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# eHealth to Improve Psychological Functioning and Self-Management of People With Chronic Kidney Disease: A Randomized Controlled Trial

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## ABSTRACT

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

**Methods:** Primary outcome of the open two-arm parallel randomized controlled trial in four Dutch hospitals was psychological distress at posttest directly after the intervention and at 3-month follow-up. Secondary outcomes were physical and mental health-related quality of life, self-efficacy, chronic disease self-management, and personalized outcomes, that is, perceived progress compared with 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, health-related quality of life, self-efficacy, and chronic condition self-management, whereas analyses of covariance showed significantly more perceived progress in the intervention group at posttest on personally prioritized areas of functioning ($b = 0.46$, 95% confidence interval = 0.07–0.85) and self-management ($b = 0.55$, 95% confidence interval = 0.16–0.95), with Cohen $d$ values of 0.46 and 0.54 (medium effects), respectively. Effects on personalized outcomes were maintained at follow-up.

**Conclusions:** Compared with regular care only, the electronic health intervention did not reduce psychological distress, whereas personalized outcomes did improve significantly after intervention. Future studies could consider personalized outcomes that reflect individually relevant areas and treatment goals, matching person-tailored treatments.

**Trial Registration:** Registered at the Netherlands Trial Register with study number NTR7555 (https://trialsearch.who.int/Trial2.aspx?TrialID=NTR7555).

**Key words:** chronic kidney disease, randomized controlled trial, psychological distress, self-management, eHealth, patient-tailored care.

**ANCOVA** = analysis of covariance, **b** = parameter estimate, **CI** = confidence interval, **CKD** = chronic kidney disease, **d** = Cohen d, **eHealth** = electronic health, **GAD-7** = Generalized Anxiety Disorder scale, **HRQoL** = health-related quality of life, **iCBT** = Internet-delivered cognitive-behavioral therapy, **PHQ-9** = Patient Health Questionnaire Depression Scale, **PHQ-ADS** = Patient Health Questionnaire Anxiety and Depression Scale, **PPP-functioning** = progress on personally prioritized areas of functioning, **PPPQ** = Personalized Priority and Progress Questionnaire, **PPP-self-management** = progress on personally prioritized areas of self-management, **RAND SF-36** = RAND 36-item Short Form Health Survey, **RCT** = randomized controlled trial, **SDC** = Supplemental Digital Content

SDC Supplemental Digital Content

## 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 nonsmoking, 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 nonadherent behaviors (8–10). Accordingly, psychological distress has been associated with suboptimal self-management among patients with CKD (11). These mechanisms are alarming because 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 bidirectional 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 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, 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, because patients focused on distinct, personally meaningful goals, they likely improved on different outcomes. Therefore, we included personalized outcome measures (Tommel et al., 2022, unpublished).

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 at posttest directly after the intervention and at 3-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; (20)), and perceived progress on personally prioritized areas of functioning (PPP-functioning) and self-management (PPP self-management) (Tommel et al., 2022, unpublished) at posttest that would be sustained till follow-up. For the latter, personalized outcomes, we expected no worsening within-group at follow-up, 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 (NTR7555), and complies with the 1964 Declaration of Helsinki. The Consolidated Standards of Reporting Trials statement (Supplemental Digital Content [SDC] 1, Table S1, http://links.lww.com/PSYMED/A888) and the Template for Intervention Description and Replication checklist were used for reporting (21,22).

### Participants

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" (28). 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

Box 1. Inclusion and Exclusion Criteria.

### Criteria screening phase
Inclusion criteria
- Under medical treatment by an internist-nephrologist
- Chronic kidney disease with an eGFR 20–89 ml/min per 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 mm Hg 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; (23,24)) 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 nonadherence based on questionnaire cutoff points)[d,e] (1)

Exclusion criteria
- Severe depressive or anxiety symptoms (PHQ-9 ≥20 or GAD-7 ≥15; (25))
- Ongoing psychological treatment elsewhere

eGFR = estimated glomerular filtration rate; PHQ-9 = Patient Health Questionnaire Depression Scale; GAD-7 = Generalized Anxiety Disorder scale.[a] Short Questionnaire to Assess Health-enhancing physical activity (26).[b] Ratio of body weight (in kilograms) and square of height (in meters).[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" (cutoff 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" (cutoff for inclusion ≤6).[e] Simplified Medication Adherence Questionnaire (cutoff for inclusion ≥2 items indicating nonadherence; (27)).

