A psychosocial intervention for regaining control in dialysis patients: design of a randomized controlled trial

ISRCTN registry (2020)
Introduction

Chronic kidney disease (CKD) affects around 10% of the global population and poses a high mortality risk worldwide (Jha et al., 2013; Tonelli, 2006; Wang et al., 2018). In the last stage of chronic kidney disease (End stage renal disease; ESRD) individuals need dialysis or transplantation to survive. Renal transplantation is the current treatment of choice in terms of long-term survival, well-being and quality of life as opposed to dialysis (Kaballo et al., 2018; Ozcan et al., 2015; Tonelli et al., 2011). However, not all patients are eligible for transplantation and there is a shortage of organs available for donation (Tonelli et al., 2011). Therefore, a substantial part of ESRD patients have to undergo dialysis.

Dialysis is a demanding treatment, given that patients are tied to a dialysis machine for approximately three days a week, four hours per session. Moreover, patients have to adhere to a strict dietary regimen and take a large amount of daily medication. Dialysis has also been related to unfavorable side effects such as extreme fatigue, itching, and nausea (Murtagh, Addington-Hall, & Higginson, 2007; Tong et al., 2014). Consequently, dialysis may greatly affect the ability to function in important life domains, such as maintaining close relationships, engaging in social activities, or continuing education and labor participation (Erickson, Zhao, Ho, & Winkelmayer, 2018; Heijmans & Rijken, 2004; Tong et al., 2014). Given these impediments, it is not surprising that dialysis poses a serious burden (Karamanidou, Weinman, & Horne, 2014; Reid, Seymour, & Jones, 2016). Dialysis patients experience lower levels of subjective well-being and quality of life compared to patients undergoing renal transplantation and the general population (Broers et al., 2018; Chen et al., 2017; Ozcan et al., 2015).

A key predictor of overall psychological functioning in general is the extent to which individuals perceive control over important life outcomes (Bandura, 1997; Gerstorf et al., 2014). Higher levels of perceived control have consistently been related to higher levels of psychological and physical functioning across different chronic illnesses and in the general population (Barry, Kasl, Lichtman, Vaccarino, & Krumholz, 2006; Bishop, Frain, & Tschopp, 2008; Gerstorf et al., 2014), whereas lower levels have been linked to elevated levels of psychological distress and poor quality of life (Bárez, Blasco, Fernández-Castro, & Viladrich, 2007; Ranchor et al., 2010). In individuals undergoing dialysis, perceiving low control over one’s illness has been related to low levels of well-being (Griva, Davenport, Harrison, & Newman, 2012; Timmers et al., 2008).

It has been demonstrated that perceptions of control can change over time, particularly when confronted with life events (Lachman & Firth, 2004; Ranchor et al., 2010). In a recent study in renal patients on a waiting list for kidney transplantation,
approximately a third of the patients reported an increase in perceived control after transplantation. Half did not experience a change in perceived control and the remaining respondents reported a decrease in perceived control (Schulz et al., 2017). Thus, perceived control does not automatically improve for all patients after transplantation.

Research on the effectiveness of psychosocial interventions has found that feelings of perceived control do not increase when patients are offered care that did not specifically focus on increases in control. In a study among heart patients, personal control over illness was not found to improve after a general cardiac rehabilitation program (Janssen, De Gucht, van Exel, & Maes, 2014). In a sample of cancer patients receiving psychological care, only 41% of the patients reported enduring improvement in perceived control, while 50% showed temporary improvement and 9% even a deterioration in personal control (Zhu et al., 2014).

In light of these findings showing moderate effects of existing medical and psychological interventions on perceived control, the detrimental effects of dialysis and the important role of perceived control in maintaining one’s well-being, we aimed to develop an intervention specifically tailored at enhancing perceptions of control in this specific dialysis population.

**Current study**

The primary aim of this study is to develop and examine the effectiveness of a psychosocial intervention specifically designed to improve perceptions of control (i.e. primary outcome) in individuals on dialysis, compared to a waitlist control condition. In addition, the underlying working mechanisms of the intervention will be examined (i.e. mediators), as well as for whom the intervention might be the most beneficial (i.e. moderators). Secondary outcomes will include quality of life, fatigue, depression, and anxiety, as previous research has shown that these factors are changeable and may be influenced by interventions and increases in perceptions of control as well (Gerstorf et al., 2014; Ghorbani, Krauss, Watson, & LeBreton, 2008; Ray, Jefferies, & Weir, 1997).

