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

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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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