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. In addition, patients with severe psychological distress were not eligible either. They were contacted by telephone 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 (29,30). The intervention had the aims to treat psychological distress, diminish psychosocial barriers and promote facilitators for adherence to self-management recommendations, and support patients in adopting and maintaining healthy and adherent behaviors. Treatment was guided by therapists, that is, 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 because of 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 (25,30). See Figure 2 for an example of modules in E-coach and SDC 2, Table S2, http://links.lww.com/PSYMED/A889, for an overview of all modules.

During the next 3 to 4 months (approximately), 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; (31)) and behavior change techniques (e.g., pros and cons, action planning; (32)). Each patient worked through modules at home and received weekly or biweekly 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,
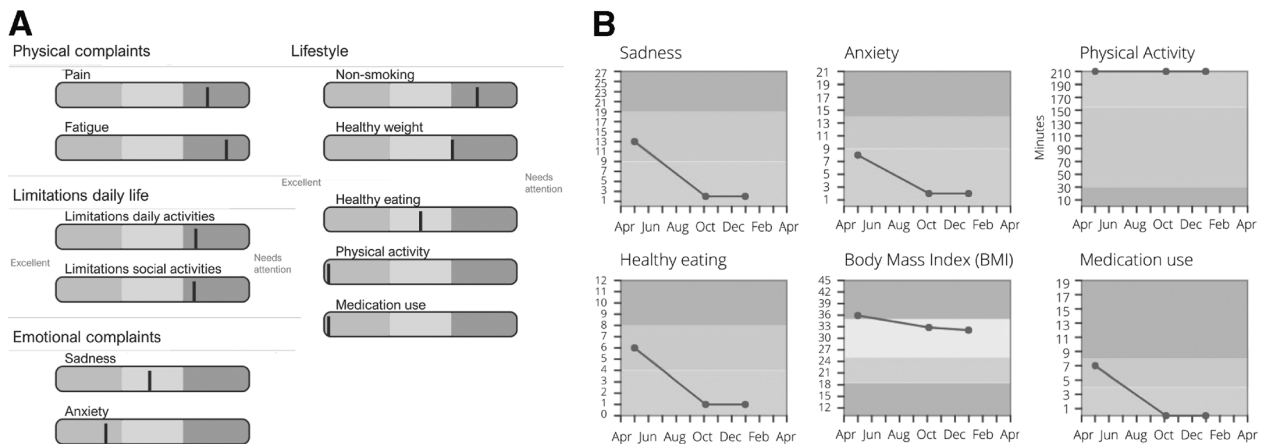
**FIGURE 1.** A and B, Examples of Personal Profile Charts at (A) one time point and (B) progress over time. Traffic light colors indicated current status on domains of functioning and self-management. Additional explanations were shown when hovering the mouse cursor over a domain. Color image is available only in online version www.psychosomaticmedicine.org.

among other things, each patient wrote a letter to themselves regarding their achievements. Afterward, 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 have been published elsewhere (18).

## Data Acquisition and Outcomes
Data were collected at baseline, at posttest directly after the intervention, and at follow-up 3 months after posttest. 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; (33)), a composite of depressive (Patient Health Questionnaire Depression Scale [PHQ-9]; (23)), and anxiety symptoms (Generalized Anxiety Disorder scale [GAD-7]; (24)). Scores range from 0 to 48, with higher scores indicating higher psychological distress. The PHQ-ADS composite was reliable with Cronbach $\alpha$ values of .78, .85, and .88 at baseline, posttest, and follow-up, respectively.