Self-regulation theory will serve as a framework for developing our intervention targeting perceptions of control. According to self-regulation theory, individuals constantly compare current circumstances with a desired situation and aim at closing this discrepancy by actively pursuing important life goals (Carver & Scheier, 1998). Self-regulation encompasses goal setting, goal process monitoring, anticipating barriers to goal attainment, problem-solving, and relapse prevention. Importantly, successful goal pursuit has been found to contribute to a sense of control over life and psychological well-being (Boudrengchien, Frenay, & Bourgeois,
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2012; Carver & Scheier, 1998; Emmons, 2003; Wrosch, Scheier, Miller, Schulz, & Carver, 2003). Severe illness can severely compromise successful goal pursuit. Such disturbances in the attainment of important life goals have been related to decreased well-being in end stage renal disease patients (including dialysis patients) (de Vries et al., 2017).

In this study it is hypothesized that an intervention that supports dialysis patients in managing new or difficult to attain goals across different life domains could increase overall perceived control (Wrosch, Schulz, & Heckhausen, 2004), and ultimately improve well-being (Emmons, 2003). For example, patients might be hindered in visiting family members given the fatigue and lack of free time due to dialysis (family life domain). The intervention will assist patients in managing these disturbances in the attainability of goals. The confrontation with a chronic illness might also be accompanied with new goals. For instance, patients might need to solve travel costs and arrangements to the hospital for their treatment. To this end, a central part of the newly developed intervention protocol will consist of helping patients to adopt helpful goal adjustment strategies (Janse et al., 2014). One strategy is characterized by giving up unattainable goals in one life domain (e.g. patients might give up their goal of having a job in the work domain), and reprioritize attainable goals in another important life domain (e.g. spending more time with their partner in the family domain). Patients might also change from one goal to another goal within the same domain (e.g. leisure time) when the goal is difficult to attain (e.g. instead of playing football, reading a book).

The intervention will be offered individually, since it is specifically tailored to the patient-defined needs, and therefore different issues might come up during the intervention. Given that dialysis is a time-consuming treatment and thus patients already spend long periods in the hospital, the intervention will be offered close to the moment of dialysis; preferrably before or during dialysis in a closed room, in order to secure the patients’ privacy. In case patients dialyse at home, arrangements will be made to combine regular hospital visits with at-home visits to give the intervention. Thus, practical implementability is considered of high importance in this overburdened population, with health professionals deciding together with patients as to which location and what time bear the lowest burden on patients. The intervention will be provided by social work or a psychologist, because these professionals are familiar with talking with patients about their functioning in different life domains.

Patient participation in developing the intervention and setting up the study is considered essential. First, patients will be involved in the development of the intervention by means of structured interviews, in which they will be asked about how they conceptualize perceived control, on what domains they perceive (a lack
of control, and what gives/decreases a sense of control. Second, people will also be asked to give feedback on the questionnaires used in the study, including the duration of filling in the questionnaires, whether important concepts are covered, and whether it is feasible for them to complete questionnaires in light of the treatment demands and time-constraints they might experience.

**Mediators**
It has become increasingly important in empirical research to identify underlying mechanisms of change in psychosocial interventions, so as to explain how and why interventions work (Windgassen, Goldsmith, & Chalder, 2016). In order to examine if the specific strategies of goal adjustment are responsible for possible changes in perceived control, different goal characteristics are assessed as mediators. Based on previous research, these characteristics consist of goal importance, goal attainability, goal hindrance, and effort in pursuing goals (Emmons, 2003; Janse et al., 2014).

Following the goal elicitation procedure as described by Emmons et al. (2003), patients will be asked to report 3 to 5 goals they currently pursue, and to rate each goal on a rating scale of 1-10 according to the abovementioned characteristics. It is expected that during the intervention, patients improve their goal adjustment skills across different life domains, as characterized by increased attainability and effort, and reduced goal hindrance. A meaningful change in goal adjustment is defined in two ways. First, an increase of at least 0.5 SD as determined by Cohen (1998) in attainability, or effort, and/or a decrease of at least 0.5 SD in goal hindrance. Secondly, a cutoff can be determined based on the Dutch grading system, in which a grade of 5 or lower is considered unsatisfactory, and a grade of 6 or higher satisfactory. That means that in case attainability and effort increase from <= 5 to >=6, and/or goal hindrance reduces from >= 6 to <=5 there is also an improvement in goal adjustment. Eventually it is expected that these improved skills will increase general perceived control over life in individuals on dialysis.

