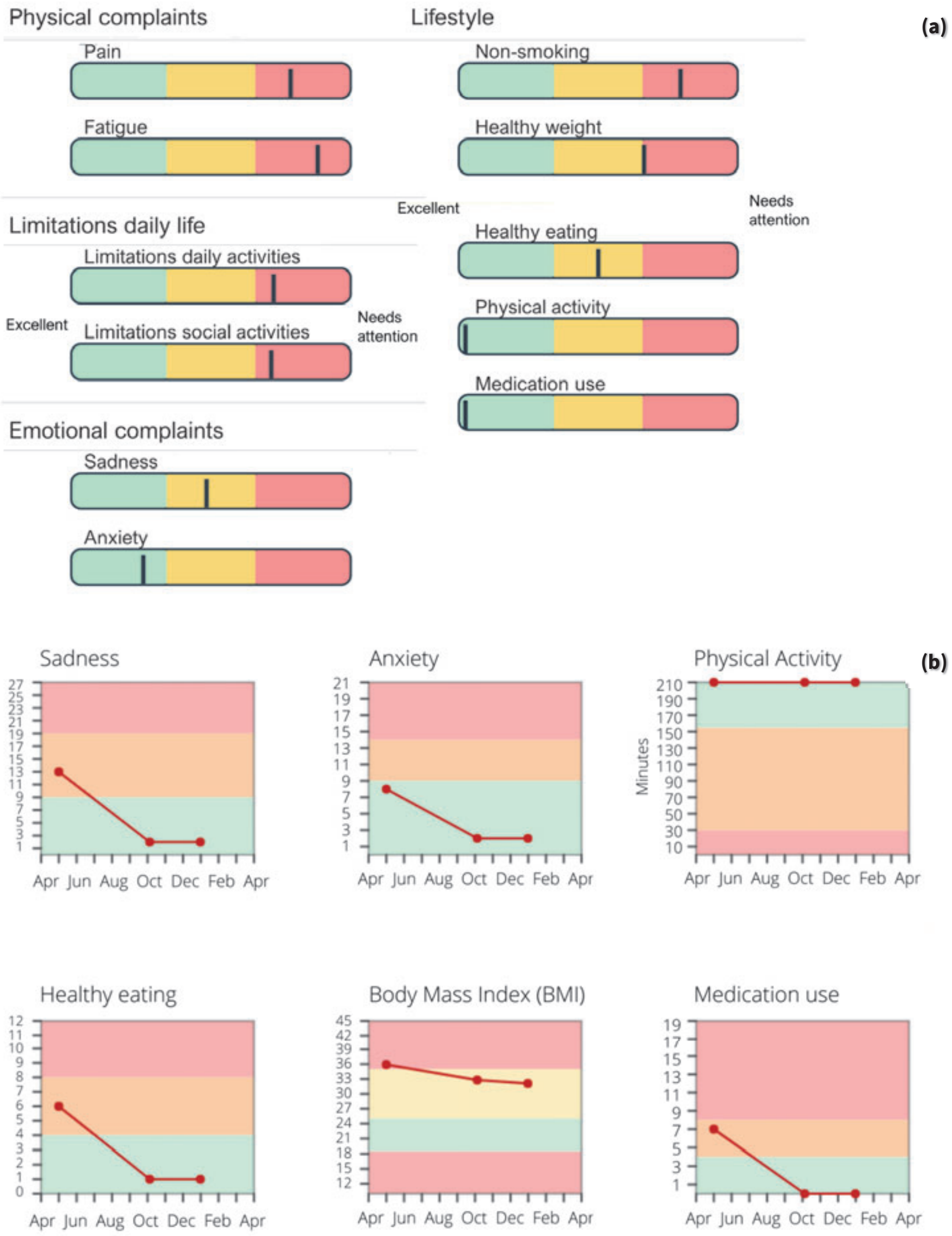
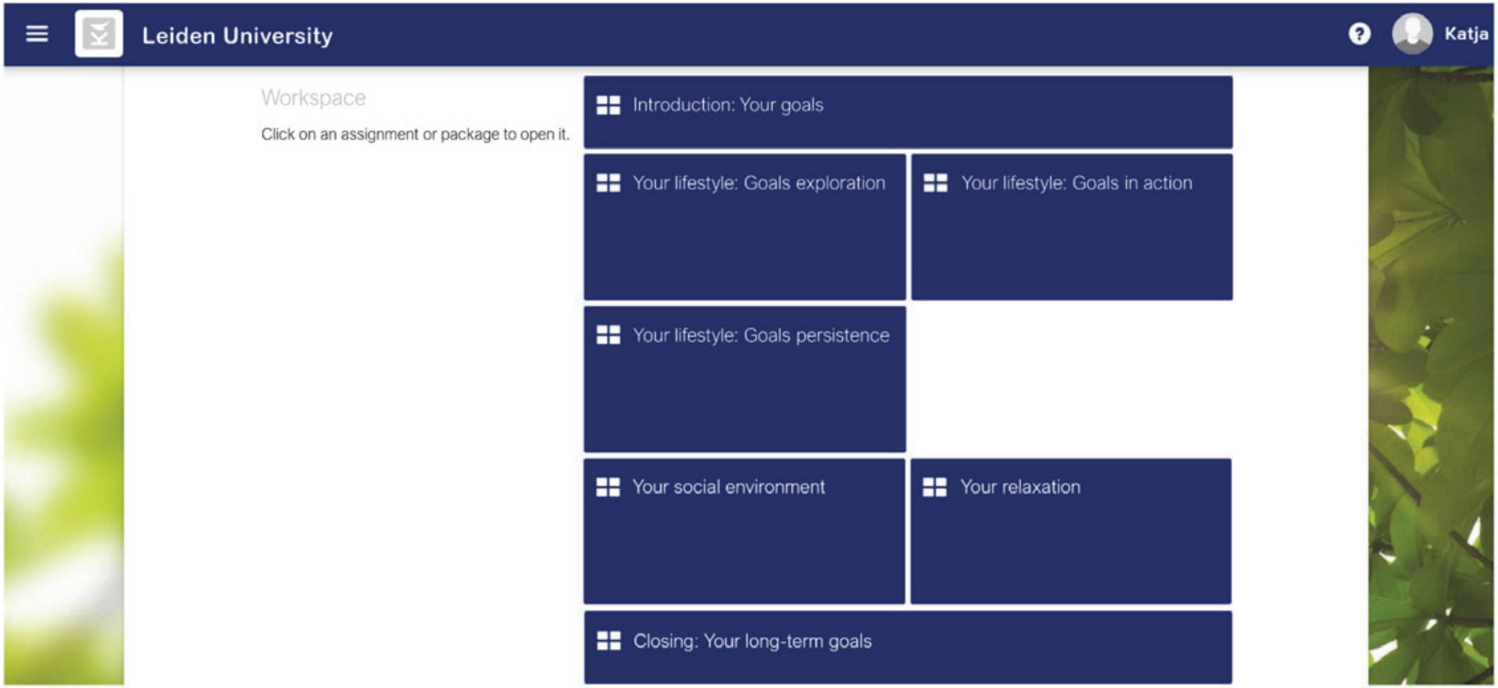


Figure 1. Examples of Personal Profile Charts at a) one time point and b) progress over time. Traffic light colors indicated current status on domains of functioning and self-management. Additional explanations were shown when hovering the mouse cursor over a domain.



Click on an assignment or package to open it.

Figure 2. An example of modules in eHealth application “E-coach”.

Data Acquisition and Outcomes

Data were collected at baseline, directly after the 3-month intervention, and at 6-month follow-up. Participants completed online screening questionnaires before randomization for sociodemographic, psychosocial, and behavioral data. All participants received Personal Profile Charts with their results at each time point. Furthermore, randomized participants were invited for medical measurements (weight, waist circumference, and blood pressure) in their medical center at all time points, carried out by trained research nurses or physician researchers. These measurements were documented in a secured online Case Report Form together with medical and biochemical data (e.g., from 24-hour urine and blood samples) extracted from hospital information systems. Adverse events were recorded in digital standardized forms to the Medical Ethics Committee in accordance with standard procedures.

Primary outcome was psychological distress, measured with the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS),[30] a composite of depressive (Patient Health Questionnaire depression scale [PHQ-9])[31] and anxiety symptoms (Generalized Anxiety Disorder scale [GAD-7]).[32] Scores range from 0 to 48, with higher scores indicating higher psychological distress. The PHQ-ADS composite was reliable with Cronbach's alphas of .78, .85, and .88 at baseline, 3-, and 6-months, respectively.

Several secondary outcomes were assessed. Physical and mental health-related quality of life (HRQoL) were measured with the RAND 36-item Short Form Health Survey (RAND SF-36).[33] Physical and mental HRQoL component summary scores range from 0 to 100, with higher scores indicating better HRQoL. Cronbach's alphas per time point were .73, .77, and .82 for physical HRQoL, and .74, .78, and .78 for mental HRQoL. Self-efficacy for disease management was measured by the Chronic Disease Self-Efficacy Scales–Manage Disease in General Scale (MDGS).[34] Scores range from 5 to 50, with higher scores indicating stronger belief in the capability of managing disease. Cronbach's alphas were .83, .82, and .87. Chronic condition self-management was assessed using the Partners in Health scale (PiH).[21] Scores range from 0 to 96, with higher scores indicating better self-management. Cronbach's alpha equaled .78, .81, and .81. For personalized outcomes (PPP-functioning and PPP-self-management), participants indicated their perceived progress on seven areas of functioning (i.e., fatigue, pain, itch, anxiety, depression, social environment, and daily activities) and five areas of self-management (i.e., medication adherence, healthy diet, physical activity, weight maintenance, and non-smoking) at 3- and 6-months, with the Personalized Priority and Progress Questionnaire (PPPQ).[20] Per item (area), scores range from -3 to +3, on which 0 indicates neither worsening nor improvement. At baseline, all participants could indicate a maximum of two areas of functioning and two areas of self-management as personal priorities for improvement. If a participant had indicated one personal priority, the personalized outcome at follow-up entailed the perceived progress score on this indicated item, and if a participant indicated two priorities, their mean was the personalized outcome. Development and validation of the PPPQ have been described in another manuscript.[20]

Last, participants in the intervention group were asked to complete evaluation questionnaires about their satisfaction and experiences with the eHealth care pathway. Other instruments used in this study have been described elsewhere.[18]

Sample Size

The sample size calculation was based on the primary outcome measure, the continuous composite variable (PHQ-ADS) of the PHQ-9 and GAD-7 scales. Other trials that evaluated psychological interventions among chronic conditions with these scales showed Cohen's *d* effect sizes from 0.28 to 0.63.[35-37] We considered Cohen's *d* between intervention and control group of 0.46 on the PHQ-ADS composite to be feasible, with a power of 0.80 at the .05 significance level. Based on this effect size, and considering a potential 15% drop-out rate, we aimed to include 120 patients.

Randomization

Randomization to either the intervention or control group (1:1) was performed using random number tables with random block sizes of four and six, created with an online number generator (random.org) and stratified by medical center and sex. Randomization tables were concealed from the main executive researcher and cells containing randomization indicators were hidden until a participant was assigned. Each participant was allocated to a condition by an independent data manager, who revealed the relevant randomization indicator. Next, the data manager notified the researcher, who communicated allocation to the participant.

Blinding

Due to the nature of the intervention, participants, researchers, and therapists were not masked to the assigned group. General practitioners and internist-nephrologists were informed about the group. Participant identification codes were used to link data to participants. Study personnel and the data manager (who conducted data monitoring) were the only people with access to personalized data.

Statistical Methods

Baseline sample characteristics were computed for the intervention and control group together and separately. Differences between complete cases and cases with missing data at any time point were examined using independent samples *t*-tests for continuous variables and χ^2-tests for categorical variables. These initial data analyses showed that cases with missing data more often completed paper-and-pencil questionnaires than complete cases (missing at random).[38] Digitally, answers were required for most items leading to few missing data. We included covariate "paper" in the main analyses, indicating whether participants completed all self-report measures digitally or filled in questionnaires on paper at any time point.[i]

To describe the intervention effect in terms of (standardized) treatment outcome differences, mean change scores over time (by subtracting the baseline score from 3- and 6-month follow-up scores) were compared between the intervention and control groups. For personalized outcomes (PPPQ), patients reported their perceived progress at 3- and 6-months as a comparison to the previous time point, which precluded subtraction of baseline scores: Means at 3- and 6-months on the PPPQ were used as mean change scores over time. Furthermore, for all outcomes, Cohen's *d* effect sizes were calculated.[ii] Effect sizes of 0.2, 0.5, and 0.8 were considered small, medium, and large, respectively.[39]

To analyze intervention effectiveness, i.e., the effect of the treatment condition (intervention or control) over time, we performed intention-to-treat analysis (including all 121 participants) combined with linear mixed-effects regression (i.e., longitudinal multilevel analysis) using the full information maximum likelihood estimation method.[38] To perform this analysis per outcome variable, we created one long format dataset with the outcome scores at baseline, 3-months and 6-months below each other. We further created a time variable with values 0 (baseline), 1 (3-months=short-term), and 2 (6-months=long-term). From this time variable two dummy variables were created with baseline as reference category, reflecting the short-term (3-months vs. baseline) and long-term (6-months vs. baseline) effect of time. Finally, we created the interaction terms between group

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[i] For variables constructed by summing up multiple items (PHQ-ADS, MDGS, and PiH), we applied person mean imputation of missing items per time point, with the requirement that at least 60% of items were available. This resulted in person mean imputed data for only one participant on the PHQ-ADS and for two participants on the MDGS and PiH, who had missing values on items assessed at both follow-up time points.

[ii] Formula for computing the Cohen's *d* effect size ($\mathrm{ES}_{\mathrm{change}}$) between-group effect sizes of the intervention group (group 1) and control group (group 2): $\mathrm{ES}_{\mathrm{change}} = \frac{\overline{x}_{\mathrm{change,group1}} - \overline{x}_{\mathrm{change,group2}}}{s_{\mathrm{change,pooled}}}$, where $s_{\mathrm{change,pooled}} = \sqrt{\frac{(n_1-1)\times \mathrm{SD}^2_{\mathrm{change,group1}} + (n_2-1)\times \mathrm{SD}^2_{\mathrm{change,group2}}}{n_1+n_2-2}}$

(intervention=1, and control=0) and these dummy variables, to investigate the short-term and long-term effect of the intervention. The linear mixed effects regression models included the following fixed effects: the two dummy variables of time, paper (a dichotomous variable indicating digital questionnaire completion versus any time point on paper), the interaction terms short-term*group and long-term*group, and the baseline covariates age and sex were included to adjust for potential influence. We assumed that the group means were equal at baseline (following the recommended strategy for longitudinal analysis in randomized controlled trials by Fitzmaurice and colleagues),[40] therefore the fixed effect of group was not included in the analysis. To improve model fit per outcome, the optimal variance-covariance matrix was selected (using restricted maximum likelihood) and the need for random intercept or slopes was tested with the Likelihood Ratio Test for nested models and the lowest Akaike's Information Criterion values for non-nested models (see Supplementary File 2 for an overview of final models). Assumptions for linear mixed-effects modeling (i.e., normally distributed random effects and error terms, no influencing outliers, and independent errors) were checked.

To assess the intervention effectiveness for personalized secondary outcomes (PPPQ), one-way analyses of covariance (ANCOVA) were conducted, with group as independent variable, paper, age, and sex as covariates, and PPP-functioning and PPP-self-management at 3- and 6-months as dependent variables, respectively. To avoid loss of power and biased results of these analyses, missing data were imputed using multiple imputation (10 repetitions) under the “missing at random” assumption. Assumptions for ANCOVA analyses (i.e., normally distributed residuals, no influencing outliers, and homogeneity of regression slopes) were checked.

