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General introduction
Chapter 1

Kidneys perform a wide range of life-sustaining functions, including the removal of waste products and fluid excess, blood pressure regulation and the production of hormones including vitamin D and erythropoietin. When the kidneys function abnormally and there is a decreased kidney function during a period of at least three months, the diagnosis of chronic kidney disease is established (National Kidney Foundation, 2020). Chronic kidney disease (CKD) comprises six different stages, as established by a measure of kidney function; i.e. glomerular filtration rate and albuminuria. The last stage of chronic kidney disease is called end stage renal disease (ESRD). In this stage, the kidney function is approximately 15% or less and renal replacement therapy is necessary to stay alive. Renal replacement therapy includes either kidney transplantation or dialysis. Although kidney transplantation is the preferred treatment over dialysis in terms of longevity and quality of life, a substantial number of ESRD patients cannot undergo transplantation because of the transplant waitinglist or due to ineligibility for transplantation. Consequently, this group needs to undergo dialysis treatment.

Dialysis is overall considered a very burdensome treatment with major consequences for individuals’ physical and psychological health. With regard to psychological functioning, dialysis patients overall experience little autonomy in their daily lives (Jansen, Rijken, Heijmans, & Boeschoten, 2010). An important component of autonomy is perceived control, which refers to the general belief that one can influence important life outcomes (Pearlin & Schooler, 1978). Perceiving control over life is an important buffer for well-being and quality of life in both the general and somatically ill populations, including dialysis patients (Griva, Jayasena, Davenport, Harrison, & Newman, 2009). However, currently there is no psychosocial intervention available aimed at enhancing perceived control in dialysis patients.

The aim of this thesis was therefore to develop and examine a psychosocial intervention specifically tailored at improving dialysis patients’ perceptions of control. First, we studied the psychological mechanisms underlying improvements in well-being in patients with end stage renal disease undergoing transplantation, including the role of perceived control in these improvements. Second, in the preparation phase of the psychosocial intervention, we studied the concept of perceived control from a patient perspective, specifically how patients themselves define perceived control and what, in their view, contributes or impedes a sense of control. Ultimately, a psychosocial intervention was developed aimed at improving perceived control and the effectiveness, feasibility and acceptability of this interventions was examined.

Hereafter, the different treatments for ESRD will be explained. Next, factors associated with improvements in well-being in ESRD patients from pre- to post-transplantation are introduced. Then, the psychosocial intervention for enhancing
perceived control and reasons for not accepting the intervention within the trial will be discussed. The chapter will conclude with the aim and outline of this thesis.

Treatments for end stage renal disease

Dialysis and kidney transplantation cannot fully restore kidney functioning and therefore do not provide a cure for end stage renal disease (Dutch Kidney Foundation, n.d.). However, they can prolong life expectancy. In 2019, approximately 6,292 patients with ESRD underwent dialysis treatment, whereas 11,641 received a kidney transplant in the Netherlands (Nefrovisie, 2019). Hereafter, dialysis and kidney transplantation will be further explained.

Dialysis

Although access to transplantation has improved over time, a substantial number of patients is still dependent on dialysis to survive. The majority of the dialysis population consists of elderly patients. In 2019, 64% of the people receiving dialysis in the Netherlands was aged above 65 years, of whom 37% was 75 years or older (Nefrovisie, 2019). There are two different kinds of dialysis treatment: hemodialysis (HD) and peritoneal dialysis (PD). See box 1 for a detailed description of the different dialysis treatment modalities. In the Netherlands, 81% of the dialyzing population in 2019 underwent in-center hemodialysis, of whom 70% was aged above 70 years. 15% received peritoneal dialysis and the rest underwent home hemodialysis (Nefrovisie, 2019).