**Moderators**
Research has also emphasized the need for information on characteristics of patients who might most benefit from psychological interventions, or for whom the intervention works less well. Because no intervention aimed at improving perceived control has been tested before, no information on moderators is currently available. Therefore, several factors will be studied in an explorative fashion. Firstly, a possible moderating influence of demographic factors will be considered, such as patients’ age, gender, and level of education. Secondly, the moderating role of disease-related factors will be studied, including time on dialysis, frequency of dialysis, co-morbidity, dialysis modality (at home or at the dialysis center), and having underwent a transplantation or being eligible for transplantation. Also, biological
moderators will be explored, such as creatinine clearance, which serves as an indicator for kidney function. Thirdly, a moderating role of the personality trait of a basic need for structure will be explored, as well as the moderating role of patients’ illness cognitions (such as helplessness, acceptance and benefit findings) and perceived support.

**Treatment integrity**
Treatment integrity refers to the extent to which an intervention has been delivered as intended and increases the validity of the findings from a randomized controlled trial. Information on treatment integrity allows to conclude whether the effectiveness of an intervention can be truly attributed to the intervention. In this study, treatment integrity will be studied by monitoring to what extent therapists adhere to the intervention manual. To this end, sessions will be audio-recorded and afterwards checked for adherence by two independent observers.

**Feasibility and acceptability**
The feasibility of the intervention will be examined by assessing recruitment, drop-out, and adherence rates. Furthermore, at T1, the participants are asked to evaluate the intervention by means of a quantitative questionnaire and qualitative interviews, in order to provide a deeper insight into the helpful and difficult components of the training.

**Study aims and hypotheses**
The main objective of this study is to examine the immediate and long-term effects of the self-regulation intervention in increasing perceptions of control in patients undergoing dialysis. It is hypothesized that the intervention will be more effective in increasing perceptions of control in the intervention condition compared to a waitlist control condition. Regarding secondary outcomes, it is expected that patients in the intervention condition will show more improvements in their quality of life and larger decrements in fatigue, depression and anxiety compared to the control condition. Moreover, we aim to examine factors that might mediate or moderate the intervention effects, so as to clarify why and for whom the intervention is (less) effective.

**Methods/design**

**Study design**
The current study is a multi-center, randomized controlled trial (RCT). Participants will be randomly assigned to the intervention condition or a waiting list control condition. Participants allocated to the intervention condition will receive questionnaires at 4 time-points: before the intervention (T0), after the intervention
(T1), 3 months after the intervention (T2) and 9 months after the intervention (T3). Participants allocated to the waiting list control condition will be asked to complete questionnaires with the same time-intervals as those allocated to the intervention condition, at T0, T1 and T2. They will receive the intervention after T2, which comes down to a waiting period of approximately 18 weeks (6 weeks of intervention and 12 weeks of follow-up until T2). The current study is conducted in accordance with the principles of the Declaration of Helsinki and the Medical Research Involving Human Subjects Act (WMO) and has been approved by the Medical Ethical Committee of the University Medical Center Groningen (UMCG).

**Recruitment and screening procedure**

Figure 1 shows the flowchart of the participant recruitment through the study. Patients currently undergoing dialysis in a center or at home are routinely screened for their levels of perceived control. Patients who dialyze in a center are approached face-to-face, given that they make regular visits to the hospital for their dialysis treatment, and can therefore be easily approached. Patients who dialyze at home however pay less frequent visits to the hospital, and therefore will receive a letter from the dialysis center with a request to fill in the questionnaire on perceptions of control and send it back by mail. Different hospitals in the North and the center of the Netherlands are approached to participate in the study.

Patients who score 23 or below on the Mastery scale (Pearlin & Schooler, 1978) are invited for an intake with a psychologist or research assistant. Patients who fulfill the inclusion criteria and wish to receive support for perceiving more control over their lives, receive more detailed written information concerning the study, an informed consent, and the first baseline assessment. Once eligible patients give written informed consent and complete the baseline questionnaire, they are included in the study.
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Excluded: N=
Did not meet screening criteria
Insufficient knowledge of Dutch:
Age < 18 years

Screened: N=

Excluded: N=
Elevated Mastery score (Mastery ≥ 24):

Below cutoff (Mastery ≤ 23): N=

Did not meet inclusion criteria: N=
Psychiatric condition
Receiving psychological treatment:
unstable pharmacological treatment:

Total Eligible N=

Refused to participate: N= (Give reasons) (n= )

Total randomized: N=

Allocated to intervention: N=
Did not receive allocated intervention (give reasons) (n= )

Post-intervention assessment (T1): N=
Incomplete assessment (n= )
(give reasons) (n=)

T1 n = T2 n = T3 n =
Lost to follow-up (give reasons) (n=)