Since the primary outcome psychological distress is a composite measure, we exploratorily analyzed linear mixed-effects models with depressive and anxiety symptoms separately, to understand whether the intervention effectiveness differed for those separate outcomes. For all outcomes, sensitivity analyses were conducted to test the robustness of our results, including analyses without adjustments for baseline covariates, ANCOVA analyses without imputing missing data, and analyses in the per-protocol sample, which excluded intervention participants who dropped out of treatment. Additional sensitivity analyses regarding floor effects are described in the supplementary material.

P-values $<.05$ were considered statistically significant. Analyses were performed with SPSS version 27.0 (IBM). Linear mixed-effects models were performed with the MIXED procedure and ANCOVA models with the UNIANOVA procedure.

Results

Participant Flow

Between April 2018 and March 2020, 460 of 2240 (20.5%) eligible patients with CKD not receiving dialysis completed screening questionnaires. Screening results of 146 patients (31.7%) showed increased-risk profiles of at least mild depressive or anxiety symptoms and at least one suboptimal self-management behavior, of whom 121 (82.9%) were randomly assigned to the intervention (*n*=60) or control group (*n*=61). Eight patients dropped out during the trial, leaving 113 (93.4%) who completed the allocated group. Eleven adverse events occurred in the intervention group and seven in the control group, which all required hospitalization. Adverse events were unrelated to study procedures and no participant withdrawals occurred due to intervention harms. Figure 3 shows the participant flow.

Baseline Characteristics

Table 1 includes baseline characteristics of the randomized sample. Most participants were men, born in the Netherlands, and had a partner. The majority (59.5%) had never received psychological treatment in the past. Ages ranged from 25.8 to 81.6 years. The mean estimated glomerular filtration rate was 49.6 ± 18.5 mL/min/1.73 m^2 and 65.3% were kidney transplant recipients. Mean office systolic and diastolic blood pressures were 138.6 ± 17.0 mm Hg and 80.9 ± 9.0 mm Hg, respectively. The mean body mass index was 27.9 ± 5.4 kg/m^2, and waist circumference 100.0 ± 15.3 cm.

Intervention Adherence, Module Use, and Evaluation

In the intervention group, 54 (90.0%) patients completed the iCBT treatment according to protocol. Reasons for non-completion were not experiencing gain (*n*=3), too high burden (*n*=2), and health reasons (*n*=1). Treatment dropouts had a significantly higher age (67.9±7.3) than completers (56.0±12.6; *p*=.026), higher baseline diastolic blood pressure (83.4±7.5 vs 72.1±6.1; *p*<.001), and more physical comorbidities (3.0±1.3 vs 1.1±1.1; *p*<.001). With regard to baseline scores on outcomes, treatment dropouts had a significantly lower physical HRQoL (28.7±7.0) than completers (35.5±7.6; *p*=.041), and poorer disease self-management 73.8±9.9 vs. 81.5±8.5; *p*=.042). One participant dropped out of treatment immediately after the intake session, before starting online modules. The mean treatment duration of the other dropouts was 5.6±4.7 weeks and they used 1.4±2.1 out of 14 modules on average. One treatment dropout did complete measurements at 3-months and one at all time points.

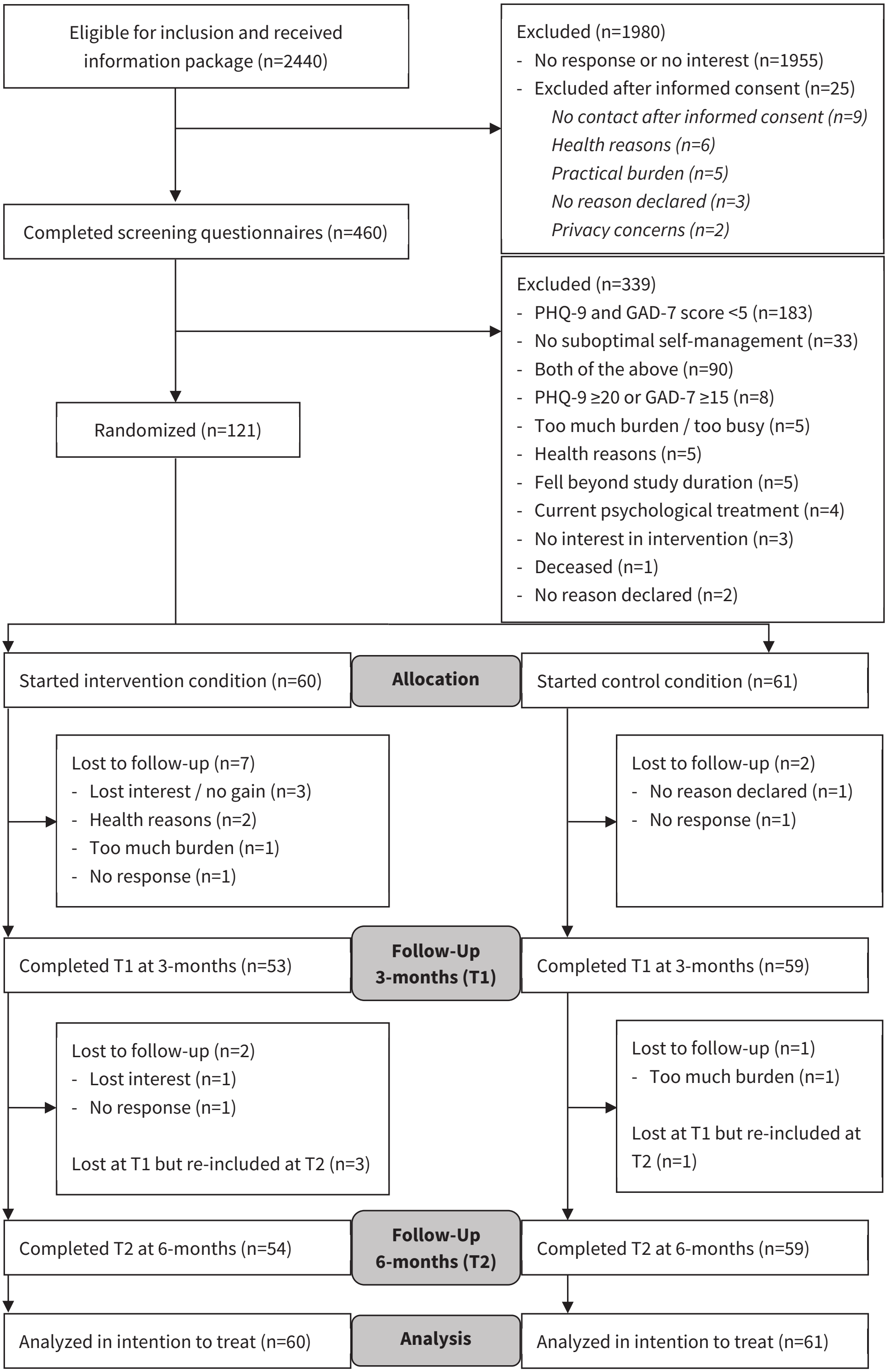

Figure 3. Participant flow.

Table 1. Baseline participant characteristics

Characteristic	Intervention (*n*=60)	Control (*n*=61)
Socio-demographic characteristics		
Age, y	57.2±12.6	54.8±15.0
Male sex, *n*(%)	32(53.3)	36(59.0)
Country of birth Netherlands, *n*(%)	54(90.0)	55(90.2)
Married/partnered, *n*(%)	44(73.3)	45(73.8)
Having children, *n*(%)	45(75.0)	42(68.9)
Low education[a], *n*(%)	32(53.3)	32(52.5)[e]
Employed[b], *n*(%)	27(45.0)	34(55.7)
Disease and treatment characteristics		
Primary cause of kidney failure, *n*(%)		
Glomerulonephritis	7(11.7)	15(24.6)
Diabetes mellitus	13(21.7)	4(6.6)
Renal vascular disease	8(13.3)	8(13.1)
Cystic kidney diseases	7(11.7)	7(11.5)
Interstitial nephritis	8(13.3)	3(4.9)
Other cause	11(18.3)[f]	21(34.4)[g]
Kidney transplant recipient, *n*(%)	40(66.7)	39(63.9)
Time since last kidney transplantation[c], y	6.8[8.8]	6.9[12.6]
History of dialysis, *n*(%)	22(36.7)	29(47.5)[e]
Nr. of physical comorbidities for which in treatment		
0	18(30.0)	19(31.1)
1	19(31.7)	17(27.9)
2	13(21.7)	12(19.7)
≥3	10(16.7)	13(21.3)
Diabetes mellitus, *n*(%)	24(40.0)	14(23.0)
Cardiovascular disease[d], *n*(%)	24(40.0)	24(39.3)
Hypertension, *n*(%)	44(73.3)	53(86.9)
Antihypertensive medication use, *n* %)	49(81.7)	49(80.3)
Treatment history psychological complaints, *n*(%)	25(41.7)	24(39.3)
Biochemical measures		
Sodium excretion rate, mmol/24h	150.1±51.1[g]	145.4±58.8[h]
Protein excretion rate, mmol/24h	0.19[3.80][h]	0.15[5.24][i]
Urea excretion rate, mmol/24h	392.0[703.1][j]	319.0[571.5][i]
Creatinine excretion rate, mmol/24h	12.6[27.2][g]	11.3[15.2][i]

Characteristic	Intervention (n=60)	Control (n=61)
Albumin excretion rate, mmol/24h	31.3[3199.3][k]	38.4[4112.1][l]
Potassium excretion rate, mmol/24h	66.6[132.0][h]	64.0[120.0][m]
eGFR, mL/min/1.73 m^2	52.1±18.7	47.2±18.1
Hemoglobin, mmol/L	8.2±0.9[n]	8.3±1.0[n]
Total cholesterol, mmol/L	4.6±1.0[g]	4.5±1.0[o]
LDL cholesterol, mmol/L	2.4[5.4][j]	2.4[1.1][j]
HDL cholesterol, mmol/L	1.4[0.6][g]	1.3[0.5][o]
Blood pressure and anthropometric measures		
Office SBP, mm Hg	140.5±16.6	136.8±17.3[e]
Office DBP, mm Hg	82.3±8.1	79.4±9.6[e]
Body mass index, kg/m^2	27.3[5.7]	26.5[6.2]
Waist circumference, cm	101.0[24.0][e]	100.0[20.5][o]
Self-management behaviors		
Dietary adherence 1-10 score	6.6±2.1	6.4±2.3
Physical activity, hours/week	14.9[17.1]	11.4[15.8]
Nonsmoking	52(86.7)	58(95.1)
Medication adherence, 1-6 score	6.0[1.0]	5.0[2.0]
Alcohol consumption, units/week	0.0[4.8]	0.0[3.0]
Depressive symptoms, 0-27 score	7.5±3.2	8.3±3.4
Anxiety symptoms, 0-21 score	5.5±3.8	5.5±3.8

Notes. Values for categorical variables are presented as count (proportion); values for continuous variables are given as mean ± standard deviation for normally distributed variables or median [interquartile range] for skewed variables; DBP=diastolic blood pressure; eGFR=estimated glomerular filtration rate; HDL=high-density lipoprotein; HRQoL=health-related quality of life; LDL=low-density lipoprotein; SBP=systolic blood pressure; [a]Low education includes primary, pre-vocational, and vocational education; High education includes advanced secondary and tertiary education; [b]Paid job, unpaid/voluntary work, or self-employed; [c]Only for kidney transplant recipients; [d]Cardiovascular disease was defined by the presence of coronary disease, angina pectoris, myocardial infarction, cerebrovascular accident, peripheral arterial disease, arrhythmia, or heart failure; [e]1 unknown, [f]6 unknown, [g]3 unknown, [h]7 unknown, [i]8 unknown, [j]5 unknown, [k]10 unknown, [l]12 unknown, [m]11 unknown, [n]2 unknown, [o]4 unknown.

The mean treatment duration (excluding planned weeks of inactivity) of completers was 15.0 ± 4.1 weeks (range 8–29) and they used 5.7 ± 2.2 modules on average (range 1–10). In addition to introduction module ‘your goals’ and final module ‘your long-term goals’, the most frequently used module was ‘your lifestyle: goal exploration’ (n=43), followed by ‘your lifestyle: goals in action’, ‘your thoughts’, and ‘your relaxation exercises’ (all n=28).

The least used modules were ‘your complaints: pain’ (*n*=3) and ‘your complaints: itch’ (*n*=1). See Supplementary File 1 for an overview of module use. Patients were very satisfied with the iCBT treatment and gave it an overall mean score of 7.7±1.4 out of 10 (range 4–10), the online environment a 7.5±1.4 (range 4–10), and contact with their therapist an 8.6±1.1 (range 5–10). Also, they found the Personal Profile Charts useful to obtain insights in their own wellbeing and lifestyle (mean 3.13±0.80 on a 1–4 scale) and as an aid in setting personal goals during the intake session (mean 3.20±0.76 on a 1–4 scale).

Primary and Secondary Outcomes

Assumptions for the statistical analyses were not violated. Logarithmic transformations were applied for strongly positively skewed outcome variables and reflect and logarithmic transformations for strongly negatively skewed outcome variables (note that for the latter, a higher value on the transformed variable is a lower value on the original variable). At baseline, mean scores on primary and secondary outcomes (Supplementary File 3) did not differ significantly between groups. Regarding our primary outcome, at baseline, 70.2% of the sample reported at least mild psychological distress (i.e., scored 10 or higher). Mean psychological distress reported by the intervention group at baseline was 13.0±6.2 and 13.8±6.2 in the control group. Mean psychological distress was lower in the intervention group than in the control group at 3- and 6-months, and dropped below the cut-off point of 10 (indicating no or minimal presence of psychological distress) in the intervention group only. Table 2 shows observed change scores on the primary and secondary outcomes, with effect sizes of the differences between groups on change scores. Positive Cohen’s *d* values indicate that the intervention group performed better (on observed mean change scores) than controls, which was the case for all outcomes, except self-management at 6-months. Medium effect sizes were observed for PPP-functioning at 3-months and 6-months as well as for PPP-self-management at 3-months (see also Table 2).

Table 3 shows the results of the linear mixed-effects analyses. No time-by-group interaction effects were found for our primary outcome, i.e., differences between groups were not significant at 3-months (*b*=-0.03, 95%Confidence Interval [41][-0.12, 0.06], *p*=.49) or at 6-months (*b*=-0.07, 95%CI[-0.18, 0.05], *p*=.26; see Figure 4). Regarding secondary outcomes, only for self-management a time-by-group interaction effect was identified at 3-months (*b*=-0.09, 95%CI[-0.17, -0.01], *p*=.030), but not at 6-months (see Figure 5): Compared to the control group, the intervention group engaged more in chronic condition self-management activities (e.g., treatment and medication adherence and healthy lifestyle behaviors) immediately after completing the intervention.

Table 2. Observed mean change scores per condition for outcome variables; with differences and effect sizes of the differences in mean change scores between conditions (complete cases).