Dialysis patients need to live with both a substantial disease and treatment burden. Regarding disease burden, main physical complaints include fatigue, muscle cramps and itchy skin. Moreover, dialysis is a burdensome treatment because it takes place multiple times per week - on average 3 times per week 4 hours per session for in-center hemodialysis. Given the frequent required travelling for in-center dialysis, patients can also face practical issues, such as transportation problems or travelling costs. Dialysis requires additional pharmacological treatment with multiple medications and strict lifestyle measures, including a strict fluid and dietary regimen. Dialysis therefore severely affects daily living and quality of life, including psychological functioning (Landreneau, Lee, & Landreneau, 2010; Rebollo Rubio, Morales Asencio, & Eugenia Pons Raventos, 2017). The treatment interferes with functioning in all life domains such as difficulties in the maintenance of (intimate) relationships, problems engaging in important free-time activities, and high unemployment rates (Ekelund & Andersson, 2010; Erickson, Zhao, Ho, & Winkelmayer, 2018; Karamanidou, Weinman, & Horne, 2014). A frequently reported problem of patients on dialysis is an experienced lack of autonomy (Jansen et al., 2010). Specifically, dialysis patients experience lower levels of perceived control over their illness compared to transplanted patients, which has in turn been associated with a decreased quality of life (Griva et al., 2009). The current treatment of choice
for ERSD (renal transplantation) does not automatically enhance perceptions of control in all patients. According to a recent study among renal transplant recipients, 50% of the patients did not report a change in perceived control and 15% even reported a decrease in perceived control after transplantation (Schulz et al., 2017). Thus, low perceived control is considered a problem among patients, but there is no intervention available that improves these perceptions of control. Therefore, we aimed at developing such an intervention. The first step in this process consisted of gaining a deeper insight in the improvements in well-being in patients with end stage renal disease undergoing transplantation, and the role of perceived control in these improvements.

**Box 1. Dialysis modalities**

**Peritoneal dialysis (PD)**
In PD, the abdomen (peritoneum), serves as a filter in removing waste products and fluid from the blood. PD should be performed every day and can be done everywhere, e.g. at home, at work or when traveling. The treatment consists of a cleansing fluid (dialysate) rinsed into the abdomen through a catheter. Waste products are absorbed in the dialysate and thereafter removed from the body. The process of removing the used dialysate and renewing the fluid with clean fluid is called “exchanging”. Within PD, there are two types: continuous ambulatory PD (CAPD) and automated PD (APD). In CAPD, patients exchange themselves by hand the cleansing fluid, approximately 4-5 times per day.

**Hemodialysis (HD)**
In HD, the blood runs through a dialysis machine outside the body. HD can take place in a dialysis center or at home. Dialysis in a dialysis center normally takes around 3-4 times per week, for 4 hours per session. Often it is also possible to dialyze at night in a dialysis center. When performing home HD, patients can adjust their dialysis schedule to their own needs (more frequent and/or shorter time periods).

**Home vs center dialysis**
Often home dialysis (PD or home HD) is considered to provide the most benefits for physical and psychological health because it allows for a more continuous treatment and it gives more freedom and flexibility compared to in-center dialysis.
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Transplantation

Kidney transplantation is the treatment of choice because it is related to lower mortality and better quality of life compared to dialysis (Griva, Davenport, Harrison, & Newman, 2012; Jansz et al., 2018; Kaballo et al., 2018; Kovacs et al., 2011; Landreneau et al., 2010; Tonelli et al., 2011). There are two different transplant options: either patients are on the waitinglist for kidney transplantation and receive a kidney from a deceased kidney donor or they find a living kidney donor. The waitinglist for renal transplantation outweighs the number of available deceased kidney donors which is reflected in an average waiting period of 3 years in the Netherlands (Dutch Kidney Foundation, n.d.). Every year patients die because they cannot be transplanted on time. That said, access to kidney transplantation has however substantially improved in the Netherlands from 400 transplants 25 years ago, to 1000 transplants per year, resulting in more patients living with a kidney transplant than patients on dialysis (Dutch Kidney Foundation, n.d.). Moreover, of those patients who received a transplant, more patients were transplanted with a living donor kidney than a deceased donor kidney. That is, in 2019 5,537 patients received a deceased donor kidney and 6,104 received a living donor kidney. This is especially important because a living donor kidney is associated with a longer graft survival (Dutch Kidney Foundation, n.d.).