Analyzed: N=
Excluded from analysis (give reasons) (n=)

Allocated to Waitinglist control: N=

T1 : N =
Incomplete assessments (n= )
(give reasons) (n=)

T1 n = T2 n = T3 n =
Lost to follow-up (give reasons) (n=)

Analyzed: N=
Excluded from analysis (give reasons) (n=)

Figure 1. Flowchart of the intervention study
Study population

*Inclusion criteria:* I) receiving dialysis treatment (at the hospital or at home), II) aged 18 years or older, III) sufficient knowledge of the Dutch Language, IV) having low perceived control as indicated by a score of 23 or below on the Mastery scale (Pearlin & Schooler, 1978).

*Exclusion criteria:* I) severe psychiatric comorbidity (e.g. psychosis, bipolar disorder, schizophrenia, severe cognitive impairment or neurological damage), II) receiving a psychological treatment at the time of inclusion. Patients are allowed to participate when they receive psychopharmacological treatment (e.g. antidepressants or anti-anxiety medication), but only when stable on the medication regimen for at least 2 months and no change in medication intake during the study (e.g. begin or end pharmacotherapy).

Treatment allocation

Randomization will take place with a computerized covariate adaptive randomization program (Kang & Park, n.d.). Patients will be stratified by hospital (where patients receive their dialysis treatment or go for their regular check-up), dialysis location (whether patients dialyze at home or at the dialysis center), and education (low, middle, or high education). These stratification variables were included since they might have a confounding influence (Mirowsky & Ross, 2007; Nezlek, 2008; Palmer et al., 2014), and thus could make it more difficult to evaluate the treatment effects.

 Intervention

This psychosocial intervention consists of a generic self-regulation intervention specifically tailored to the dialysis population, by including information on dialysis and a flexible delivery in light of the treatment burden. Patients can come up with either disease-related or general goals during the intervention. This way, patients can apply the learned self-regulation strategies in different situations and across various life domains.

The treatment consists of four individual sessions, in a time frame of four to eight weeks, and duration of 45 to 60 minutes per session. Patients receive a workbook, in which they can complete assignments before the next session. Given that some patients are severely ill or disabled, it is stressed that homework is not obligatory for participation in the study.

The intervention will be given by medical social workers or a psychologist, experienced with the dialysis population and with providing psychosocial
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interventions. The psychologist has a master’s degree in clinical psychology. Before the start of the study, the trainers receive training for applying the protocol.

The first two sessions of the goal intervention are dedicated to the assessment of personal values and patients’ levels of importance, perceived control, and hindrance in different life domains (intimate relationship, family life, social life, leisure time, (voluntary) work, and the dialysis treatment). Patients are asked to set a realistic and attainable goal directed at feeling more control over their lives. In the third and fourth session of the intervention, different steps for attaining the patient-defined goal will be monitored, and barriers and aids for attaining the goal will be discussed. Ultimately, relapse prevention will be addressed. There will be a booster session one month after the last session, so as to monitor changes during the last month and reflect on the strategies for maintaining behavioral change and overcome obstacles and possible relapse.

Outcome assessment

Table 1 shows an overview of the concepts, measurements, and time points on which the measurements are assessed. The treatment sessions are audiotaped, and patients are asked for consent to retrieve medical data from their hospital records. In case patients do not give permission to audiotape the sessions, or do not want their medical data to be retrieved, they can also participate in the study. Participants in the waiting list control condition receive the treatment after a waiting period of 18 weeks. The burden of completing questionnaires is accounted for by giving patients the possibility to fill in the questionnaires during the dialysis treatment. The coordinating investigator maintains contact with the patient during the study period.

Sample size

The calculation of the sample size is based on the primary outcome measure: the Mastery scale. According to an existing database of 379 dialysis patients on a waiting list for transplantation, a mean score of 22.1 and a standard deviation of 5.0 on the Mastery scale has been reported. In order to establish a difference of 0.5 SD (clinical relevant difference) between the waiting list and the intervention condition, with a power of .80, two-sided testing and an alpha of 0.05 (Cohen, 2003), the total sample size should comprise 67 patients. This size allows examining the effectiveness, and the effects of mediators and moderators in the intervention compared to the waiting list control condition. The analysis will be based on the intention-to-treat procedure.
**Analysis plan**

In order to answer the primary research question (the effectiveness of the self-regulation intervention compared to a waitlist-control condition in improving perceived control), general linear modeling analyses will be performed. Primary and secondary outcome measures will be introduced as dependent variables and the condition (intervention or control) as independent variable. Correlations between important (demographic) measures and outcome variables will be calculated so as to control for possible confounding variables. Mediation and moderation analyses will be performed with the PROCESS macro for SPSS.
Table 1. Concepts, instruments to measure the concepts, and moment of assessment.