Outcome variable	3-months (post-intervention)						6-months (follow-up)					
	Change score (*SD*)			95% CI			Change score (*SD*)			95% CI		
	Intervention	Control	Dif.	LL	UL	*d*	Intervention	Control	Dif.	LL	LB	*d*
Psychological distress	-3.7(6.7) (*n*=52)	-3.3(6.5) (*n*=59)	0.47	-2.02	2.95	0.07	-3.8(6.3) (*n*=54)	-2.4(8.4) (*n*=59)	1.36	-1.43	4.14	0.18
Physical HRQoL	3.3(6.9) (*n*=52)	1.9(6.3) (*n*=58)	1.38	-1.10	3.86	0.21	2.9(7.1) (*n*=52)	2.6(8.8) (*n*=58)	0.27	-2.77	3.30	0.03
Mental HRQoL	3.5(8.7) (*n*=52)	2.3(8.7) (*n*=58)	1.19	-2.11	4.50	0.14	2.7(9.9) (*n*=52)	2.2(9.5) (*n*=59)	0.54	-3.11	4.20	0.06
Self-efficacy	2.1(5.8) (*n*=52)	1.5(5.9) (*n*=58)	0.61	-1.59	2.82	0.11	2.5(6.7) (*n*=53)	0.9(6.3) (*n*=58)	1.61	-0.83	4.05	0.25
Self-management	3.7(7.0) (*n*=53)	2.1(7.5) (*n*=58)	1.58	-1.16	4.33	0.22	2.0(8.2) (*n*=53)	2.5(8.7) (*n*=58)	-0.50	-3.70	2.71	-0.06
Progress on priorities for functioning	0.6(1.1) (*n*=53)	0.1(1.0) (*n*=59)	0.48	0.09	0.87	0.46	0.3(1.2) (*n*=53)	-0.3(1.1) (*n*=59)	0.62	0.20	1.05	0.55
Progress on priorities for self-management	0.6(1.0) (*n*=52)	-0.0(1.1) (*n*=58)	0.58	0.17	0.98	0.54	0.1(1.2) (*n*=53)	0.1(1.4) (*n*=59)	0.02	-0.47	0.50	0.01

Notes. CI=confidence Interval; Dif.=Difference in mean change scores (baseline scores subtracted from 3- and 6-month follow-up scores, respectively) between conditions; LL=Lower Limit; UL=Upper Limit; *d*=Cohen's *d*. For psychological distress, depressive and anxiety symptoms, negative change scores indicate improvement; For all other outcomes, positive change scores indicate improvement. For all outcomes, positive differences in mean change scores between conditions and positive Cohen's *d* values indicate that the intervention group improved more than controls. For progress on priorities for functioning and self-management, means (perceived progress as compared to previous time point) instead of change scores are shown and used to calculate differences and effect sizes.

Table 3. Main analyses of the E-GOAL intervention. Estimated coefficients and confidence intervals based on linear mixed-effects models of primary and secondary outcomes adjusted for baseline covariates, assuming equal scores at baseline in the intervention (*n*=60) and control group (*n*=61).

Outcome variable	Psychological distress		Physical HRQoL		Mental HRQoL		Self-efficacy		Self-management	
	b	95% CI	*b*	95% CI	*b*	95% CI	*b*	95% CI	*b*	95% CI
Intercept	1.21	1.07 to 1.34	46.02	39.90 to 52.15	41.59	35.63 to 47.56	34.20	30.50 to 37.91	1.31	1.11 to 1.51
Short-term	-0.15	-0.21 to -0.08	2.40	0.66 to 4.14	2.44	0.44 to 4.45	1.64	0.23 to 3.05	-0.04	-0.10 to 0.01
Long-term	-0.14	-0.22 to -0.06	3.01	1.27 to 4.74	2.06	-0.26 to 4.38	0.95	-0.46 to 2.37	-0.05	-0.11 to 0.02
Short-term*group	-0.03	-0.12 to 0.06	0.56	-1.86 to 2.97	1.12	-1.63 to 3.87	0.43	-1.47 to 2.33	-0.09	-0.17 to -0.01
Long-term*group	-0.07	-0.18 to 0.05	-0.24	-2.66 to 2.17	0.84	-2.24 to 3.92	1.43	-0.47 to 3.33	-0.03	-0.12 to 0.05

Notes. *b*=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, and for whether participants completed all measurements digitally versus any time point on paper.

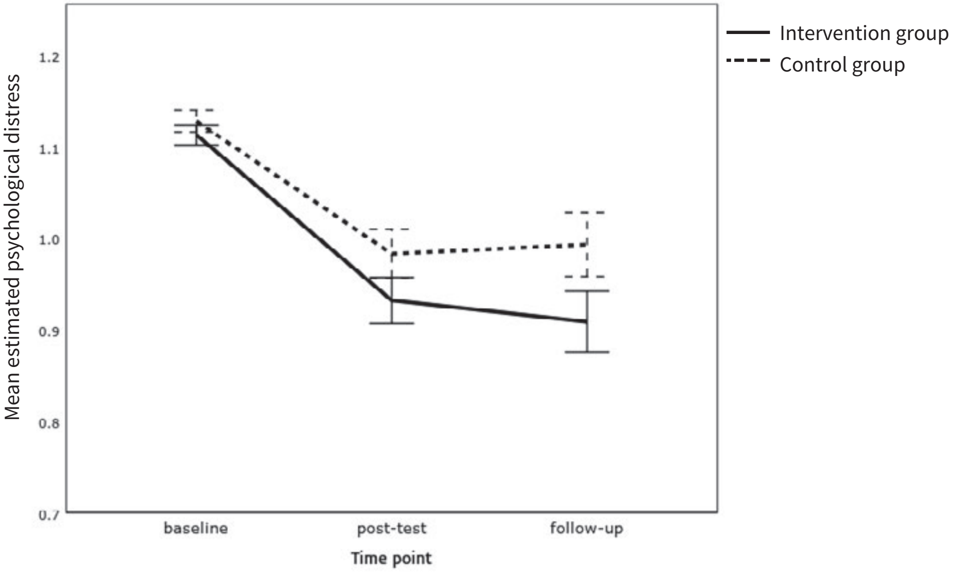

Figure 4. Time-by-group interaction effects for psychological distress (logarithmic transformation of Patient Health Questionnaire Anxiety and Depression Scale; PHQ-ADS) in linear mixed-effects models adjusted for baseline covariates. Error bars +/- 1 standard error. The mean reduction in psychological distress symptoms from baseline to 3-months (*p*=0.49) and from baseline to 6-months (*p*=0.26) did not significantly differ between groups.

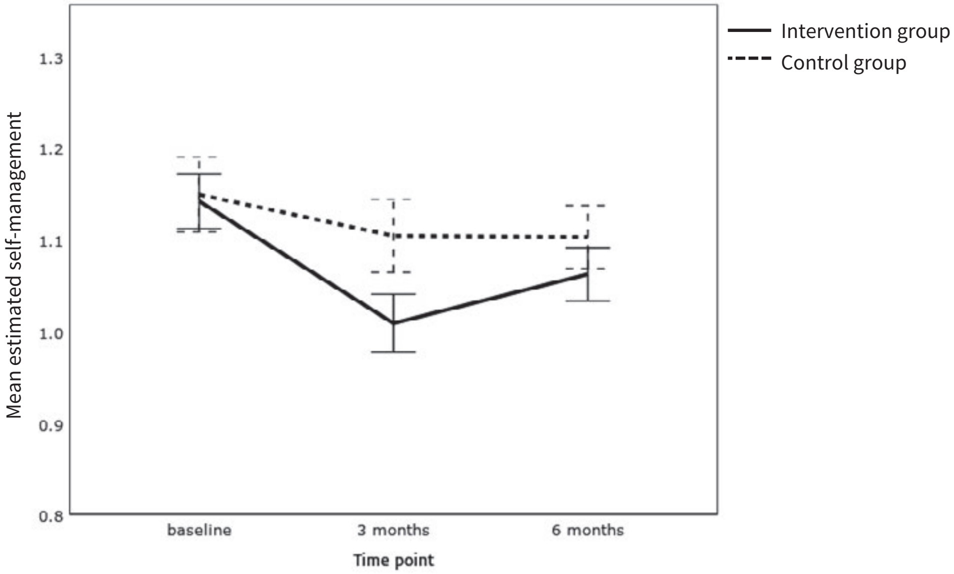

Figure 5. Time-by-group interaction effects for self-management (reflect and logarithmic transformation of Partners in Health scale; PiH) in linear mixed-effects models adjusted for baseline covariates. Error bars +/- 1 standard error. The improvement in self-management from baseline to 3-months was significantly larger in the intervention group than in the control group (*p*=0.03). This difference between groups was not significant from baseline to 6-months (*p*=0.44).

For personalized outcome measures, in both groups, the areas of functioning that were most frequently prioritized for improvement at baseline were fatigue or sleep (*n*=90), daily activities (*n*=39), and anxiety or worry (*n*=30). Regarding self-management, the main personal priorities were physical activity (*n*=76), weight maintenance (*n*=70), and healthy diet (*n*=59). See Supplementary File 4 for an overview of reported priorities.

The ANCOVA results showed statistically significant differences between groups in PPP-functioning at both the 3-months assessment (progress compared to baseline; *b*=0.46, 95%CI[0.07, 0.85], *p*=.021), and 6-months assessment (compared to 3-months; *b*=0.59, 95%CI[0.16, 1.02], *p*=.007), with the intervention condition showing significantly more improvements than controls. Similarly, the intervention group reported more perceived improvement on PPP-self-management at 3-months (*b*=0.55, 95%CI[0.16, 0.95], *p*=.006). At the 6-months assessment the difference between groups was not significant (*b*=0.02, 95%CI[-0.48, 0.53], *p*=.93), as both groups reported neither perceived improvement nor worsening compared to 3-months; this indicates that the intervention effect achieved at short-term was maintained at long-term (see Figure 6). For an overview of ANCOVA results, see also Supplementary File 5.

Exploratory and Sensitivity Analyses

Linear mixed-effects models of depressive and anxiety symptoms (Tables S6 and S7 in Supplementary File 6) showed no significant intervention effects for depressive symptoms, in line with the primary analysis of psychological distress. However, a significant time-by-group interaction effect was found for anxiety at short-term: The reduction in anxiety symptoms from baseline to 3-months was significantly larger in the intervention group than in the control group (*b*=-0.11, 95%CI[-0.21, -0.00], *p*=.041). This difference remained of borderline significance from baseline to 6-months (*b*=-0.11, 95%CI[-0.22, 0.00], *p*=.059, see also Figure 7).

Finally, sensitivity analyses showed that the results were stable in the analyses without adjustments for baseline covariates age and sex, without multiple imputation, and in the per-protocol sample without intervention dropouts, and similar in subgroup analyses (Tables S8 to S16 in Supplementary File 6).

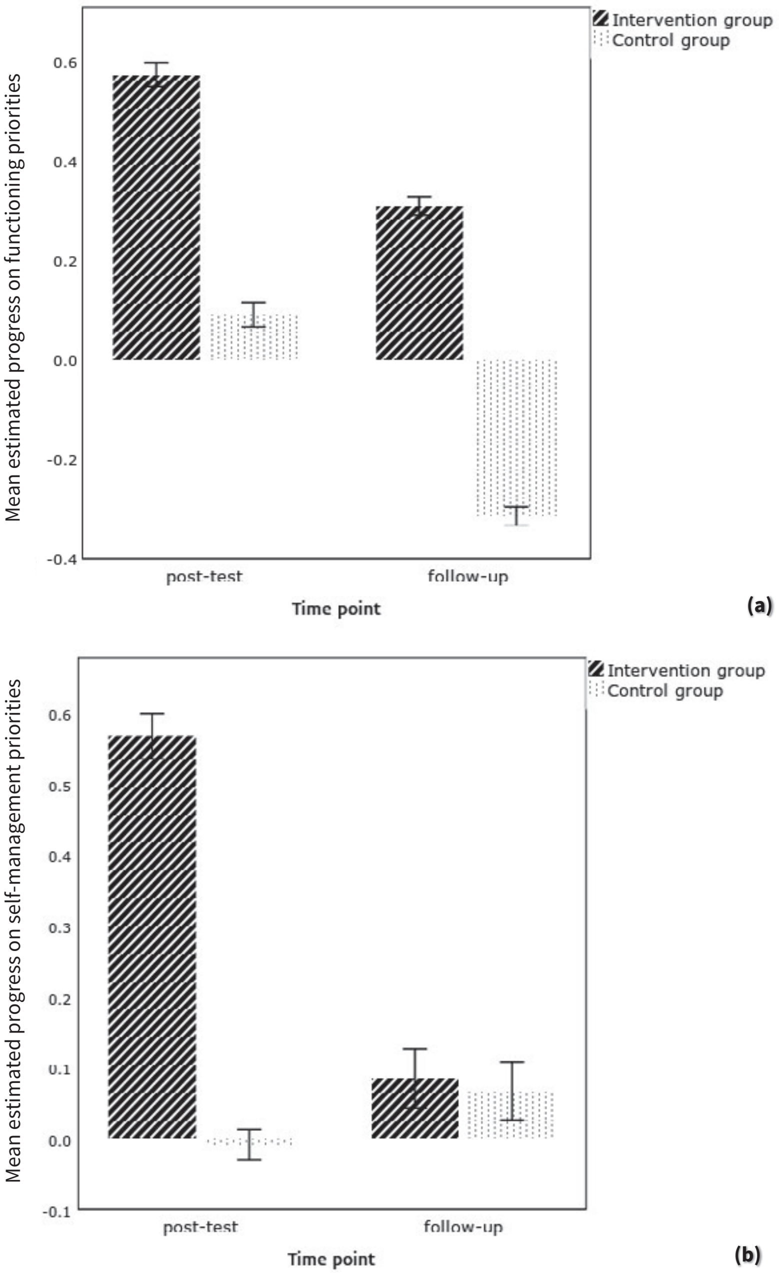

Figure 6. Mean perceived progress as compared to previous time point on personally prioritized areas of a) functioning and b) self-management per randomization group. Estimated marginal means from one-way analyses of covariance are shown, adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper. Error bars +/- 1 standard error. Scores on the Personal Priority and Progress scale (PPPQ) could range from -3 to +3, on which 0 indicates neither worsening nor improvement.

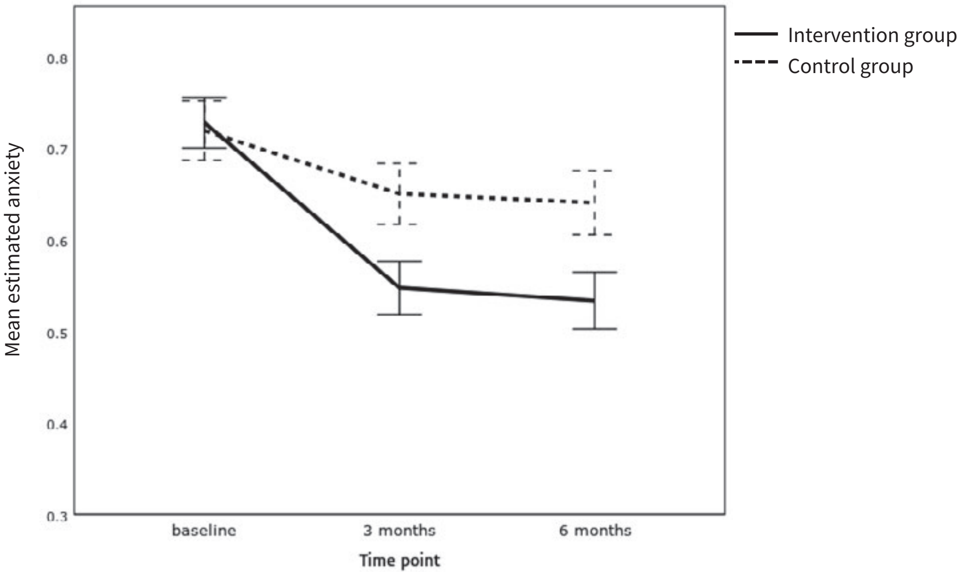

Figure 7. Time-by-group interaction effects for anxiety symptoms (logarithmic transformation of Generalized Anxiety Disorder scale; GAD-7) in linear mixed-effects models adjusted for baseline covariates. Error bars +/- 1 standard error. The mean reduction in anxiety symptoms from baseline to 3-months was significantly larger in the intervention group than in the control group ($p=0.04$). This difference between the groups remained of borderline statistical significance from baseline to 6-months ($p=0.06$).