Kidney transplantation is generally associated with better quality of life and well-being compared to dialysis (Landreneau et al., 2010; Tonelli et al., 2011). However, it also presents challenges. For example, patients need to take immunosuppressants their whole life in order to prevent kidney rejection from happening. Importantly, immunosuppressants have side effects, such as an increased risk of infections, high blood pressure or the risk of developing skin cancer (NHS) as well as other forms of cancer. Moreover, although far less compared to dialysis patients, individuals with a kidney transplant also need to adhere to lifestyle changes such as medication intake and a strict dietary regimen (American Kidney Fund). Transplant recipients might also experience negative psychological effects, such as feelings of guilt or fear of losing the new kidney (Rodrigue et al., 2018; Schipper et al., 2014).

Factors associated with improvements in well-being across renal transplantation

We explored two different mechanisms potentially underlying improvements in well-being across transplantation: changes in self-regulation and in benefit finding. Both concepts have been widely studied in the context of a health deterioration. However, these concepts have rarely been examined in the event of a positive life change, which is the case in renal transplantation. Therefore, we studied changes in self-regulation and benefit finding from pre- to post-transplantation and their associations with psychological and health indicators.
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**Self-regulation**
Self-regulation refers to the complex process of efforts and behaviours that people undertake in order to reach their life goals (Bandura, 1977). Advancing towards and attaining important life goals is essential for maintaining a sense of meaning and well-being (Scheier & Carver, 1985). However, chronic illness can disturb the pursuit and attainment of important life goals, leading to higher levels of distress (Joekes, Maes, Boersma, & Van Elderen, 2005; Stefanic, Caputi, & Iverson, 2014). As indicated, patients with end stage renal disease face severe impediments in daily life. Given that patients who undergo transplantation are not dependent on dialysis anymore and might therefore experience less day-to-day restrictions, it can be expected that kidney transplantation decreases disturbances and consequently improves well-being. Understanding the role of self-regulation and its association with perceived control in the context of renal transplantation could offer practical and concrete guidelines for the development of a psychosocial intervention in dialysis patients. As such, this thesis examined changes in goal disturbance from pre- to post- transplantation, its association with distress changes, and the mediating role of perceived control.

**Benefit finding**
Another psychological concept that has gained empirical interest in the context of negative life changes is Benefit finding. Benefit finding refers to the capacity to identify positive changes following a negative life event such as illness (Tedeschi & Calhoun, 2004). It includes the experience of personal strength, the ability to learn from one’s illness and realizing what is important in life (Evers et al., 2001).

Benefit finding has been regularly studied in the context of a health threat, such as AIDS or cancer (Danhauer et al., 2013; Koutrouli, Anagnostopoulos, & Potamianos, 2012; Milam, 2004). These studies generally show that it is possible to construe benefits when faced with a serious illness (Helgeson, Reynolds, & Tomich, 2006). However, Benefit finding has never been studied in the process of a health improvement. This thesis contributes to the current gap in the literature by examining changes in Benefit finding across renal transplantation, as well as the association between Benefit finding and psychological and clinical correlates and by disentangling the relation between Benefit finding and distress over time.

After gaining more knowledge on the background of end stage renal disease and factors associated with increases in well-being across transplantation, the next step was to develop an intervention specifically aimed at enhancing perceptions of control in dialysis patients.
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A psychosocial intervention enhancing perceived control in dialysis patients with low perceived control

The development and evaluation of the psychosocial intervention for enhancing perceived control in dialysis patients with low perceived control consisted of different phases: first, exploring the concept of perceived control from a patients’ perspective. Second, the actual development of the intervention based on firm theoretical underpinnings, resulting in the evaluation of its effectiveness, feasibility and acceptability. Subsequently, exploring a common pitfall in psychological intervention research; i.e. the lack of acceptance of care in the context of intervention research.