Several secondary outcomes were assessed. Physical and mental HRQoL were measured with the RAND 36-item Short Form
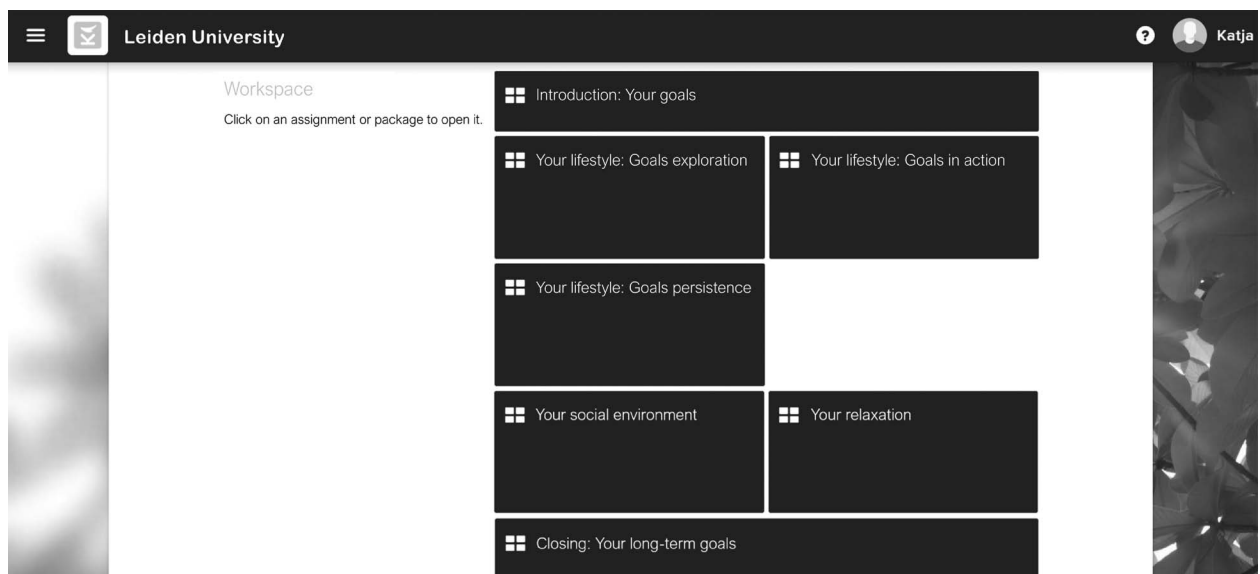


**FIGURE 2.** An example of modules in eHealth application "E-coach." eHealth = electronic health. Color image is available only in online version www.psychosomaticmedicine.org.

Health Survey (34). Physical and mental HRQoL component summary scores range from 0 to 100, with higher scores indicating better HRQoL. Cronbach α values 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 (35). Scores range from 5 to 50, with higher scores indicating stronger belief in the capability of managing disease. Cronbach α values were .83, .82, and .87. Chronic condition self-management was assessed using the Partners in Health scale (20). Scores range from 0 to 96, with higher scores indicating better self-management. Cronbach α 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 nonsmoking) at posttest and follow-up, with the Personalized Priority and Progress Questionnaire (PPPQ) (Tommel et al., 2022, unpublished). From the original 13-item personalized instrument, items (areas) can be added or removed depending on their relevance for the population under study. An example used in this study is the following: "Compared to the last time I completed this questionnaire, I have managed less well/better to eat healthily." Per item (area), scores range from −3 ("much less well") to +3 ("much better"), on which 0 indicates neither worsening nor improvement ("equally well"). 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. The PPPQ was evaluated in two kidney disease samples, showing to be feasible and easy to complete in 2 to 4 minutes. The questionnaire items showed acceptable construct validity and few floor or ceiling effects. Also, in the current study, the scales showed acceptable to good internal consistency with Cronbach α values of .88 and .83 at posttest and follow-up for functioning, and .69 and .73 for self-management. Development and validation of the PPPQ have been further described in another article (Tommel et al., 2022, unpublished).

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 $d$ effect sizes from 0.28 to 0.63 (36–38). We considered Cohen $d$ between the intervention and control groups 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% dropout 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 4 and 6, 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

Because of 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 groups 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 $\chi^2$ tests for categorical variables. These initial data analyses showed that cases with missing data more often completed paper-and-pencil questionnaires than complete cases (39). 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.[1]

To describe the intervention effect in terms of (standardized) treatment outcome differences, mean change scores over time (by subtracting the baseline score from posttest and follow-up scores) were compared between the intervention and control groups. For personalized outcomes (PPPQ), patients reported their perceived progress at posttest and follow-up as a comparison to the previous time point, which precluded subtraction of baseline scores: Means at posttest and follow-up on the PPPQ were used as mean change scores over time. Furthermore, for all outcomes, Cohen $d$ effect sizes were calculated.[2] Effect sizes of 0.2, 0.5, and 0.8 were considered small, medium, and large, respectively (40).