Discussion

Psychological distress is common among patients with CKD not receiving dialysis and kidney transplant recipients, and can interfere with disease self-management. Similar to previous research,[12] over a third of participants in this study reported depressive or anxiety symptoms, and the large majority of these patients had difficulties to engage in recommended self-management behaviors. To improve both psychological functioning and self-management, personalized, multicomponent interventions are advocated in literature and desired by patients.[42,43] To our knowledge, E-GOAL is the first study to investigate the effectiveness of such a tailored eHealth care pathway with guided iCBT and self-management support among patients with CKD. The findings varied. Compared to regular care only, this personalized approach did not reduce overall psychological distress significantly. For secondary outcomes, compared to usual care, chronic condition self-management and personalized outcomes of functioning and self-management that were prioritized by individual patients themselves significantly improved more post-intervention. Moreover, effects on personalized outcomes of functioning were further enhanced after the intervention ended and improvements on personalized outcomes of self-management were maintained over time. No differences between groups in health-related quality of life and self-efficacy were observed.

Although the intervention did not reduce patients' psychological distress significantly compared with patients in the control condition, the mean symptom reduction of the intervention group dropped to no or minimal symptoms at short- and longer-term.[30] Psychological distress was assessed as a composite: The intervention seemed to be successful in significantly reducing anxiety but not depressive symptoms. Comparing these results to similar interventions among patients with CKD not receiving dialysis is complicated, since previous studies either just focused on self-management and did not assess psychological distress as an outcome, or included participants with kidney failure treated by dialysis. For instance, in a recent systematic review and meta-analysis that evaluated the effects of psychosocial interventions on depressive and anxiety symptoms in individuals with CKD, only studies were found that included people with kidney failure receiving dialysis, palliative care, or awaiting kidney transplantation.[44] In this review, moderate reductions of depressive and anxiety symptoms have been found after psychosocial intervention, although the results varied: Out of five studies, three reported significant reductions post-intervention. Studies that failed to find beneficial intervention effects did not use clinical cut-off scores as inclusion criteria, which may have led to difficulties in reducing symptoms due to low baseline symptom levels.[44] Similarly, a floor effect may have been present for our primary outcome: Although we pre-selected patients by our screening procedure and did include participants with at least mild depressive or anxiety symptom scores (PHQ-9 ≥5 or GAD-9 ≥5), almost 30% of our participants had scores in the lowest category on the composite (PHQ-ADS <10), i.e., they reported no or only minimal psychological distress at baseline.[30] This may partly explain the lack of significant findings, although exploratory subgroup analysis among participants with at least mild psychological distress did not show remarkable differences. Furthermore, observed mean change scores showed that, although the intervention group reported somewhat stronger improvements, controls also improved over time on primary and secondary outcomes. This also happened in previous self-management trials,[6,7] and may be explained by assessment reactivity or Hawthorne effect:[45] Participants' awareness of trial participation and exposure to measurements may have worked as an implicit intervention in the control condition. For instance, participants in the control group were also invited to reflect on their health and behavior and received visual feedback of questionnaire results, which may have motivated them to change and could have contaminated outcomes.[45]

A last explanation may be that we predominantly relied on generic measures, whereas the personalized nature of our intervention actually requires personalized outcome measures. In contrast to traditional one-size-fits-all approaches for "the average patient", personalized interventions identify the best support for each individual.[46] Individuals work on personal goals, implying differences in treatment focus and outcomes of importance per patient.[46] Accordingly, our results revealed significantly more improvements on personally prioritized areas in the intervention group compared to controls with medium-sized effects. In comparison, for generic outcomes, the intervention condition only showed significantly reduced anxiety and better self-management compared to controls at 3-months and effect sizes were small. These findings indicate a current problem regarding personalized interventions in RCTs, which often turn out to have limited effects on generalized outcomes that still belong to traditional one-size-fits-all treatments.[46,47] In line with personalization of interventions, effectiveness should be evaluated by focusing on outcomes that matter to each individual patient. Patients themselves should also determine their perceived change, making it personally meaningful.[46] To our knowledge, this is the first study using personalized outcomes in a trial among patients with CKD.

Limitations and Strengths

Limitations were the short-term follow-up of only three months post-intervention and limited statistical power. In hindsight, we may have needed a larger sample or a higher cut-off for psychological distress to demonstrate statistical significance, as the power calculation was based on studies in which participants were eligible if they had somewhat higher psychological distress levels at baseline compared to ours.[35-37] A larger sample size would also allow for a wider array of analyses of subgroups, mediators, and moderators of treatment effects that could explain the mixed findings, such as specific mechanisms of action or active treatment components.[26,47] Another limitation was the open-label approach, as blinding was not possible due to the active nature of the intervention. Patient's awareness of participation and their assigned group may have led to several biases, including assessment reactivity explained above, as well as response biases that could have contributed to potential positive effect exaggerations in the intervention group.[45,48] As a last limitation, we did not take multiple testing into account, since we tested only one primary research question. If we would perform Holm-Bonferroni correction for multiple testing[49] on the linear mixed-effects analyses with our primary and secondary outcomes, the intervention effect on self-management would not be regarded statistically significant. The ANCOVA findings regarding personalized outcomes would remain unchanged (i.e., the three significant effects are also significant when we apply the multiple test correction with an overall alpha level of .05).

Strengths of this study were the high response rate for the intervention, as 82.9% percent were willing to be randomized, and the lower than expected drop-out rate (6.6%). High participation, treatment adherence, and positive evaluations may be explained as follows: First, the intervention was developed systematically and in co-creation with health professionals and patients with CKD or other chronic conditions, to ensure its relevance to their needs.[18,50] This frequent feedback and prototype testing by stakeholders may have aided in making the E-GOAL eHealth care pathway acceptable and feasible. Co-creation could be further enhanced by an even more active stakeholder participation—including minority groups—in all research stages, including design, implementation, evaluation, and dissemination.[50] Second, the intervention was tailored to personalized needs and used personalized progress measures. This person-tailoring was appreciated by participants and makes the E-GOAL eHealth care pathway easily applicable to other patients and populations.

Implications

For future research and implementation in clinical practice, two success factors of the current trial should be considered. First, advanced personalization was the fundament, with treatment goals based on personal screening outcomes and priorities for improvement, customized treatment modules, and flexibility in pace, intensity, and mode of contact with the E-coach therapist. With this tailorability to individuals' unique needs, eHealth innovations hold promise for more accessible, acceptable, and sustainable healthcare.[43,51] Second, in the screening procedure in our study, about a third of patients with CKD reported psychological complaints in combination with difficulties to adhere to self-management recommendations. This high co-occurrence strengthens the need for a holistic healthcare system, with attention for the intertwinement of psychological distress and self-management. Conversely, in current hospital care, there is often a one-sided focus on physiological functioning with referrals to external mental healthcare for psychological complaints. Patients may perceive referrals and mental disorder diagnoses as stigmatizing, i.e., as pathologizing normal distress in response to living with chronic disease.[9] Multicomponent interventions integrated in hospital care may be more acceptable and effective, by stimulating bi-directional improvements: On the one hand, enhancing psychological functioning facilitates adherence to self-management recommendations; on the other hand, optimizing self-management protects against psychological distress.[10,11]

We recommend several steps to improve the intervention, in order to potentially be successful in reducing psychological distress. First, it has been found that the severity of psychological complaints could moderate response to treatments.[52] Therefore, the adequate cut-off point for inclusion should be determined, for example by offering our intervention to patients with higher baseline levels of distress.[53] Second, additional treatment components or techniques could be included in the iCBT treatment that have been found effective in reducing psychological distress symptoms. For instance, in CBT among various other chronically ill populations, treatment effects have been mediated by acceptance of psychological or physical complaints.[54,55] Techniques from acceptance and commitment therapy (ACT), a third-wave wing of CBT, could be included in our iCBT treatment to alleviate psychological distress by promoting its acceptance.[56] Third, to understand the mechanisms of action in the current intervention, the data of our E-GOAL trial could be further explored by analyses of potential mediators or process variables, such as the therapeutic relationship, that may have influenced the intervention's effectiveness.[54,57]

Last, generalizability of the intervention to populations with other lifestyle-related chronic diseases is suggested by the considerable presence of multimorbidity in our sample and participants' most commonly reported priorities (e.g., fatigue, physical activity, diet, and weight), which are also prominent in other diseases, such as type 2 diabetes.[58] Currently, several promising components of the eHealth care pathway are being further developed and investigated for implementation among different patient populations, including asthma[24] and kidney failure.[59]

Conclusions

The personalized E-GOAL eHealth care pathway is an example of a person-centered and multicomponent intervention, innovative in targeting both psychological functioning and chronic disease self-management that are often intertwined. Compared to regular care only, this eHealth intervention did not significantly improve psychological distress, quality of life, and self-efficacy, whereas significant effects were observed for anxiety and chronic disease self-management immediately after the intervention period. Importantly for this personalized intervention, personally relevant outcomes did also improve significantly post-intervention and improvements were maintained over time. The RCT results provided insights in priorities of people with CKD and suggest that future studies could consider personalized outcomes for patient-tailored interventions that reflect individually meaningful treatment goals and improvements.

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Supplementary File 1

Module Use

Table S1. Use of intervention modules in application E-coach by treatment completers (*n* = 54).

Module	Description	Use
Your goals	Treatment goal setting	38
Your lifestyle: goal exploration	Motivation and self-efficacy for self-management behavior change	41
Your lifestyle: goals in action	Planning and carrying out self-management behavior change	27
Your lifestyle: goal persistence	Evaluation and maintenance of self-management behavior change	20
Your mood	Negative mood and depressive symptoms	23
Your thoughts	Maladaptive cognitions and worry	28
Your relaxation	Anxiety and stress symptoms	9
Your relaxation exercises	Stress-reducing mediations and visualizations	28
Your activities	Activity planning and balance in daily life	25
Your environment	Social environment and functioning	8
Your complaints: fatigue and sleep	Physical symptoms and limitations (fatigue)	18
Your complaints: pain	Physical symptoms and limitations (pain)	3
Your complaints: itch	Physical symptoms and limitations (itch)	1
Your long-term goals	Evaluation with relapse prevention	40

Supplementary File 2

Overview of Final Linear Mixed-Effects Models

Table S2. Linear mixed-effects models for main analyses of the E-GOAL intervention adjusted for baseline covariates.

Outcome variable	Variance-covariance matrix	Random intercept	Random slopes
Psychological distress	Heterogenous first-order autoregressive	No	Yes
Physical HRQoL	Scaled identity	Yes	No
Mental HRQoL	First-order autoregressive	No	Yes
Self-efficacy	Scaled identity	Yes	No
Self-management	Heterogenous first-order autoregressive	No	Yes
Depressive symptoms	Scaled identity	Yes	No
Anxiety symptoms	First-order autoregressive	No	Yes

Notes. Best model fit with adequate variance-covariance matrix and use of random intercept or random slopes were determined by the Likelihood Ratio Test for nested models and the lowest Akaike's Information Criterion values for non-nested models. All analyses were adjusted for baseline covariates age and sex, and for whether participants completed all measurements digitally versus any time point on paper.

Supplementary File 3

Observed Mean Scores on Outcome Variables

Table S3. Observed means for outcome variables.

Outcome variable	Observed mean (*SD*)					
	Intervention group			Control group		
	0 mo (*n* = 60)	3 mo (*n* = 53)	6 mo (*n* = 54)	0 mo (*n* = 61)	3 mo (*n* = 59)	6 mo (*n* = 59)
Psychological distress	13.0 (6.2)	8.9 (5.3)[a]	9.1 (5.7)	13.8 (6.2)	10.5 (6.9)	11.5 (8.0)
Depressive symptoms	7.5 (3.2)	5.6 (3.6)	5.6 (3.5)[b]	8.3 (3.4)	5.9 (3.9)	6.6 (4.4)
Anxiety symptoms	5.5 (3.8)	3.2 (2.4)[a]	3.4 (2.9)	5.5 (3.8)	4.6 (3.6)	4.9 (4.1)
Physical HRQoL	34.8 (7.8)[c]	38.7 (8.4)	38.2 (9.3)[b]	37.1 (9.3)	39.3 (10.4)[e]	40.0 (11.4)[d]
Mental HRQoL	39.7 (8.9)[c]	43.9 (8.8)	37.5 (6.2)[b]	39.9 (8.5)	42.4 (10.0)[d]	41.9 (10.1)
Self-efficacy	37.5 (6.2)	39.9 (6.2)[a]	40.1 (6.7)[b]	37.8 (6.0)	39.3 (5.8)	38.7 (5.2)[d]
Self-management	80.8 (8.8)	84.7 (8.1)	83.3 (8.8)[b]	79.3 (10.4)	81.0 (9.9)	81.8 (9.1)[d]
Progress on priorities for functioning	-	0.58 (1.1)	0.31 (1.2)[b]	-	0.09 (1.0)	-0.31 (1.1)
Progress on priorities for self-management	-	0.58 (1.0)[a]	0.09 (1.2)[b]	-	-0.01 (1.1)[d]	0.07 (1.4)

Notes. HRQoL = health-related quality of life. To compare groups on mean change scores over time of complete cases, see Table 2.

[a]*n* = 52, [b]*n* = 53, [c]*n* = 59, [d]*n* = 58.

Supplementary File 4

Personalized Treatment Priorities

Table S4. Pre-treatment priorities for intervention and post-treatment actively targeted areas as assessed with the Personalized Priority and Progress Questionnaire (PPPQ).

Area	Pre-treatment (*n*)		Post-treatment (*n*)	
	Intervention	Control	Intervention	Control
Functioning				
Fatigue	41	49	21	12
Pain	9	11	6	6
Itch	3	4	4	3
Anxiety	15	15	12	7
Depression	12	8	9	1
Social environment	9	5	6	9
Daily activities	25	24	22	14
Self-management				
Medication adherence	3	4	6	0
Healthy diet	26	33	23	22
Physical activity	34	42	25	23
Weight maintenance	39	31	12	12
Non-smoking	7	2	5	1

Supplementary File 5

ANCOVA Results of Personalized Outcome Measures

Table S5. Estimated coefficients and confidence intervals of one-way analyses of covariance between the intervention (*n*=60) and control group (*n*=61) at 3- and 6-months, on mean perceived progress as compared to previous time point on personally prioritized areas of functioning and self-management as indicated at baseline, adjusted for baseline covariates.

Outcome variable	*b*	95% CI
Progress on priorities of functioning at 3-months	0.46	0.07 to 0.85
Progress on priorities of self-management at 3-months	0.55	0.16 to 0.95
Progress on priorities of functioning at 6-months	0.59	0.16 to 1.02
Progress on priorities of self-management at 6-months	0.02	-0.48 to 0.53

Notes. *b*=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Supplementary File 6

Exploratory and Sensitivity Analyses

Exploratory Analyses of Depressive and Anxiety Symptoms

Table S6. Observed mean change scores per condition for depressive and anxiety symptoms; with differences and effect sizes of the differences between groups on the change scores (complete cases).

Outcome variable	3-months (post-intervention)						6-months (follow-up)					
	Change score (*SD*)			95% CI			Change score (*SD*)			95% CI		
	Intervention	Control	Dif.	LL	UL	*d*	Intervention	Control	Dif.	LL	UL	*d*
Depressive symptoms	-1.6 (3.9) (*n* = 53)	-2.4 (4.0) (*n* = 59)	-0.79	-2.27	0.68	-0.20	-1.7 (3.7) (*n* = 54)	-1.7 (4.8) (*n* = 59)	-0.01	-1.62	1.61	-0.00
Anxiety symptoms	-2.1 (3.9) (*n* = 52)	-0.8 (3.4) (*n* = 59)	1.27	-0.09	2.63	0.35	-2.0 (3.8) (*n* = 54)	-0.7 (4.4) (*n* = 59)	1.36	-0.16	2.89	0.33

Notes. CI = Confidence Interval; Dif. = Difference in mean change scores (baseline scores subtracted from 3- and 6-month follow-up scores, respectively) between conditions; LL = Lower Limit; UL = Upper Limit; *d* = Cohen’s *d*. Negative change scores indicate improvement. Positive differences in mean change scores between conditions and positive Cohen’s *d* values indicate that the intervention group improved more than controls.