<table>
<thead>
<tr>
<th>Concept</th>
<th>Measurement (number of items)**</th>
<th>Measurement in time points*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome measure</strong></td>
<td></td>
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<tr>
<td>Perception of control</td>
<td>Mastery Scale (7)</td>
<td>x x x x x x</td>
</tr>
<tr>
<td><strong>Secondary outcome measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domain specific Mastery</td>
<td>Self-constructed (11)</td>
<td>x x x x x</td>
</tr>
<tr>
<td>Quality of life</td>
<td>SF-12 (12), EQ5D (5)</td>
<td>x x x x x</td>
</tr>
<tr>
<td>Fatigue</td>
<td>CIS-20 (20)</td>
<td>x x x x x</td>
</tr>
<tr>
<td>Depression</td>
<td>PHQ-9 (9)</td>
<td>x x x x</td>
</tr>
<tr>
<td>Anxiety</td>
<td>GAD-7 (7)</td>
<td>x x x x</td>
</tr>
<tr>
<td>Perceived Stress</td>
<td>PSS (5)</td>
<td>x x x x</td>
</tr>
<tr>
<td>Meaning in Life</td>
<td>LET (6)</td>
<td>x x x x</td>
</tr>
<tr>
<td>Well-being</td>
<td>WHO-5</td>
<td>x x x x</td>
</tr>
<tr>
<td><strong>Moderators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Dialysis related factors</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of dialysis and location</td>
<td>Medical record</td>
<td>x</td>
</tr>
<tr>
<td>Time on dialysis</td>
<td>Medical record</td>
<td>x</td>
</tr>
<tr>
<td>Frequency of dialysis</td>
<td>Medical record</td>
<td>x</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Eligibility/underwent</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>transplantsations</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Personality characteristics</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illness cognitions</td>
<td>ICQ (18)</td>
<td>x x x x x</td>
</tr>
</tbody>
</table>
### Table 1. Concepts, instruments to measure the concepts, and moment of assessment. (continued)

<table>
<thead>
<tr>
<th>Concept</th>
<th>Measurement (number of items)**</th>
<th>Measurement in time points*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal need for Structure</td>
<td>PNS (12)</td>
<td>S</td>
</tr>
<tr>
<td>Important others</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Relationship with Partner</td>
<td>ABO (19)</td>
<td>x</td>
</tr>
<tr>
<td>Mediators</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Goal characteristics</td>
<td>Personal striving assessment (5)</td>
<td>x</td>
</tr>
</tbody>
</table>

*S screening; T0 Baseline; T1 post intervention; T2 three months post intervention; T3 nine months post intervention.

** SF 12- Short From Health Survey; EQSD- Euro Quality of Life 5 dimensions; CIS Fatigue- Checklist Individual Strength; PHQ-9- Perceived Health Questionnaire; GAD-7- Generalized Anxiety Disorder Scale; PSS – Perceived Stress Scale; LET-6 – Life Engagement Test; WHO-5- World Health Organization Well-Being Index; KDQOL-SF – Kidney Disease Quality of Life Short Form; ICQ – Illness Cognitions Questionnaire; PNS – Personal Need for Structure Questionnaire; APO – Active engagement, Protective Buffering, and Overprotection.
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Discussion

This is the first study aimed at investigating the effectiveness of a self-regulation intervention in improving general perceptions of control in dialysis patients, by means of a randomized controlled trial. The self-regulation intervention is expected to improve patients’ perceptions of control compared to a waitlist control condition. The waitlist control condition will receive the psychosocial treatment after a waiting period of approximately 18 weeks.

The primary outcome of this study is perceptions of control, yet also other important secondary outcomes will be considered, such as quality of life and fatigue. In order to minimize the burden on patients, they will be offered the possibility to complete questionnaires during the dialysis treatment. Moreover, the self-regulation intervention can also be delivered during the dialysis treatment, which makes it more suitable for integration in current medical care.

In addition to examining the effectiveness of the intervention, this study also aims to examine the factors which moderate and mediate the treatment effects of the protocol, and to study the relationship between treatment integrity and improvements in perceptions of control. These additional questions allow us to provide more insight in the way interventions work (why and for whom). In case the intervention helps to increase perceived control, it might be of additional value to the usual care of patients undergoing dialysis.
References


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Design of a RCT


Design of a RCT