To analyze intervention effectiveness, that is, the effect of the treatment condition (intervention or control) over time, we performed intention-to-treat analysis (including all 121 participants; Figure 3) combined with linear mixed-effects regression (i.e., longitudinal multilevel analysis) using the full-information maximum likelihood estimation method (39). To perform this analysis per outcome variable, we created one long format data set with the outcome scores at baseline, posttest, and follow-up below each other.

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[1] 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. If more than 40% of a participant's data on a variable were missing, the sum score on this variable was missing for this person.

[2] Formula for computing the Cohen $d$ effect size ($\text{ES}_{\text{change}}$) between-group effect sizes of the intervention group (group 1) and control group (group 2): $\text{ES}_{\text{change}}$

$$= \frac{\bar{x}_{\text{change, group1}} - \bar{x}_{\text{change, group2}}}{s_{\text{change, pooled}}}, \text{ where } s_{\text{change, pooled}} = \sqrt{\frac{(n_1-1) \times \text{SD}^2_{\text{change, group1}} + (n_2-1) \times \text{SD}^2_{\text{change, group2}}}{n_1 + n_2 - 2}}$$
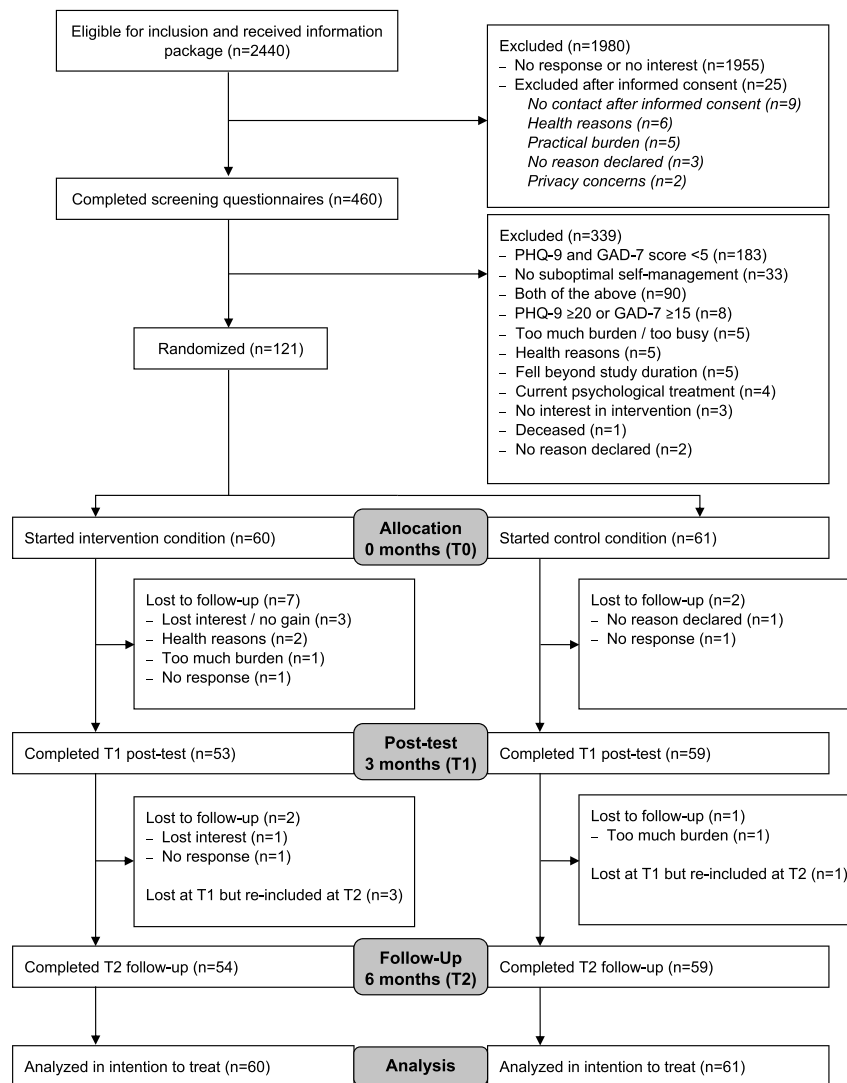
**FIGURE 3.** Participant flow. PHQ-9 = Patient Health Questionnaire Depression Scale; GAD-7 = Generalized Anxiety Disorder scale.