Table S7. Estimated coefficients and confidence intervals based on linear mixed-effects models of depressive and anxiety symptoms adjusted for baseline covariates, assuming equal scores at baseline in the intervention (*n* = 60) and control group (*n* = 61).

Outcome variable	Depressive symptoms		Anxiety symptoms	
	b	95% CI	*b*	95% CI
Intercept	0.99	0.84 to 1.14	0.86	0.67 to 1.06
Short-term	-0.16	-0.23 to -0.10	-0.07	-0.15 to 0.00
Long-term	-0.13	-0.19 to -0.07	-0.08	-0.17 to 0.00
Short-term*group	0.02	-0.06 to 0.10	-0.11	-0.21 to -0.00
Long-term*group	-0.03	-0.11 to 0.05	-0.11	-0.22 to 0.00

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Analyses Without Adjustments for Baseline Covariates Age and Sex

In Tables S8 to S10, the results are shown of the analyses without adjusting for the potential influence of baseline covariates age and sex. We did include covariate “paper”, indicating whether participants completed all measurements digitally versus any time point on paper, to adjust for the influence of missing data.

Table S8. Main analyses of the E-GOAL intervention. Estimated coefficients and confidence intervals based on linear mixed-effects models of primary and secondary outcomes, without adjusting for age and sex, assuming equal scores at baseline in the intervention (*n* = 60) and control group (*n* = 61).

Outcome variable	Psychological distress		Physical HRQoL		Mental HRQoL		Self-efficacy		Self-management	
	b	95% CI	*b*	95% CI	*b*	95% CI	*b*	95% CI	*b*	95% CI
Intercept	1.13	1.10 to 1.17	35.70	33.90 to 37.49	39.77	38.02 to 41.52	37.75	36.62 to 38.88	1.14	1.08 to 1.20
Short-term	-0.15	-0.21 to -0.08	2.42	0.68 to 4.16	2.46	0.46 to 4.47	1.60	0.19 to 3.01	-0.04	-0.10 to 0.01
Long-term	-0.14	-0.22 to -0.06	3.03	1.29 to 4.78	2.09	-0.22 to 4.41	0.90	-0.51 to 2.32	-0.04	-0.11 to 0.02
Short-term*group	-0.03	-0.13 to 0.06	0.50	-1.93 to 2.93	1.08	-1.67 to 3.83	0.53	-1.38 to 2.44	-0.09	-0.17 to -0.01
Long-term*group	-0.07	-0.18 to 0.05	-0.29	-2.72 to 2.14	0.78	-2.30 to 3.86	1.51	-0.39 to 3.42	-0.04	-0.12 to 0.05

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for whether participants completed all measurements digitally versus any time point on paper.

Table S9. Estimated coefficients and confidence intervals of one-way analyses of covariance between the intervention (*n*=60) and control group (*n*=61) at 3- and 6-months, on mean perceived progress on personally prioritized areas of functioning and self-management, without adjusting for age and sex.

Outcome variable	*b*	95% CI
Progress on priorities of functioning at 3-months	0.47	0.08 to 0.85
Progress on priorities of self-management at 3-months	0.55	0.16 to 0.94
Progress on priorities of functioning at 6-months	0.60	0.17 to 1.02
Progress on priorities of self-management at 6-months	0.02	-0.48 to 0.52

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for whether participants completed all measurements digitally versus any time point on paper.

Table S10. Estimated coefficients and confidence intervals based on linear mixed-effects models of depressive and anxiety symptoms, without adjusting for age and sex, assuming equal scores at baseline in the intervention (*n* = 60) and control group (*n* = 61).

Outcome variable	Depressive symptoms		Anxiety symptoms	
	b	95% CI	*b*	95% CI
Intercept	0.92	0.87 to 0.97	0.73	0.67 to 0.79
Short-term	-0.16	-0.23 to -0.10	-0.07	-0.14 to 0.00
Long-term	-0.13	-0.19 to -0.07	-0.08	-0.17 to 0.00
Short-term*group	0.02	-0.06 to 0.10	-0.11	-0.21 to -0.01
Long-term*group	-0.03	-0.11 to 0.05	-0.11	-0.22 to 0.00

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for whether participants completed all measurements digitally versus any time point on paper.

Analyses Without Multiple Imputation

Below, the results of the ANCOVA analyses can be found, repeated on the original dataset without multiple imputation.

Table S11. Estimated coefficients and confidence intervals of one-way analyses of covariance between the intervention (*n*=60) and control group (*n*=61) at 3- and 6-months, on mean perceived progress as compared to previous time point on personally prioritized areas of functioning and self-management as indicated at baseline, adjusted for baseline covariates.

Outcome variable	*b*	95% CI
Progress on priorities of functioning at 3-months	0.47	0.07 to 0.87
Progress on priorities of self-management at 3-months	0.55	0.14 to 0.96
Progress on priorities of functioning at 6-months	0.62	0.18 to 1.05
Progress on priorities of self-management at 6-months	0.04	-0.46 to 0.53

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Analyses in the Per-Protocol Sample

In Tables S12 to S14, the results of the analyses in the per-protocol sample are shown, in which the intervention participants who dropped out of treatment $(n = 6)$ were excluded.

Table S12. Main analyses of the E-GOAL intervention in the per-protocol sample (*N* = 115). Estimated coefficients and confidence intervalsbased on linear mixed-effects models of primary and secondary outcomes adjusted for baseline covariates, assuming equal scores at baseline in the intervention and control group.

Outcome variable	Psychological distress		Physical HRQoL		Mental HRQoL		Self-efficacy		Self-management	
	b	95% CI	*b*	95% CI	*b*	95% CI	*b*	95% CI	*b*	95% CI
Intercept	1.20	1.07 to 1.33	45.94	39.78 to 51.11	41.59	35.58 to 47.60	33.85	30.12 to 37.58	1.34	1.14 to 1.54
Short-term	-0.15	-0.21 to -0.08	2.32	0.58 to 4.07	2.37	0.37 to 4.37	1.65	0.23 to 3.07	-0.04	-0.10 to 0.02
Long-term	-0.14	-0.22 to -0.05	2.93	1.18 to 4.67	1.96	-0.35 to 4.27	0.97	-0.46 to 2.39	-0.04	-0.11 to 0.02
Short-term*group	-0.03	-0.13 to 0.0.06	0.57	-1.87 to 3.01	0.93	-1.83 to 3.69	0.53	-1.39 to 2.45	-0.10	-0.18 to -0.01
Long-term*group	-0.07	-0.19 to 0.05	-0.14	-2.57 to 2.29	0.86	-2.22 to 3.95	1.46	-0.45 to 3.37	-0.04	-0.12 to 0.05

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Table S13. Estimated coefficients and confidence intervals of one-way analyses of covariance between groups at 3- and 6-months in the per-protocol sample (*N* = 115), on mean perceived progress on personally prioritized areas of functioning and self-management, adjusted for baseline covariates.

Outcome variable	*b*	95% CI
Progress on priorities of functioning at 3-months	0.44	0.04 to 0.83
Progress on priorities of self-management at 3-months	0.55	0.14 to 0.95
Progress on priorities of functioning at 6-months	0.59	0.15 to 1.02
Progress on priorities of self-management at 6-months	0.06	-0.44 to 0.56

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Table S14. Estimated coefficients and confidence intervals based on linear mixed-effects models in the per-protocol sample (*N* = 115) of depressive and anxiety symptoms adjusted for baseline covariates, assuming equal scores at baseline in the intervention and control group.

Outcome variable	Depressive symptoms		Anxiety symptoms	
	b	95% CI	*b*	95% CI
Intercept	0.99	0.83 to 1.15	0.87	0.67 to 1.07
Short-term	-0.16	-0.23 to -0.10	-0.07	-0.14 to 0.01
Long-term	-0.13	-0.19 to -0.07	-0.08	-0.17 to 0.00
Short-term*group	0.02	-0.07 to 0.10	-0.11	-0.21 to -0.00
Long-term*group	-0.03	-0.11 to 0.05	-0.11	-0.22 to -0.00

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Subgroup Analyses

In Tables S15 and S16, results of three subgroup analyses are shown. As we included patients who showed at least mild depressive or anxiety symptoms at baseline (either PHQ-9 ≥ 5 or GAD-7 ≥ 5, or both), participants could have only minimal symptoms on either the PHQ-9 or the GAD-7, and only minimal psychological distress on the composite outcome (PHQ-ADS < 10), which could lead to floor effects. To assess whether the intervention may be more effective for subgroups with at least mild symptoms, we conducted three subgroup linear mixed-effects model analyses: concerning subgroups of participants with at least mild psychological distress symptoms (PHQ-ADS ≥ 10, $n = 85$), depressive symptoms (PHQ-9 ≥ 5, $n = 109$), and anxiety symptoms (GAD-7 ≥ 5, $n = 67$), showing intervention effectiveness for the corresponding outcomes.

Table S15. For subgroups with at least mild symptoms per outcome at baseline: observed mean change scores per condition for psychological distress, depressive and anxiety symptoms; with differences and effect sizes of the differences between groups on the change scores (complete cases).

Outcome variable	3-months (post-intervention)						6-months (follow-up)					
	Change score (*SD*)			95% CI			Change score (*SD*)			95% CI		
	Intervention	Control	Dif.	LL	UL	*d*	Intervention	Control	Dif.	LL	UL	*d*
Psychological distress	-5.1 (7.7) (*n* = 33)	-4.1 (7.1) (*n* = 44)	1.05	-2.34	4.44	0.14	-5.3 (7.1) (*n* = 36)	-3.8 (8.2) (*n* = 45)	1.50	-1.92	4.93	0.20
Depressive symptoms	-1.9 (4.0) (*n* = 47)	-2.6 (4.1) (*n* = 53)	-0.74	-2.37	0.88	-0.18	-1.9 (3.8) (*n* = 48)	-1.9 (5.1) (*n* = 53)	0.03	-1.76	1.82	0.01
Anxiety symptoms	-3.7 (4.1) (*n* = 30)	-2.1 (3.8) (*n* = 31)	1.57	-0.46	3.60	0.40	-3.3 (4.1) (*n* = 33)	-2.3 (4.0) (*n* = 32)	1.03	-0.99	3.04	0.25

Notes. CI = Confidence Interval; Dif. = Difference in mean change scores (baseline scores subtracted from 3- and 6-month follow-up scores, respectively) between conditions; LL = Lower Limit; UL = Upper Limit; *d* = Cohen's *d*. Negative change scores indicate improvement. Positive differences in mean change scores between conditions and positive Cohen's *d* values indicate that the intervention group improved more than controls.

Table S16. For subgroups with at least mild symptoms per outcome at baseline: estimated coefficients and confidence intervals based on linear mixed-effects models of psychological distress ($n = 85$), depressive ($n = 109$) and anxiety symptoms ($n = 67$) adjusted for baseline, assuming equal scores at baseline in the intervention and control group.

Outcome variable	Psychological distress		Depressive symptoms		Anxiety symptoms	
	b	95% CI	*b*	95% CI	*b*	95% CI
Intercept	1.28	1.17 to 1.40	1.00	0.87 to 1.12	0.99	0.81 to 1.17
Short-term	-0.17	-0.24 to -0.09	-0.16	-0.22 to -0.10	-0.15	-0.24 to -0.06
Long-term	-0.18	-0.28 to -0.08	-0.12	-0.18 to -0.06	-0.17	-0.27 to -0.07
Short-term*group	-0.04	-0.15 to 0.08	-0.01	-0.10 to 0.07	-0.15	-0.27 to -0.03
Long-term*group	-0.06	-0.20 to 0.08	-0.04	-0.12 to 0.04	-0.14	-0.26 to -0.02

Notes. b=Parameter Estimate; CI=Confidence Interval. All analyses were adjusted for baseline covariates age and sex, as well as for whether participants completed all measurements digitally versus any time point on paper.

Supplementary File 7

E-GOAL Study Group

Drs. Cinderella K. Cardol, Leiden University
Dr. Henriët van Middendorp, Leiden University
Dr. Paul J.M. van der Boog, Leiden University Medical Center
Prof.dr. Gerjan Navis, University Medical Center Groningen
Prof.dr. Luuk B. Hilbrands, Radboud university medical center
Dr. Yvo W.J. Sijpkens, Haaglanden Medical Center
Dr. Yvette Meuleman, Leiden University Medical Center
Drs. Karin Boslooper-Meulenbelt, University Medical Center Groningen
Dr. Sasja Huisman, Leiden University Medical Center
Jan A.M. Luijten, patient research partner
Carla van Dorp, patient research partner
Prof.dr. Friedo W. Dekker, Leiden University Medical Center
Dr. Joris I. Rotmans, Leiden University Medical Center
Prof.dr. Ton J. Rabelink, Leiden University Medical Center
Prof.dr. Niels H. Chavannes, Leiden University Medical Center
Dr. Jacob K. Sont, Leiden University Medical Center
Dr. Eduard M. Scholten, Haaglanden Medical Center
Prof.dr. Andrea W.M. Evers, Leiden University
Dr. Sandra van Dijk, Leiden University

Chapter 7

Summary and General Discussion

Summary

Individuals with chronic kidney disease (CKD) generally suffer from permanent damage to the kidneys. In most cases, this damage gradually gets worse over time. In the current dissertation, we focus on patients who are not receiving dialysis treatment, including kidney transplant recipients. These patients can slow down the loss of kidney function by adopting a healthy lifestyle and adhering to a range of self-management recommendations—dietary adherence, physical activity, medication adherence, weight maintenance, and non-smoking.[1] Unfortunately, many patients do not manage to carry out all these tasks,[2,3] which may be partly explained by the considerable impact of the disease and its management on patients' daily lives and future perspectives:[4] Many patients suffer from psychological complaints,[5] which can hinder successful self-management.[6] Most interventions that offer support address either psychological complaints or self-management behavior, and it could possibly be more effective if both types of interventions would be concurrently targeted. As every person is unique, there is a large variability in patients' psychological and self-management difficulties, needs, preferences, and priorities.[7] These individual needs may be taken into account by personalizing interventions,[8] which could be facilitated by using electronic Health (eHealth) applications as modes of intervention delivery.[9] Therefore, the main aim of this dissertation was to develop and evaluate the effectiveness of an eHealth care pathway to provide personalized support for people with CKD not receiving dialysis. In the development and evaluation, we used different research methods, including focus groups, interviews, and an open randomized controlled trial (RCT). The E-GOAL eHealth care pathway included:

3) a screening tool with questionnaires and results visualized in personalized profile charts. Main screening purposes were to identify patients who experience psychological distress and suboptimal self-management and who thus may benefit from treatment, to tailor treatment, and to monitor progress over time,
4) blended and guided treatment which integrates Internet-delivered cognitive-behavioral therapy (iCBT) and self-management support. Main treatment purposes were to treat psychological distress, to diminish psychosocial barriers and promote psychosocial facilitators for adherence to self-management recommendations, and to support patients in adopting and maintaining healthy and adherent behaviors.

In order to develop an eHealth care pathway that was adequately tailored to the needs of people with CKD, we first explored which barriers and facilitators for engaging in healthy self-management behaviors patients experience according to patients themselves and their healthcare providers. In addition, we assessed which intervention strategies would be

suitable to address those barriers and facilitators to enhance patients' capabilities, opportunities, and motivation for health behavior change (**Chapter 2**). With this information and in collaboration with patients, we systematically developed the eHealth care pathway tailored to the needs and characteristics of individual patients with a chronic disease (**Chapter 3**). Subsequently, individuals with CKD participated in the eHealth care pathway. Using their answers on the initial screening questionnaires, we investigated how many people with CKD experienced psychological distress, depressive, or anxiety symptoms and difficulties in dietary adherence, physical activity, medication adherence, weight maintenance, and non-smoking. Additionally, we explored whether suffering from psychological distress was associated with experiencing self-management problems (**Chapter 4**). For patients who were affected by a combination of psychological distress and suboptimal self-management, we developed a personalized instrument to be able to assess their individual priorities for improvement (**Chapter 5**). These personally relevant priorities were used to set treatment goals and monitor personally meaningful change for patients who participated in the personalized iCBT treatment compared to patients who did not. We evaluated the iCBT treatment in a randomized study for patients who were identified during the screening procedure. We studied the treatment effectiveness in reducing psychological distress, and in improving physical and mental health-related quality of life (QoL), self-efficacy for disease management, chronic condition self-management, and personalized functioning and self-management outcomes (**Chapter 6**).