Perceived control

Perceived control is considered a key predictor of psychological functioning and has received substantial attention in the general population as well as in somatically ill patients, including individuals on dialysis (Griva et al., 2009). Perceived control is defined as a general belief or expectation that one can influence important life outcomes (Pearlin & Schooler, 1978). Perceived control is dynamic and can change over time. For example, older age and a higher educational level have been related to more perceived control (Mirowsky & Ross, 2007). Studies have shown that it is possible to experience control in spite of highly uncontrollable life events, which is the case when receiving a diagnosis of severe illness such as cancer (Ranchor et al., 2010).

Given the overwhelming evidence for the importance of experiencing control for one’s well-being in combination with the experienced lack of autonomy that dialysis patients face, there has been a growing emphasis on perceiving control over one’s life and illness. This is evidenced by a growing focus on patients’ self- and illness management within medical health care for dialysis patients. Despite the growing interest in this topic it is however not known how dialysis patients themselves think about the concept of perceived control, which is imperative to provide the necessary care tailored to the needs and wishes of individual patients. Qualitative methodology provides the opportunity to understand the meaning of perceived control from a patient’s perspective. Therefore, the current thesis qualitatively examined the meaning of perceived control, factors facilitating and factors impeding perceived control in dialysis patients.

Development of an intervention to enhance perceptions of control in dialysis patients

Given that perceived control does not automatically improve after general psychosocial interventions aimed at improving psychological and physical health (Janssen, De Gucht, van Exel, & Maes, 2014; Schulz et al., 2017; Zhu et al., 2014), specific psychosocial care targeting perceptions of control in dialysis patients is warranted.
In order to enhance perceived control, a psychosocial intervention was developed based on self-regulation theory and specifically tailored to increase control perceptions in dialysis patients. A diagnosis of severe illness can impede the pursuit and attainment of important life goals, consequently decreasing quality of life and well-being (Boersma, Maes, & van Elderen, 2005; Offerman, Schroevers, van der Velden, de Boer, & Pruyn, 2010). According to self-regulation theory, letting go of unattainable goals and instead engaging in important and attainable goals is imperative to maintain a sense of control and safeguard one’s well-being (Emmons, 2003; Wrosch, Schulz, & Heckhausen, 2004). Goal adjustment strategies as empirically identified in the literature were adopted in the intervention protocol (Janse et al., 2016). This thesis describes the protocol and the findings of the randomized controlled trial (RCT) examining the effectiveness, feasibility and acceptability of the psychosocial intervention for regaining perceptions of control in dialysis patients who report low perceived control.

Despite reported problems/complaints and the availability of psychosocial care, there is a group of patients that does not accept psychosocial care (Mosher et al., 2014; van der Donk et al., 2019). Information on care needs primarily stems from studies on cancer patients, but is largely lacking in the dialysis population. A deeper insight in the reasons and predictors of not accepting care among dialysis patients might inform health care providers and eventually bridge the gap between empirical research and clinical care for dialysis patients. Therefore, this thesis also examined the proportion and characteristics of dialysis patients with low perceived control who do not accept care for regaining control and their reasons for not accepting care in the context of the RCT.

**Aim and outline**
The first aim of this thesis was to explore factors associated with improved well-being across transplantation. The second aim was the development and evaluation of a psychosocial intervention for enhancing perceived control in end stage renal disease patients undergoing dialysis. Chapters 2 and 3 explore the underlying role of self-regulation and benefit finding in distress declines from pre- to post-transplantation. Chapter 4 examines the concept of perceived control from a patient perspective, as well as the factors facilitating and impeding a sense of control. Chapters 5 describes the protocol of the psychosocial intervention for enhancing perceived control and Chapter 6 reports on its effectiveness, feasibility and acceptability. Chapter 7 further explores the proportion, characteristics and reasons of dialysis patients with low perceived control to not accept care for regaining perceived control within the RCT. Finally, chapter 8 provides a general discussion of the conclusions drawn from the studies, the clinical implications of the findings and suggestions for future research in the field of psychosocial care in end stage renal disease.
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