We further created a time variable with values 0 (baseline), 1 (post-test = short-term), and 2 (follow-up = long-term). From this time variable, two dummy variables were created with baseline as reference category, reflecting the short-term (posttest versus baseline) and long-term (follow-up versus baseline) effect of time. Finally, we created the interaction terms between group (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 by group and long-term by 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 RCTs by Fitzmaurice and colleagues; (41)); therefore, the fixed effect of group was not included in the analysis. To improve model fit per outcome, the best 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 information criterion values for nonnested models (see SDC 3, Table S3, http://links.lww.com/PSYMED/A890, 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. We performed Holm-Bonferroni correction for multiple testing (42) on the 10 tests in total (i.e., two tests per primary and secondary outcome) to determine significance with an overall type 1 error rate of $\alpha = .05$.

To assess the intervention effectiveness for personalized secondary outcomes (PPPQ), one-way analyses of covariance (ANCOVAs) were conducted, with group as the independent variable; paper, age, and sex as covariates; and PPP-functioning and PPP-self-management at posttest and follow-up 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. Significance of the four ANCOVA analyses with our personalized outcomes was determined using the Holm-Bonferroni multiple test correction (42) with an overall α level of .05.

Because 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 these exploratory analyses, we did not focus on significance testing and therefore did not apply a multiple test correction. 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.

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 7 in the control group, which all required hospitalization. Adverse events were unrelated to study procedures, and no participant withdrawals occurred because of 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 (standard deviation) estimated glomerular filtration rate was 49.6 (18.5) ml/min per 1.73 m², and 65.3% were kidney transplant recipients. Mean office systolic and diastolic blood pressures were 138.6 (17.0) and 80.9 (9.0) mm Hg, respectively. The mean body mass index was 27.9 (5.4) kg/m², and waist circumference was 100.0 (15.3) cm.

### Intervention Adherence, Module Use, and Evaluation

In the intervention group, 54 patients (90.0%) completed the iCBT treatment according to protocol. Reasons for noncompletion were not experiencing gain ($n = 3$), too high burden ($n = 2$), and health reasons ($n = 1$). Treatment dropouts had a significantly higher age (mean [standard deviation] = 67.9 [7.3]) than completers (56.0 [12.6]; $p = .026$), higher baseline diastolic blood pressure (83.4 [7.5] versus 72.1 [6.1]; $p < .001$), and more physical comorbidities (3.0 [1.3] versus 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] versus 81.5 [8.5]; $p = .042$).

**TABLE 1.** Baseline Participant Characteristics

| Characteristic | Intervention ($n = 60$) | Control ($n = 61$) |
|---|---|---|
| Sociodemographic characteristics | | |
| Age, y | 57.2 (12.6) | 54.8 (15.0) |
| Male sex, n (%) | 32 (53.3) | 36 (59.0) |
| Country of birth, the 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)[b] |
| Employed[c], 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)[d] | 21 (34.4)[e] |
| Kidney transplant recipient, n (%) | 40 (66.7) | 39 (63.9) |
| Time since last kidney transplantation[f], y | 6.8 [8.8] | 6.9 [12.6] |
| History of dialysis, n (%) | 22 (36.7) | 29 (47.5)[b] |
| No. physical comorbidities for which in treatment, n (%) | | |
| 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[g], 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/24 h | 150.1 (51.1)[e] | 145.4 (58.8)[h] |
| Protein excretion rate, mmol/24 h | 0.19 [3.80][h] | 0.15 [5.24][i] |
| Urea excretion rate, mmol/24 h | 392.0 [703.1][j] | 319.0 [571.5][i] |
| Creatinine excretion rate, mmol/24 h | 12.6 [27.2][e] | 11.3 [15.2][i] |
| Albumin excretion rate, mmol/24 h | 31.3 [3199.3][k] | 38.4 [4112.1][l] |
| Potassium excretion rate, mmol/24 h | 66.6 [132.0][h] | 64.0 [120.0][m] |
| eGFR, ml/min per 1.73 m² | 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)[e] | 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][e] | 1.3 [0.5][o] |
| Blood pressure and anthropometric measures | | |
| Office SBP, mm Hg | 140.5 (16.6) | 136.8 (17.3)[b] |
| Office DBP, mm Hg | 82.3 (8.1) | 79.4 (9.6)[b] |