Overall, this dissertation systematically covered relevant steps in the process of intervention development and evaluation. The results provide insights in the psychological health and self-management of people with CKD and their priorities for treatment: Psychological distress and non-adherence to self-management recommendations are highly prevalent and co-occurrent. Also, individual patients experience a rather large variation in different personally relevant barriers and priorities for treatment. The E-GOAL eHealth care pathway is an example of a person-centered and multicomponent intervention with screening and treatment, innovative in detecting and treating psychological distress and non-adherence to self-management recommendations jointly, in targeting individual needs and preferences, and in using personalized priority and outcome measures. The iCBT treatment with self-management support resulted in mixed findings regarding effectiveness when comparing the intervention group with a care as usual control group. The main conclusions were that the E-GOAL intervention was not effective in reducing psychological distress, whereas patients did experience improvements in their personal priorities with regard to their functioning and self-management compared to regular care only. Moreover, the results demonstrated the acceptability, feasibility, and usability of eHealth applications to provide person-centered care.

In short, this dissertation has added to the scientific understanding of psychological distress and self-management among people with CKD not on dialysis. The results may explain adverse health outcomes and provide opportunities to intervene, in order to prevent complications and to slow down disease progression. The findings encompass intervention needs of individuals with CKD that can be incorporated in clinical practice. In doing so, more personalized nephrology care can be attained, to aid patients in improving their psychological and physical health and wellbeing.

In this final chapter, a general discussion of the main findings will be provided. Thereafter, the overarching strengths and limitations of the conducted research will be discussed, followed by recommendations for future studies and practice.

Overview of the Main Findings

Barriers and Facilitators of Self-Management

In **Chapter 2**, we performed focus groups with patients and health professionals to gain insights into psychosocial barriers and facilitators for adherence to self-management recommendations regarding dietary adherence, physical activity, medication adherence, weight maintenance, and non-smoking. We found many barriers and facilitators, such as patients' knowledge and intrinsic motivation, emotional wellbeing and psychological distress, optimism, and disease acceptance. The findings matched the fourteen domains of the Theoretical Domains Framework (TDF), of which the most prominently reported domains were 'social influences' 'and 'environmental context and resources', reflecting how patients' environments hinder or support engagement in a healthy lifestyle. The great amount of mainly environmental, motivational, and emotional barriers experienced by patients may explain why many of them do not succeed in adhering to the CKD self-management recommendations. These findings suggest that psychosocial and self-management support should be combined, since one can hinder the other and targeting both may lead to better health outcomes among individuals with CKD. Considering the great variation between individuals in perceived barriers and facilitators, the results indicate a need for personally tailored behavioral interventions to support disease self-management. As the TDF domains can be translated to matching behavior change techniques, the domains can guide development of adequate strategies to identify and target individually experienced psychosocial barriers and facilitators.

E-GOAL eHealth Care Pathway

In **Chapter 3**, we described the development of an innovative eHealth care pathway aimed at detecting and treating psychological distress and self-management difficulties that fits the needs and preferences of individual patients across various lifestyle-related chronic diseases, including CKD. Each component of the eHealth care pathway was developed systematically by (1) developing initial versions based on previously developed and evaluated interventions from our research team, scientific evidence (e.g., focus group results described before), and on theoretical frameworks of behavior change (i.e., the TDF and Behavior Change Wheel); (2) acquiring feedback from patients and health professionals by interviews; and (3) refining to address users' needs. In the final eHealth care pathway, patients could complete brief online screening questionnaires to detect psychological distress and self-management difficulties. In this screening tool, scores were visualized in Personal Profile Charts. Patients with psychological distress and self-management non-adherence were automatically provided with complementary questionnaires, which were administered to tailor a 3-month guided iCBT intervention to their priorities and goals. Progress over time could be assessed with the screening tool. The systematic process and development stages that are outlined in this chapter can be applied to guide future complex intervention development and form a fundament for further steps of an intervention's evaluation, continued development, and implementation.

Psychological Distress and Self-Management

In **Chapter 4**, we investigated relationships between psychological distress and self-management with the results of the screening questionnaires, which were completed by 460 individuals with CKD. We found that 27.2% of patients self-reported psychological distress, that is, mild to severe depressive or anxiety symptoms or both. In addition, over two-thirds were non-adherent to one or more self-management recommendations regarding dietary adherence, physical activity, medication adherence, weight maintenance, and non-smoking. In total, four out of five patients with psychological distress also reported non-adherence. We also found small associations of psychological distress with poorer dietary and medication adherence as well as with less physical activity, but not with body mass index and smoking. Findings were similar for depressive symptoms, whereas anxiety was only associated with poorer dietary and medication adherence. Furthermore, we developed a CKD self-management index by summing five binary indicators of adherence to the recommendations (adherent vs. non-adherent), with which we determined that an increase in psychological distress was associated with an increased likelihood of being non-adherent to a higher number of different recommendations. For example, patients who suffered from moderate to severe distress were relatively more often non-adherent to three or more recommendations compared to patients with no or mild distress symptoms. The associations that were observed suggest that psychological distress can be a potential barrier for self-management, although the cross-sectional design precludes conclusions about causality. The high co-occurrence rates emphasize the need to treat psychological distress and self-management jointly, and thus provide support for the fundament of the E-GOAL eHealth care pathway as a potentially desirable intervention for people with CKD.

Personalized Priority and Progress Questionnaire

In **Chapter 5**, we developed and validated the Personalized Priority and Progress Questionnaire (PPPQ), a brief personalized instrument that (1) defines patients' priorities for improvement, (2) measures progress on functioning and self-management outcomes that are prioritized by the individual patient, and (3) fosters person-centered care in both clinical trials and practice. We developed the instrument based on literature on personalized assessment and patient priorities, interviews with patients, and feedback by medical psychologists, and evaluated its psychometric properties. The questionnaire assesses patients' priorities for improvement on areas of functioning and self-management, as well as progress on these personally prioritized areas. The PPPQ showed to be feasible and valid. The questionnaire facilitates detection of functioning and self-management outcomes that are personally meaningful to the individual patient. This benefit makes the PPPQ a suitable instrument to evaluate personalized interventions in trials in which patients work on different treatment goals: Personalized outcome assessment allows for general conclusions on treatment effectiveness, while taking each patient's unique treatment trajectory into account. In clinical settings, the PPPQ could be used as a quick and easy tool to identify patients' priorities, to enhance shared-decision making and tailor treatments, and to monitor functioning on these personally meaningful areas. With these characteristics, the PPPQ could aid in delivering and evaluating person-centered care that is tailored to the unique needs and priorities of every individual patient.

Internet-Delivered Cognitive-Behavioral Therapy

In **Chapter 6**, we assessed the effectiveness of the treatment part of the personalized E-GOAL eHealth care pathway in an open, multicenter RCT, in which 121 people with CKD participated. Care as usual only was compared with care as usual plus the guided iCBT over a 3-month intervention period and at 6-month follow-up. Compared to regular care only, this eHealth intervention did not reduce primary outcome psychological distress significantly. No intervention effects were found for depressive symptoms, health-related QoL, or self-efficacy, whereas anxiety symptoms, chronic condition self-management, and personally relevant outcomes of functioning and self-management did improve significantly at 3-months compared to regular care only. Effects on personalized outcomes were maintained at 6-months. Patients were very satisfied with the iCBT treatment: they gave it an overall mean score of 7.7 and evaluated the collaboration with their therapist with an 8.6 out of 10. The RCT results also provided insights in the most commonly reported priorities for improvement of people with CKD, including fatigue, physical activity, healthy diet, weight maintenance, and limitations in daily activities. More research is needed to understand the lack of effect on our primary outcome and to enhance the intervention in potentially reducing psychological distress. The limited effectiveness to improve generic outcomes, compared to the significant and sustained improvements of personally relevant outcomes, suggests that future studies could consider personalized outcomes for person-tailored interventions, which reflect individually meaningful treatment goals and improvements. Furthermore, the high response and treatment completion rates, as well as positive evaluations by participants, suggest a good acceptability and feasibility of the intervention for people with CKD not receiving dialysis.

Strengths and Limitations

The E-GOAL study presented in the current dissertation has multiple strengths and limitations that should be mentioned. Strengths and limitations of each study conducted in this dissertation are discussed in the corresponding chapters and overarching considerations will be provided in the following paragraphs.

Strengths

Strengths of the studies that are described in this dissertation were the remarkably high response rates and low dropout. We were able to meet the intended sample size for the RCT, in which the intervention was evaluated positively by participants and treatment completion rates were high. This willingness to participate and high levels of satisfaction, the high prevalence rates of psychological distress and non-adherence, and the large amount of barriers for self-management that were reported, indicate that wellbeing and disease management are of great relevance for our population. The studied population in itself is another strength: Psychological health and self-management of people with CKD not receiving dialysis are relatively understudied, as most research among people with kidney disease focuses on populations with kidney failure treated by dialysis.[10,11] Expanding on recent trials that evaluated dietary self-management interventions (SodiUm Burden lowered by Lifestyle Intervention: self-Management and E-health technology [SUBLIME] and Effects of Self-monitoring on Outcome of Chronic Kidney Disease [ESMO]),[12,13] the current dissertation adds to the slowly increasing body of research among patients not on dialysis, for whom adequate self-management plays a vital role in disease outcomes.[1] We used broad inclusion criteria (e.g. wide eGFR range, comorbidities) in order to promote inclusivity and generalizability to clinical hospital care and general practice.[14] Generalizability of our results is further optimized by the multicenter nature of our studies, since participants were recruited from both academic hospitals and one non-academic hospital throughout the Netherlands.

In the E-GOAL study, we used a variety of research designs, with qualitative and quantitative methods, including a randomized experiment with multiple time points. Combining methodologies provides more breadth and depth than a single design to understand the self-management needs of people with CKD, and as a specific strength, qualitative studies can aid to develop and optimize an intervention before conducting an RCT.[15] Furthermore, the outcomes of this dissertation are mainly based on a variety of self-report measures, including qualitative data and questionnaires. Although literature stresses that self-report measures can have certain methodological downsides that will be discussed in the limitations section,[16] patient-reported outcome measures can also be regarded as a strength and inevitable part of personalized approaches: Subjective measures are vital to facilitate person-centered care and were essential in our studies, as we recognized and provided insights into participants' own perspectives, experiences, and outcomes that actually matter to them.[4] In addition, our use of personalized outcomes based on each trial participants' priorities, which they indicated prior to randomization, enabled a comparison of the intervention and control condition, while taking into account personalized treatment goals.

Limitations

The studies that are presented in this dissertation have several limitations. A potential limitation could be that all trial participants set personal priorities for improvement regarding their functioning and self-management: Reflecting on priorities and goals can work as some sort of intervention in itself, by focusing patients' attention, increasing motivation, and directing their efforts towards desired behaviors. Participants in the control group may therefore have searched for support in regular care or worked on their priorities by themselves during the study period. Thus, change may have been fostered in both groups and therewith, these self-reported priorities may have contaminated the “true” effect measurement of the actual intervention.[17] Furthermore, although we did also assess clinical and biomedical measurements in our trial and we outlined the strengths of self-report measures above, mainly using self-report measures as outcomes risks response biases, such as socially desirable responding.[16] For instance, participants may be hesitant to disclose psychological complaints due to associated shame or stigma.[18,19] A possible indication of stigma-related response bias in our studies may be that participation rates and reported prevalence of psychological distress varied per center: one of the possible explanations for these differences may be that stigmatizing attitudes vary by region, which may possibly have led to underreporting.[19,20] Furthermore, even though we emphasized the strengths of our sample above, generalizability may as well be diminished by the large proportion of kidney transplant recipients among our participants. Half up to two-thirds of participants in our studies had received a kidney transplant, which is considerably more than the proportion of kidney transplant recipients in the Dutch population with CKD.[21] A thorough comparison of patients not on dialysis with and without a kidney transplant was out of the scope of this dissertation and could be further examined. Also, representativeness may be influenced by the low response rate for the online screening, in which only a fifth of the invited patients participated. The digital nature of our eHealth care pathway may have been dissuasive for some individuals without a computer or with a lack of digital skills, who often belong to groups from a cultural minority or with a low socioeconomic status.[22,23] As a consequence, these groups may have been underrepresented in our sample.

The E-GOAL eHealth care pathway is a complex intervention with a broad array of intervention components and behavior change techniques, of which the actual use and exposure differed per individual patient. This broadness and flexibility fostered personalization, however, a limitation is that we could only assess the effectiveness of the intervention as a whole, without being able to measure working mechanisms or active treatment ingredients and how these may have varied across individuals.[24] Additionally, we used a screening procedure to identify patients with psychological distress and suboptimal self-management for trial participation with cut-off points that were predominantly based on previous literature,[1,25] but were unable to investigate whether these criteria were accurate, that is, whether the included patients were indeed the ones who would benefit most from treatment. The adequate cut-off points could have been determined by comparing the same treatment to groups of patients with different psychological distress levels in a sufficiently large sample. In addition, the psychological distress and nonadherence rates found in our studies may have differed if we would have used other cut-off points or instruments.[26-28] Also, the trial duration with a follow-up period of three months post-intervention could be considered too brief to draw conclusions about long-term treatment effectiveness–which is especially important since self-management intervention effects often vanish over time.[29,30] Furthermore, since we did not compare our intervention to standardized or non-tailored iCBT, we cannot formally conclude that the personalized character is needed or more effective than a standardized treatment would be.[31] Although benefits of personalization over non-personalized approaches have been emphasized in literature,[8,32] we could for example not assess whether standardized programs may suffice for certain people, such as patients with only mild psychological distress symptoms.[31] Future research with sufficient statistical power should investigate working mechanisms of the different intervention components, for example by taking potential mediators or process variables into account that may be associated with intervention effectiveness,[33] in order to gain more insights in what works exactly, how and how well, for whom, in what settings, and with what degree of exposure.[24]

Future Directions for Research and Practice

The results of this dissertation have various implications for future research and practice: First, given the co-occurrence of and associations between psychological distress and non-adherence to self-management recommendations found, we recommend targeting psychological distress and self-management jointly. As suggested in literature, reducing psychological distress could facilitate adherence, and vice versa, optimizing adherent and healthy lifestyle behaviors could reduce or protect against psychological distress.[34-36] Second, since we have found that patients have their own unique barriers, facilitators, priorities, and treatment goals, individual differences must be considered in screening and treatment, to offer patients support that matches their personal needs and preferences. As emphasized in recent reviews regarding people with CKD, patient-centered support with a focus on personally meaningful goals and changes may empower each individual patient to cope with disease-related stressors and well-manage their disease.[4,36]

Thus, the findings suggest that personalized, multicomponent interventions that take into account psychological distress as well as adherence to self-management recommendations could potentially improve the quality, acceptability, and effectiveness of CKD care. We propose several recommendations to optimize 1) screening, 2) treatment, and 3) eHealth. Furthermore, for successful continued development, evaluation, and implementation of the eHealth care pathway or similar self-management interventions, we recommend using 4) ongoing co-creation and 5) implementation strategies to integrate interventions in regular care. These five future directions for research and practice will be outlined here.