**TABLE 1.** *(Continued)*

| Characteristic | Intervention ($n = 60$) | Control ($n = 61$) |
|---|---|---|
| Body mass index, kg/m$^2$ | 27.3 [5.7] | 26.5 [6.2] |
| Waist circumference, cm | 101.0 [24.0]$^b$ | 100.0 [20.5]$^o$ |
| Self-management behaviors | | |
| Dietary adherence 1–10 score | 6.6 (2.1) | 6.4 (2.3) |
| Physical activity, h/wk | 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/wk | 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) |

eGFR = estimated glomerular filtration rate; LDL = low-density lipoprotein; HDL = high-density lipoprotein; SBP = systolic blood pressure; DBP = diastolic blood pressure.

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.

$^a$ Low education includes primary, prevocational, and vocational education; high education includes advanced secondary and tertiary education.

$^b$ One unknown.

$^c$ Paid job, unpaid/voluntary work, or self-employed.

$^d$ Six unknown.

$^e$ Three unknown.

$^f$ Only for kidney transplant recipients.

$^g$ Cardiovascular disease was defined by the presence of coronary disease, angina pectoris, myocardial infarction, cerebrovascular accident, peripheral arterial disease, arrhythmia, or heart failure.

$^h$ Seven unknown.

$^i$ Eight unknown.

$^j$ Five unknown.

$^k$ Ten unknown.

$^l$ Twelve unknown.

$^m$ Eleven unknown.

$^n$ Two unknown.

$^o$ Four unknown.

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 posttest and one at all time points.

The mean treatment duration (excluding planned weeks of inactivity) of completers was 15.0 (4.1) weeks (range, 8–29 weeks) 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 life-style: 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 SDC 2, Table S2, http://links.lww.com/PSYMED/A889, 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, 7.5 (1.4) (range, 4–10); and contact with their therapist,

8.6 (1.1; range, 5–10). Also, they found the Personal Profile Charts useful to obtain insights in their own well-being 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). At baseline, mean scores on primary and secondary outcomes (SDC 4, Table S4, http://links.lww.com/PSYMED/A891) 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 posttest and follow-up, and dropped below the cutoff 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 $d$ 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 follow-up. Medium effect sizes were observed for PPP-functioning at posttest and follow-up as well as for PPP-self-management at posttest (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; that is, differences between groups were not significant at posttest ($b = -0.03$, 95% confidence interval [CI] = $-0.12$ to 0.06, $p = .49$) or at follow-up ($b = -0.07$, 95% CI = $-0.18$ to 0.05, $p = .26$; Figure 4). Regarding generic secondary outcomes, no significant time-by-group interaction effects were found.

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 SDC 5, Table S5, http://links.lww.com/PSYMED/A892, for an overview of reported priorities.

The ANCOVA results showed statistically significant differences between groups in PPP-functioning at both the posttest assessment (progress compared with baseline; $b = 0.46$, 95% CI = 0.07 to 0.85, $p = .021$) and follow-up assessment (compared with posttest; $b = 0.59$, 95% CI = 0.16 to 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 posttest ($b = 0.55$, 95% CI = 0.16 to 0.95, $p = .006$). At the follow-up assessment, the difference between groups was not significant ($b = 0.02$, 95% CI = $-0.48$ to 0.53, $p = .93$), as both groups reported neither perceived improvement nor worsening compared with posttest; this indicates that the intervention effect achieved at short-term was maintained at long-term (Figures 5A, B). For an overview of ANCOVA results, see also see SDC 6, Table S6, http://links.lww.com/PSYMED/A893.