Screening

The findings of this dissertation show the importance of screening for psychological distress and self-management difficulties as a first step in an eHealth care pathway. Our studies show that people with CKD experience a broad variety of difficulties that may hinder their adherence to self-management recommendations. Also, they vary in areas of functioning and self-management that they prioritize for improvement. Therefore, in the future, screening could be broadened to identify a more extensive range of potential barriers and priorities. For instance, a standardized minimum set of patient-reported outcomes (PROs) that are important to patients could be assessed with recommended PRO-measures (PROMs),[37] which are currently being implemented in Dutch routine nephrology care.[38] Also, the Personalized Priority and Progress Questionnaire (PPPQ) developed in this dissertation provides an opportunity for rapid screening in a range of areas regarding patients' functioning, wellbeing, and health behaviors. Items could be added or removed to assure relevance to different contexts and populations. Importantly, we used a stepped approach of two successive screening parts and recommend using a similar approach in the future, in order to not unnecessarily overburden patients: a brief initial screening to detect problems and symptoms and, only if indicated, a more extensive assessment to decide which patients may benefit from which kind of treatment, that is, to tailor treatment to an individual's needs and priorities.[8]

Based on screening results, treatment recommendations can be tailored to each individual's impairments, resources, and needs. In our eHealth care pathway, tailoring was done in different ways: First, the iCBT treatment with self-management support was only offered to patients who needed it, that is, whose screening results showed co-occurring psychological distress and suboptimal self-management. Second, visualized screening results (Personal Profile Charts) were used at the start of treatment to guide the conversation between patient and therapist and to set personally relevant goals. Ideally, to enhance shared-decision making, both patients and their healthcare providers should have direct insights in screening results and discuss possibilities for referral to different kinds of support. That is, health professionals from our participating centers suggested that screening could be a starting point to facilitate selecting the most suitable from a palette of interventions. Our iCBT mainly targeted individual patients themselves, however, as patients in our study also reported many barriers and facilitators for self-management related to their physical and social environments, interventions could be included that address social or environmental determinants. An example of such a palette of interventions exists in the field of cardiovascular prevention and rehabilitation: A personalized digital platform has been made by the Dutch BENEFIT-for-all consortium, that integrates a variety of evidence-based interventions, aiding the matchmaking between patients and interventions.[39,40] In current Dutch nephrology research, to facilitate decision-making based on screening or PRO results in CKD, a patient-centered communication and treatment guide is being developed (Dutch Kidney Foundation 21OM+002). This ‘PRO-guide’ will provide health professionals guidance on how to act upon patient-reported outcome results, and may facilitate referral to the most suitable intervention or health professional, in order to improve personally relevant health outcomes.

Treatment

Within our iCBT intervention with self-management support, patients selected, in collaboration with a therapist, their own treatment content from a range of treatment modules and exercises, in order to tailor treatment content to their goals and preferences. In the future, several adaptations could be made and additional content could be included to provide even more options for personalization and to potentially enhance effectiveness. First, as mentioned before, each intervention trajectory was focused on a single individual. Participants in our studies indicated an important role of social support in determining the success of their self-management, and some patients would have valued group treatment or peer sharing elements. Therefore, social support systems between patients, such as online forums or live chats, could be used to exchange experiences and information, as well as to motivate and emotionally support each other.[41-43] This reciprocal peer-to-peer support can empower patients and enhance their self-efficacy for behavior change.[42,43] Also, ongoing availability of contact between patients after termination of the intervention can aid to sustain newly adopted behaviors and thus improve long-term outcomes.[41] Since our participating patients had contrasting opinions with regard to contact with fellow patients, peer-to-peer support could be included as an optional treatment element for patients to choose if they perceive an added value for their personal treatment trajectory.

Second, participants emphasized the importance of disease acceptance and optimism in reducing psychological distress and achieving adherent self-management behaviors. Therefore, intervention techniques that attend to acceptance of negative thoughts and feelings and that promote personal values and meaningful behaviors may be suitable additions. These kinds of techniques (e.g., value identification or mindfulness exercises) are offered in Acceptance and Commitment Therapy (ACT)—a “third wave” wing of CBT.[44] In our treatment, we also included positive psychology techniques (e.g., identifying character strengths) with a focus on patients’ personal and protective resources, as well as on positive emotions, to strengthen resilience to cope with stressors, increase positive affect, and alleviate psychological distress symptoms.[45] Adding additional ACT and positive psychology components to a CBT intervention can further enhance opportunities for personalizing treatment, by providing patients the freedom to choose which techniques they prefer to cope with psychological distress and facilitate their self-management behaviors.[44,45]

eHealth

Our results demonstrate the acceptability, feasibility, and usability of eHealth applications to provide person-centered care that is adaptable to different settings and circumstances. For instance, our blended intervention proved to be sufficiently flexible to continue providing online care during the COVID-19 pandemic, when face-to-face consultations were hampered. These benefits of eHealth are also stressed in literature: Patients and health professionals value the relatively easy access, flexibility, and time saved when using eHealth interventions from home, where patients are can easily implement newly learned skills and habits in their daily environments.[36,46,47] However, it has been emphasized that interactions with health professionals should not be entirely replaced by eHealth,[36] particularly considering patients’ digital health literacy or eHealth literacy.[48] eHealth literacy includes the skills needed to search, select, and use online health information and healthcare-related digital applications and interventions.[49] To maximize the benefits of eHealth interventions, designs should be accessible for patients with different levels of eHealth literacy, by designing user-friendly applications and providing tailored instructions or support to use the intervention.[48,50] Furthermore, tailored alternatives should be provided for people with low eHealth literacy, such as different delivery modes and amounts of blending with face-to-face care.[51,52] In our intervention, we tailored the modes of delivery to an individual participant’s needs and skills. For instance, we offered paper-and-pencil alternatives for the online questionnaires and face-to-face or telephone consults in addition to online messages to those who needed it. In the future, to fit the understanding and skills of different users, more diverse and interactive intervention content can be developed by going beyond texts and visual images. For example audio, video, and even voice recognition and automated conversation elements (e.g., automated audio feedback that can be tailored to a patient’s recorded voice messages) can be included.[41] In short, accessible and tailorable approaches should be offered in eHealth interventions to respond to individual differences.[53]

Co-Creation

When further developing the eHealth care pathway, co-creation with stakeholders should remain a priority. First and foremost, patient needs with regard to every intervention component should be assessed. In our research, people with CKD provided feedback on the intervention in the development stages, which probably enhanced the intervention's relevance for the target group and contributed to participants' satisfaction and positive experiences. Also, in the evaluation stages, we used questionnaires and interviews based on the Unified Theory of Acceptance and Use of Technology[54] to evaluate participants' experiences regarding the eHealth screening and treatment. In a future research project, these process data could be used to create an improved version of the existing intervention. For future research we recommend involving patients even to a larger extend by using additional or more advanced co-creation methods, for example guided by the CeHRes Roadmap.[55] This roadmap entails different phases to develop and implement eHealth interventions in a participatory process, in which end-users share their wants and needs with regard to both intervention design and content. The co-creation process is iterative, that is, formative evaluation takes place in continuous cycles to examine whether the intervention works or needs further adaptations.[55,56] Not only patients, but also other relevant stakeholders including health professionals should actively participate, to examine opportunities for a beneficial integration into their daily practice.[57] Also, healthcare organization management should be invited to participate in co-creation to achieve sustainable and economic integration in regular care.[57] Thus, user-centered and stakeholder-driven innovation cycles are recommended to keep on improving eHealth interventions to their optimal design and content, to improve their adoption, acceptability, effectiveness, and implementation.[41,48,56]

Specific attention is needed for collaboration with and tailoring to the needs of 'hard-to-reach' minority groups, such as patients with low socioeconomic status.[22] These vulnerable and under-served groups are often challenged by numerous stressors in their daily lives (e.g., financial strain),[58] and therefore usually experience higher stress levels than people from more affluent backgrounds.[59] In line with our findings regarding the co-occurrence of distress and difficulties in self-management, these stressors have been associated with unhealthy lifestyles, which increase risks of adverse health outcomes (see also Figure 2 in the General introduction).[58,59] That is, under-served groups may need self-management support the most,[60] however, they tend to benefit less from interventions[60] and many feel hesitant or incapable of using eHealth applications.[22] When eHealth support is not adapted to or used by such vulnerable groups, it thus has a risk of exacerbating health inequalities.[48] Therefore, co-creation processes with different patients, including minority groups, are needed throughout the process of development and evaluation. In this way, co-creation can result in more inclusive interventions that are tailorable to participants with different backgrounds, challenges, and needs.[22,48]

Integration in Regular Care

In addition to continued development and evaluation, the impact of eHealth interventions depends on their sustainable implementation in regular clinical care.[57] A screening tool with visualized feedback may form an easily implementable tool at reasonable costs,[61] and previous research shows that eHealth and iCBT interventions could be cost-effective too.[62,63] Due to the standardized research procedures, the E-GOAL eHealth care pathway was not yet fully incorporated into regular care in the hospital departments. For instance, external psychologists guided treatments. In future research and implementation steps, more engagement of regular healthcare providers (e.g., direct referrals by treating nephrologists and routine follow-up on assessments of screening and treatment outcomes during hospital visits) could further increase intervention uptake and motivate maintenance of patients' behavior changes once the intervention ended.[38,64] Long-term effectiveness after cessation of behavior change interventions is challenging to achieve and therefore, integrating an intervention in a 'real world' setting from early research stages on should receive more attention to prevent sporadic care and to achieve sustainability over time.[29,64] Promising opportunities to realize sustainable implementation are eHealth living labs, that is, real-life test environments in which patients, health professionals, policymakers, and scientists can collaborate to develop, evaluate, and implement eHealth innovations as a part of regular healthcare.[48,65]

The present dissertation yielded an eHealth care pathway consisting of different intervention components that could be further investigated or implemented in clinical practice. Currently, several promising components of the E-GOAL eHealth care pathway are being further developed and investigated for implementation among different patient populations. The screening tool in eHealth application PatientCoach has been translated to a mobile app version, and is used in various studies to enhance health outcomes and quality of care for patients with severe asthma in The Netherlands (Pulmonary Rehabilitation of Asthma: a Trial of sustained Internet-based Self-management Support [PRACTISS])[66] and

Europe (Severe Heterogeneous Asthma Research collaboration, Patient-centred [SHARP]).[67] The effectiveness and cost-effectiveness of the iCBT intervention in eHealth application E-coach is currently being evaluated among patients with kidney failure (E-HEalth treatment in Long-term Dialysis [E-HELD]).[68] In addition, E-coach, including the treatment modules developed in this dissertation, is being used in regular care in the Leiden University Treatment and Expertise Center (LUBEC). In the academic treatment center LUBEC, people with chronic physical diseases (e.g., cardiovascular, kidney, and rheumatic diseases) and persistent somatic symptoms (e.g., irritable bowel syndrome, fibromyalgia, and chronic fatigue) receive blended and personalized psychological healthcare.

Conclusions

The aim of this dissertation was to develop and evaluate the effectiveness of a personalized and blended eHealth care pathway to improve psychological health and self-management among people with CKD not receiving dialysis. We addressed the aim by using qualitative methods and stakeholder involvement for systematic questionnaire and intervention development, and quantitative and experimental research designs to detect psychological and self-management difficulties and evaluate the multicomponent intervention effectiveness. The dissertation provided multiple insights. 1) Many individuals with CKD experience problems in self-management, which can be hindered by many different barriers of which a highly prevalent one is psychological distress. Therefore, interventions should be implemented that screen for and treat both psychological distress and non-adherence to self-management recommendations. 2) Compared to regular care only, our personalized eHealth treatment did not significantly improve psychological distress, depressive symptoms, quality of life, or self-efficacy, whereas anxiety symptoms, chronic condition self-management, and personalized outcomes did improve significantly, and effects on the latter were maintained over time. These mixed results indicate that screening and treatment strategies could be implemented that are personalized to individual priorities and needs. 3) eHealth solutions are feasible and acceptable to provide this type of person-centered care. This dissertation has broadened knowledge regarding psychological health and self-management of people with CKD, and provides insights in their priorities and support needs, which can be of use to take the next steps in promoting personalized nephrology eHealth care.

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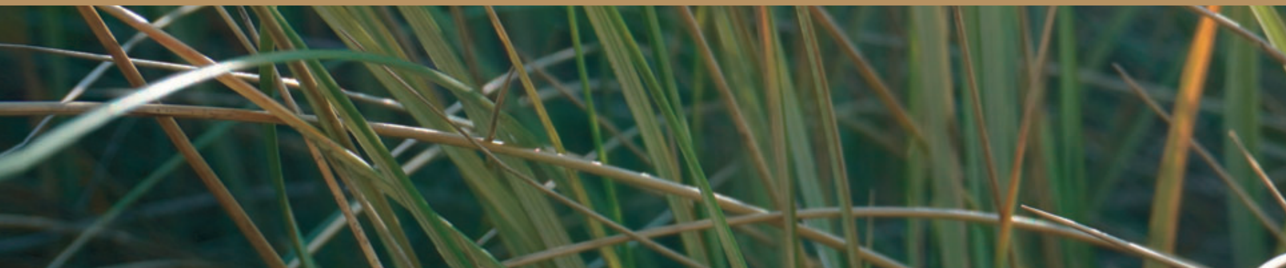

Appendix

Nederlandse samenvatting (Dutch summary)

Publications

Curriculum vitae

Dankwoord (Acknowledgments)

Nederlandse samenvatting (Dutch summary)

Barrières Doorbreken, Paden Personaliseren
Mentale gezondheid en zelfmanagement van mensen met chronische nierschade

Dit proefschrift gaat over de mentale gezondheid en zelfmanagement van mensen met chronische nierschade (CNS). In **Hoofdstuk 1**, de introductie, wordt dit onderwerp toegelicht. Mensen met CNS hebben over het algemeen permanente schade aan de nieren. In de meeste gevallen wordt deze schade geleidelijk erger. De nieren functioneren dus steeds minder goed. In het huidige proefschrift richten we ons op patiënten die geen nierfunctievervangende dialysebehandeling ondergaan, inclusief mensen die een niertransplantatie hebben gehad. Deze patiënten kunnen het verlies van nierfunctie vertragen door zich te houden aan een reeks aanbevelingen voor zelfmanagement: het naleven van een gezond en zoutbeperkt dieet, voldoende bewegen, medicijnen volgens voorschrift nemen, het handhaven van een gezond gewicht en niet roken.

Helaas is het voor veel patiënten moeilijk om al deze aanbevelingen op te volgen. Dit kan deels worden verklaard door de aanzienlijke impact van de ziekte en behandeling op het dagelijks leven en de daarmee gepaard gaande zorgen van patiënten: veel van hen hebben psychische klachten, zoals somberheid of depressieve klachten, stress, spanning of angstklachten. De meeste interventies (dat wil zeggen: aanvullende ondersteuning vanuit de zorg) richten zich ofwel voornamelijk op psychische klachten ofwel voornamelijk op zelfmanagementtaken. Het werkt mogelijk beter als beide typen interventies worden gecombineerd: het verminderen van psychische klachten kan het uitvoeren van de zelfmanagementtaken makkelijker maken. Andersom kan succesvolle zelfmanagement en dus een gezonde leefstijl iemands psychische klachten verminderen.

Omdat ieder individu uniek is, zijn er grote verschillen in de psychische en zelfmanagementproblemen, belemmeringen, behoeften, voorkeuren en prioriteiten van patiënten. Met deze individuele behoeften kan rekening worden gehouden door interventies op maat te maken, oftewel te personaliseren. Personalisatie kan worden vergemakkelijkt door interventies via digitale zorg (eHealth-toepassingen) aan te bieden. Daarom was het hoofddoel van dit proefschrift het ontwikkelen en evalueren van de effectiviteit van een eHealth-zorgpad om gepersonaliseerde psychosociale en zelfmanagementondersteuning te bieden aan mensen met CNS die geen dialyse ondergaan. Bij de ontwikkeling en evaluatie hebben we verschillende kwalitatieve en kwantitatieve onderzoeksmethoden gebruikt. Het

E-GOAL (*E-health Guidance in identifying and Overcoming psychological barriers for Adopting a healthy Lifestyle among patients with chronic kidney disease*) eHealth-zorgpad omvatte:

1) een screeningsinstrument met vragenlijsten waarvan de resultaten grafisch werden samengevat in gepersonaliseerde profielkaarten. De uitkomsten van de screenings dienden om patiënten te identificeren die psychische klachten en moeite met zelfmanagement ervaarden en die dus baat konden hebben bij de behandeling, om de behandeling te personaliseren en om de voortgang in de tijd te volgen,
2) een begeleide psychosociale behandeling via internet bestaande uit cognitieve gedragstherapie en zelfmanagementondersteuning. De belangrijkste behandelingsdoelen waren het behandelen van psychische klachten, het verminderen van psychosociale belemmeringen en het bevorderen van psychosociale helpende factoren voor het naleven van zelfmanagementtaken, en het ondersteunen van patiënten bij het aannemen en volhouden van een gezonde leefstijl.

Belemmeringen en Helpende Factoren voor Zelfmanagement

In **Hoofdstuk 2** hielden we groepsgesprekken met patiënten en zorgverleners in focusgroepen, om inzicht te krijgen in psychosociale belemmeringen en helpende factoren voor het naleven van zelfmanagementtaken met betrekking tot dieet, lichaamsbeweging, medicijngebruik, gewicht en niet-roken. We vonden veel belemmeringen en helpende factoren, zoals kennis en intrinsieke motivatie van patiënten, emotioneel welbevinden en psychische klachten, optimisme en ziekteacceptatie. De bevindingen kwamen overeen met de veertien domeinen van het theoretische raamwerk *Theoretical Domains Framework* (TDF). De domeinen die het meest besproken werden, waren 'sociale invloeden' 'en 'omgevingscontext en middelen', namelijk hoe de (sociale) omgeving van patiënten het naleven van de zelfmanagementtaken en een gezonde leefstijl hindert of ondersteunt. De grote hoeveelheid van voornamelijk omgevings-gerelateerde, motivatie-gerelateerde en emotionele belemmeringen die patiënten ervaren, kan verklaren waarom het velen niet lukt om zich aan de aanbevelingen voor zelfmanagement bij CNS te houden. Deze bevindingen suggereren dat psychosociale ondersteuning en zelfmanagementondersteuning gecombineerd zouden moeten worden, omdat het ene het andere kan bemoeilijken en/of vergemakkelijken. Een interventie die zich richt op zowel het verminderen van psychische klachten als het verbeteren van zelfmanagement kan daarmee leiden tot betere gezondheidsuitkomsten bij mensen met CNS. Gezien de grote variatie tussen individuen in waargenomen belemmeringen en helpende factoren, duiden de resultaten op een behoefte aan persoonlijk op maat gemaakte gedragsinterventies om zelfmanagement te ondersteunen. De TDF-domeinen kunnen worden vertaald naar bijpassende technieken voor gedragsverandering in dergelijke interventies. Zo kunnen de domeinen een leidraad zijn in de ontwikkeling van geschikte strategieën om individueel ervaren psychosociale belemmeringen en helpende factoren op te sporen en aan te pakken.

E-GOAL eHealth-Zorgpad

In **Hoofdstuk 3** beschreven we de ontwikkeling van een innovatief eHealth-zorgpad gericht op het opsporen en behandelen van psychische klachten en suboptimale zelfmanagement, passend bij de behoeften en voorkeuren van individuele patiënten met leefstijl-gerelateerde chronische ziekten, waaronder mensen met CNS. Elk onderdeel van het eHealth-zorgpad werd systematisch ontwikkeld door (1) initiële versies te maken op basis van eerder door ons onderzoeksteam ontwikkelde en geëvalueerde interventies, wetenschappelijke kennis (waaronder de hierboven beschreven bevindingen uit groepsgesprekken) en theoretische kaders voor gedragsverandering (bijv. TDF en het Gedragsveranderingswiel); (2) co-creatie om feedback te vergaren van patiënten en zorgverleners; en (3) verfijning van het zorgpad om tegemoet te komen aan de behoeften van gebruikers. In het uiteindelijke eHealth-zorgpad konden patiënten online korte screeningsvragenlijsten invullen om psychische klachten en suboptimale zelfmanagement op te sporen. Met dit screeningsinstrument werden scores grafisch samengevat in zogenaamde Persoonlijke Profielkaarten. Patiënten met psychische klachten en moeite met zelfmanagement kregen automatisch aanvullende vragenlijsten, die werden afgenomen om een psychosociale interventie van drie maanden af te stemmen op hun prioriteiten en behoeften. Met het screeningsinstrument kon de voortgang over tijd in kaart worden gebracht. De systematische ontwikkelingsfasen die in dit hoofdstuk worden geschetst, kunnen worden toegepast bij toekomstige complexe interventie-ontwikkeling en vormen een basis voor de vervolgstappen van evaluatie, verdere ontwikkeling en implementatie van een eHealth-zorgpad.

Psychische Klachten en Zelfmanagement

In **Hoofdstuk 4** onderzochten we de relaties tussen psychische klachten en zelfmanagement met de resultaten van de screeningsvragenlijsten, die werden ingevuld door 460 mensen met CNS. We zagen dat 27.2% van de patiënten aangaf psychische klachten te ervaren, dat wil zeggen, milde tot ernstige depressie- of angstklachten, of allebei. Bovendien gaf meer dan twee-derde aan één of meer aanbevelingen voor zelfmanagement niet op te volgen, met betrekking tot dieet, lichaamsbeweging, medicijngebruik, gewicht en niet-roken. We vonden dat psychische klachten samenhingen met het minder goed naleven van dieet- en medicijnvoorschriften en met minder lichaamsbeweging, maar niet met gewicht of roken. De bevindingen waren vergelijkbaar voor depressieve klachten, terwijl angstklachten alleen samenhingen met minder goede naleving van dieet- en medicijnvoorschriften. In totaal rapporteerden vier op de vijf patiënten met psychische klachten ook suboptimale zelfmanagement. Om dit verder te onderzoeken, ontwikkelden we een CNS-zelfmanagementindex door vijf binaire indicatoren voor het naleven van de aanbevelingen op te tellen (wel- versus niet-naleving). Daarmee stelden we vast dat een toename van psychische klachten samenhing met een verhoogde kans op niet-naleving van een groter aantal verschillende aanbevelingen. Zo gaven patiënten die leden aan matige tot ernstige psychische klachten relatief vaker aan drie of meer aanbevelingen niet na te leven in vergelijking met patiënten met geen of milde klachten. De resultaten suggereren dat psychische klachten een mogelijke belemmering kunnen zijn voor zelfmanagement, hoewel we geen conclusies kunnen trekken over oorzaak en gevolg. De bevinding dat psychische klachten en moeite met zelfmanagement vaak samengaan, onderstreept de wenselijkheid om psychische klachten en zelfmanagement gezamenlijk te behandelen, en onderbouwt dus de basis van het E-GOAL eHealth-zorgpad met de gecombineerde aanpak als een potentieel geschikte interventie voor mensen met CNS.

Persoonlijke Prioriteiten- en Progressievragenlijst

In **Hoofdstuk 5** hebben we de *Personalized Priority and Progress Questionnaire* (PPPQ) ontwikkeld en gevalideerd (dat wil zeggen: geëvalueerd of het instrument betrouwbaar is en meet wat het zou moeten meten). De PPPQ is een kort gepersonaliseerd instrument dat (1) de prioriteiten voor verbetering van de individuele patiënt in kaart brengt, (2) de voortgang meet op de door iemand zelf geprioriteerde gebieden van functioneren en zelfmanagement, en (3) persoonsgerichte zorg bevordert in zowel klinisch onderzoek als in de praktijk. We ontwikkelden het instrument op basis van literatuur over gepersonaliseerde metingen en patiëntprioriteiten, interviews met patiënten en feedback van medisch psychologen. Vervolgens evalueerden we de psychometrische eigenschappen ervan. De PPPQ bleek een gemakkelijk in te vullen en valide instrument. De vragenlijst vergemakkelijkt het opsporen van uitkomsten in functioneren en zelfmanagement die persoonlijk betekenisvol zijn voor de individuele patiënt. Dit maakt de PPPQ een geschikt instrument om gepersonaliseerde interventies te evalueren in onderzoeken waarin patiënten werken aan verschillende behandeldoelen: het meten van gepersonaliseerde uitkomsten maakt het mogelijk om de effectiviteit van een interventie te evalueren, rekening houdend met de unieke doelen en behandeltrajecten van elke patiënt. In de klinische praktijk zou de PPPQ kunnen worden gebruikt als een snel en eenvoudig hulpmiddel om de prioriteiten van patiënten in kaart te brengen, de gedeelde besluitvorming over de gewenste behandeling te verbeteren en behandelingen op maat te maken. Vervolgens kan de PPPQ worden ingezet om iemands functioneren op deze persoonlijk relevante gebieden te monitoren. Met deze kenmerken draagt de PPPQ bij aan het leveren en evalueren van persoonsgerichte zorg.

Psychosociale Behandeling via Internet

In **Hoofdstuk 6** hebben we de effectiviteit van het behandelgedeelte van het gepersonaliseerde E-GOAL eHealth-zorgpad geëvalueerd in een interventiestudie waaraan 121 mensen met CNS deelnamen. De patiënten in de controlegroep kregen alleen de reguliere zorg, terwijl patiënten in de interventiegroep aanvullend de psychosociale eHealth-behandeling aangeboden kregen over een periode van drie maanden. Vergeleken met alleen de reguliere zorg verminderde deze eHealth-interventie de primaire uitkomst psychische klachten niet. De interventie had ook geen gunstige effecten op depressieve klachten, gezondheids-gerelateerde kwaliteit van leven of zelfeffectiviteit. Wel zagen we licht gunstige effecten op angstklachten en zelfmanagement evenals sterkere effecten op persoonlijk relevante gebieden van functioneren en zelfmanagement na drie maanden in vergelijking met enkel de reguliere zorg. Effecten op deze laatstgenoemde, gepersonaliseerde uitkomsten bleven na zes maanden behouden. Patiënten waren verder zeer tevreden over de behandeling: ze gaven het een gemiddelde score van 7.7 en evalueerden de samenwerking met hun therapeut met een 8.6. De bevindingen gaven ook inzicht in de veelvoorkomende prioriteiten voor verbetering van mensen met CNS, waaronder vermoeidheid, lichaamsbeweging, dieet, gewicht en beperkingen in dagelijkse activiteiten. De hoge bereidheid tot deelname aan de behandeling, evenals de positieve evaluaties door deelnemers, suggereren een goede bruikbaarheid en geschiktheid van de interventie voor mensen met CNS die geen dialyse ondergaan. Er is echter meer onderzoek nodig om het gebrek aan een gunstig effect op psychische klachten te begrijpen en om de interventie te verbeteren. Dat de interventie niet goed de algemene uitkomsten zoals psychische klachten en juist wel persoonlijk relevante uitkomsten leek te verbeteren, suggereert dat toekomstige studies gepersonaliseerde uitkomsten voor persoonsgerichte interventies zouden kunnen overwegen, die individueel betekenisvolle behandeldoelen en verbeteringen weergeven.

Conclusies

In **Hoofdstuk 7** staat een samenvatting van de andere hoofdstukken, die overeenkomt met deze Nederlandse samenvatting. Ook worden de bevindingen van dit proefschrift samengebracht, de zwakke en sterke punten van het onderzoek bediscussieerd, evenals de implicaties voor de praktijk en voor toekomstig onderzoek. Samengevat omvat dit proefschrift de verschillende stappen in het proces van interventie-ontwikkeling en evaluatie. De resultaten geven verschillende inzichten. 1) Veel mensen met CNS hebben moeite met het naleven van aanbevelingen voor zelfmanagement. Dit kan komen door allerlei verschillende belemmeringen, waarvan psychische klachten een veelvoorkomende is. Daarom zijn innovatieve, gepersonaliseerde interventies nodig met screening en behandeling van zowel psychische klachten als suboptimale zelfmanagement. 2) Het E-GOAL eHealth-zorgpad is een voorbeeld van een dergelijke innovatieve interventie. De psychosociale behandeling via internet met cognitieve gedragstherapie en zelfmanagementondersteuning was niet effectief in het verminderen van psychische klachten (de primaire uitkomst) in vergelijking met alleen reguliere zorg. Daarnaast zagen we dat patiënten wel verbeteringen ervaarden in hun persoonlijke prioriteiten in zowel functioneren als zelfmanagement. Deze gemengde resultaten laten zien dat interventies zouden kunnen worden aangeboden die op maat zijn voor elke individuele patiënt, met gepersonaliseerde uitkomsten die individueel betekenisvolle behandeldoelen en verbeteringen weergeven. 3) Om zulke persoonsgerichte zorg te verlenen, zijn eHealth-toepassingen potentieel geschikt en wenselijk.

Kortom, dit proefschrift heeft bijgedragen aan het wetenschappelijke begrip van mentale gezondheid en zelfmanagement bij mensen met CNS. De bevindingen geven inzicht in hun prioriteiten en zorgbehoeften, die in de medische praktijk kunnen worden geadresseerd om patiënten te ondersteunen bij het verbeteren van hun mentale en fysieke welzijn. Hiermee kunnen de volgende stappen worden gezet in het bevorderen van persoonsgerichte eHealth-zorg binnen de nefrologie.

Publications

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Curriculum vitae

Katja Cardol was born on 10 September 1991 in Haarlem, the Netherlands. After obtaining her Gymnasium diploma (cum laude) in 2009 at Fioretti College in Lisse, she learned Spanish abroad and worked before starting her Bachelor in Psychology at Leiden University in 2010. In 2014, she finished her Bachelor (cum laude) with an exchange year at the University of Granada in Spain, where she also started the research for her Master thesis on the relationships between physical activity and self-regulation problems under supervision of Dr. José C. Perales and Dr. Winifred A. Gebhardt. In January 2016, Katja graduated in the Master specialization Health Psychology (cum laude) at Leiden University, which she concluded with a clinical practice internship in Santiago de Compostela, Spain. There she obtained the Family Therapy accreditation (Basisopleiding Systeemtherapie, 2016) and Sports Psychologist accreditation (Basisaantekening Sportpsycholoog, 2016), and continued working as a (sports) psychologist after graduation.

In 2016, Katja returned to Leiden University to start working on her doctoral thesis at the Health, Medical and Neuropsychology Unit. For her PhD project, she co-designed an eHealth care pathway with psychological and lifestyle behavior change modules, coordinated a large study in four hospitals, and provided psychological and lifestyle treatment (e-coaching) for patients with chronic kidney disease. For their paper on the development of the eHealth care pathway (Chapter 3), Katja and her co-author Judith Tommel received a Team Science Award (2021, Faculty of Social and Behavioural Sciences, Institute of Psychology).

During her PhD, Katja was involved in various research initiatives, including a literature survey of regular screening and adequate symptom response of people with or at risk of cardiovascular disease, and a qualitative study to explore treatment experiences of individuals with persistent Lyme disease. She also worked as a psychologist and eHealth developer in a social enterprise to support people with kidney diseases in maintaining a healthy lifestyle.

Katja started teaching at Leiden University in 2017. She taught various courses (e.g., Basic Therapeutic Skills, Cognitive Behaviour Interventions) within the Bachelor in Psychology and within Master specializations, and supervised Master students during their theses and clinical internships. Additionally, she educated healthcare professionals at Leiden University

Medical Center in health behavior change and motivational interviewing techniques. She obtained the Cognitive Behavioral Therapy accreditation (Basisopleiding Cognitieve Gedragstherapie, 2018) and partial University Teaching Qualification (Basiskwalificatie Onderwijs, 2020).

Currently, Katja holds a teaching position at the Health, Medical and Neuropsychology Unit, and started as a project leader in a project to promote a healthy lifestyle among healthcare professionals at Leiden University Medical Center. She continues her work as a self-employed sports psychologist, which she has been doing since 2017.

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