**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 | Posttest | | | | | | Follow-up | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Change Score (SD) | | Dif. | 95% CI | | d | Change Score (SD) | | Dif. | 95% CI | | d |
| | Intervention | Control | | LL | UL | | Intervention | Control | | LL | UL | |
| 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 |

SD = standard error; CI = confidence interval; Dif. = difference in mean change scores (baseline scores subtracted from posttest and follow-up scores, respectively) between conditions; LL = lower limit; UL = upper limit; d = Cohen d.
For psychological distress, 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 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 with previous time point) instead of change scores are shown and used to calculate differences and effect sizes.

## Exploratory and Sensitivity Analyses

Linear mixed-effects models of depressive and anxiety symptoms (SDC 7, Tables S7 and S8, http://links.lww.com/PSYMED/A894) showed no significant intervention effects for depressive symptoms, in line with the primary analysis of psychological distress. However, a time-by-group interaction effect was found for anxiety at short-term: the reduction in anxiety symptoms from baseline to posttest was larger in the intervention group than in the control group ($b = −0.11$, 95% CI = −0.21 to −0.00). This difference seemed to be maintained from baseline to follow-up ($b = −0.11$, 95% CI = −0.22 to 0.00).

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 (SDC 7, Tables S9–S15, http://links.lww.com/PSYMED/A894).

## 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 the literature and desired by patients (43,44). 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 with regular care only, this personalized approach did not reduce overall psychological distress significantly. For secondary outcomes, compared with usual care, personalized outcomes of functioning and self-management that were prioritized by individual patients themselves significantly improved more after 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 HRQoL, self-efficacy, and chronic disease self-management 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 (33). Psychological distress was assessed as a composite: Our exploratory results suggest that the intervention may have been more successful in reducing anxiety than depressive symptoms, although effects were small. Comparing these results with similar interventions among patients with CKD not receiving dialysis is complicated, because 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 (45). In this review, moderate reductions of depressive and anxiety symptoms have been found after psychosocial intervention, although the results varied: of five studies, three reported significant reductions after

**TABLE 3.** Main Analyses of the E-GOAL Intervention: Estimated Coefficients and CIs 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 Groups ($n = 61$)

| 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 by 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 by 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 |

HRQoL = health-related quality of life; $b$ = 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.

intervention. Studies that failed to find beneficial intervention effects did not use clinical cutoff scores as inclusion criteria, which may have led to difficulties in reducing symptoms due to low baseline symptom levels (45). Similarly, a floor effect may have been present for our primary outcome: Although we preselected 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); that is, they reported no or only minimal psychological distress at baseline (33). This may partly explain the lack of significant findings. 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 (46): 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 (46).

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 (47). Individuals work on personal goals, implying differences in treatment focus and outcomes of importance per patient (47). Accordingly, our results revealed significantly more improvements on personally prioritized areas in the intervention group compared with controls with medium-sized effects. In comparison, the groups did not show
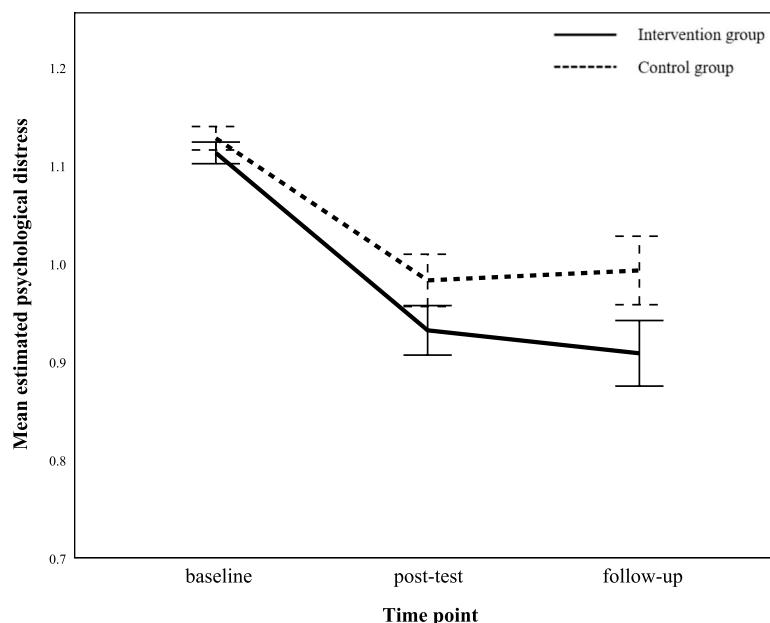


**FIGURE 4.** Time-by-group interaction effects for psychological distress (logarithmic transformation of Patient Health Questionnaire Anxiety and Depression Scale) in linear mixed-effects models adjusted for baseline covariates. Error bars ± 1 standard error. The mean reduction in psychological distress symptoms from baseline to posttest ($p = .49$) and from baseline to follow-up ($p = .26$) did not significantly differ between groups.
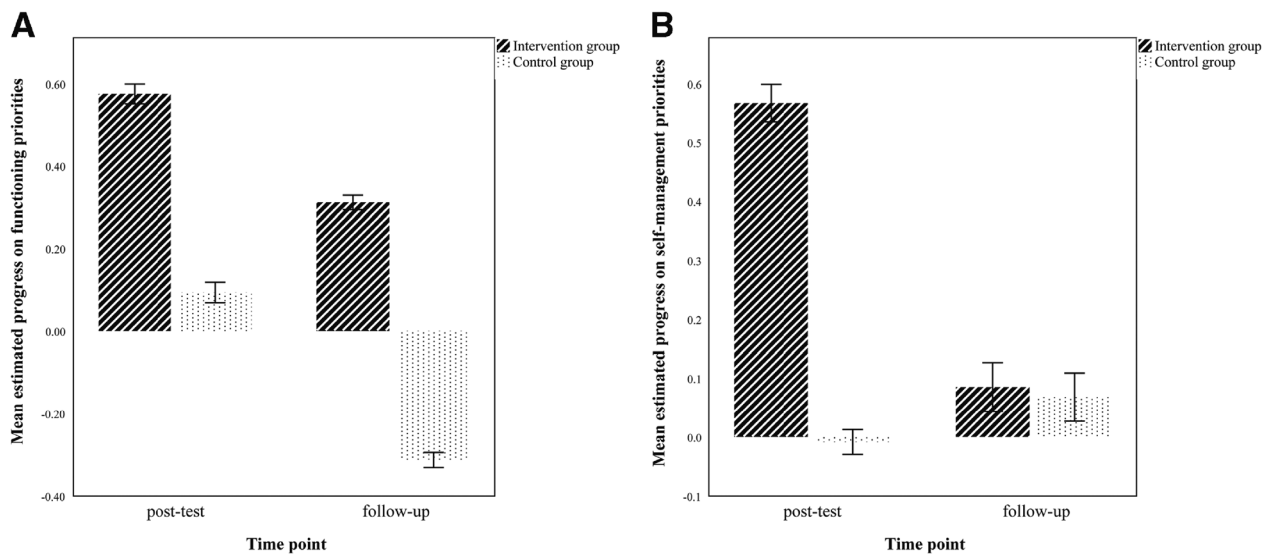
**FIGURE 5.** A and B, Mean perceived progress as compared with previous time point on personally prioritized areas of (A) functioning and (B) self-management per randomization group. Estimated marginal means from one-way analyses of covariance are shown, adjusted for baseline covariates age and sex, 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 could range from −3 to +3, on which 0 indicates neither worsening nor improvement.

significant differences on generic outcomes. 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 (47,48). 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 (47). 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 3 months after intervention and limited statistical power. In hindsight, we may have needed a larger sample or a higher cutoff 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 with ours (36–38). 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 (30,48). Another limitation was the open-label approach, as blinding was not possible because of 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 previously, as well as response biases that could have contributed to potential positive effect exaggerations in the intervention group (46,49).

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 dropout 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 (44,51). 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, that is, 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 bidirectional 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, 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 cutoff 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 that have been found effective in reducing psychological distress symptoms could be included in the iCBT treatment. 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, 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 (28) 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 with regular care only, this eHealth intervention did not significantly improve psychological distress, quality of life, self-efficacy, and chronic disease self-management, whereas—importantly for this personalized intervention—personally relevant outcomes did improve significantly after intervention and improvements were maintained over time. The RCT results provided insights into 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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