Patient-relevant outcomes after kidney transplantation

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Chapter 7

Summary and general discussion of this dissertation

This dissertation aimed to broaden our understanding of patient-relevant outcomes after kidney transplantation with a special focus on the patients' perspectives. By conducting different studies in Dutch kidney transplant recipients (KTRs) and by synthesizing existing evidence, we explored several post-transplant patient-relevant outcomes and investigated pathways to improve these outcomes, hereby adding to the existing body of knowledge in kidney transplantation. In **Chapter 1,** we briefly introduced the status quo of patient-relevant outcomes in KTRs, discussed potential pathways to improve patient-relevant outcomes in KTRs, and provided an overview of the studies presented in this dissertation. In this chapter, **Chapter 7**, we will provide a summary of our main findings (please also see **Figure 1** for a graphic summary), the clinical implication of our main findings, and suggestions for future research.

Summary of main findings

Medication non-adherence to immunosuppressants is a well-known risk factor for suboptimal graft function and graft loss in patients after kidney transplantation. **Chapter 2** presents the results of a cross-sectional study that investigated the impact of patients' illness perceptions on their self-reported medication non-adherence to the immunosuppressive treatment in prevalent Dutch KTRs. We found a high prevalence (32.4%) of medication non-adherence in our study population, with the most common non-adherence behavior being 'taking mediations 2 hours beyond the prescribed dosing time'. More importantly, our study revealed significant associations between several stronger negative illness perceptions and medication non-adherence to immunosuppressants, namely: illness identity, concern, and illness coherence. The associations between illness perceptions and medication non-adherence did not differ depending on the time since kidney transplantation. Our findings underline the need to improve medication adherence to immunosuppressants in KTRs and indicate that providing support for patients to shape their illness perceptions into more positive perceptions can help them achieve better medication adherence and, consequently, better health outcomes.

In **Chapter 3**, we investigated the risk factors for hospital readmission after kidney transplantation, an indicator for the burden of disease. In particular, we investigated whether donor type was a risk factor for 3-month hospital readmission in Dutch KTRs using data from the Netherlands Organ Transplant Registry. Our study showed at least one hospital readmission in one-third of the KTRs within 3 months after the initial discharge for kidney transplantation. KTRs with living donors had a significantly lower risk of 3-month hospital readmission compared to those with deceased donors. In KTRs with deceased donors, receiving a donation after cardiac death or after brain death did not influence the

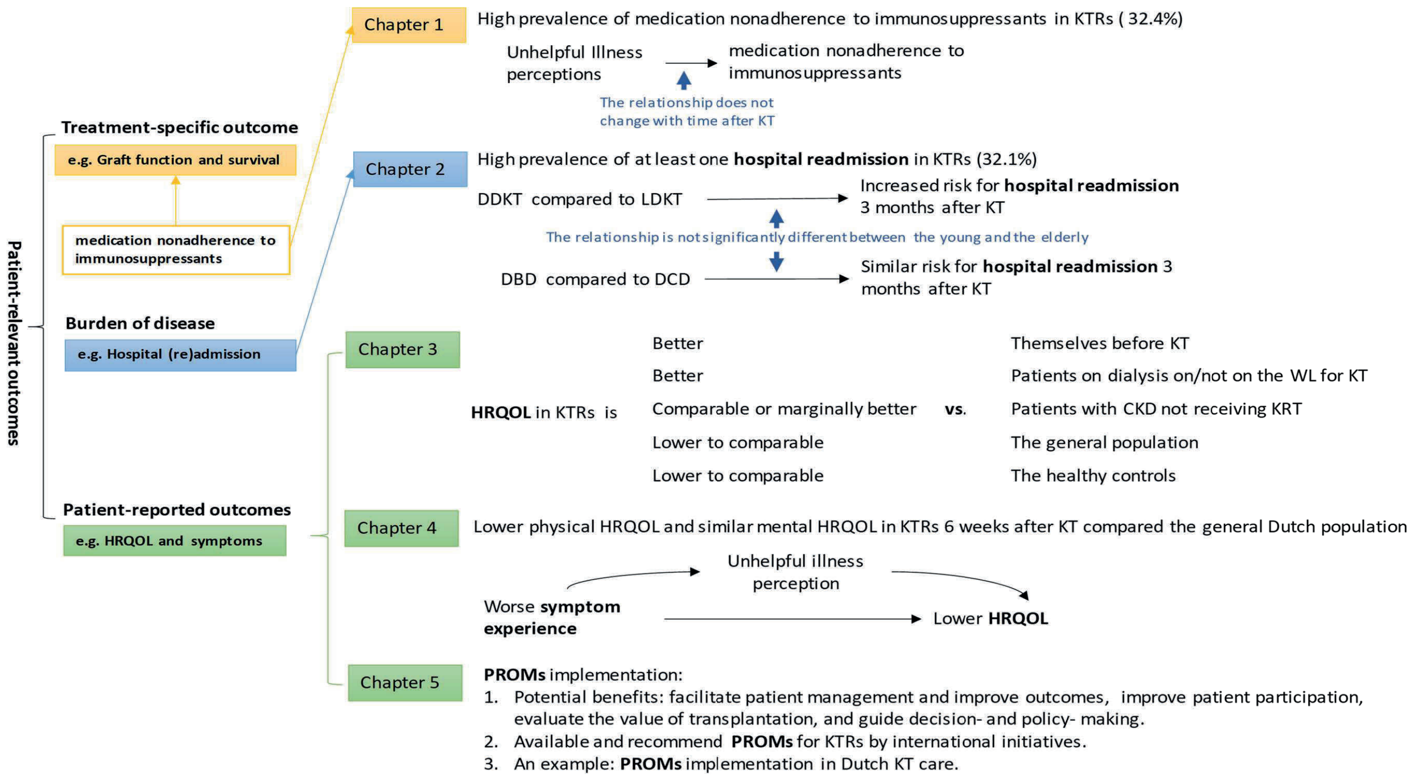

Figure 1. A brief graphic summary of the main findings of this dissertation.

Abbreviation: CKD, chronic kidney disease; DBD, donation after brain death; DCD, donation after cardiac death; DDKT, deceased donor kidney transplantation; LDKT, living donor kidney transplantation; HRQOL, health-related quality of life; PROMs, patient-reported outcome measures; KT, kidney transplantation; KTRs, kidney transplant recipients.

risk of 3-month hospital readmission. Our subgroup analysis revealed no significant difference in the association between donor type and hospital readmission between the young (< 65 years) and elderly KTRs (≥65 years). These findings support the benefit of living donor kidney transplantation. Furthermore, despite the fact that the donor type is not always a modifiable risk factor, knowledge of such risk factors can help healthcare professionals to identify high-risk patients and tailor clinical management plans.

Chapter 4 presents the results of a systematic review that described the health-related quality of life (HRQOL) in KTRs via comparison to other relevant populations, namely: patients receiving dialysis treatment, patients on the waiting list for kidney transplantation, patients with chronic kidney disease (CKD) not receiving kidney replacement therapy, the general population, healthy controls and themselves before kidney transplantation. We found that KTRs had better HRQOL than themselves before kidney transplantation and patients on dialysis with or without being on a waiting list, and similar or marginally better HRQOL than patients with CKD not receiving kidney replacement therapy. When compared to the general population and healthy controls, KTRs can reach comparable HRQOL in the first one or two years but lower physical HRQOL and lower to comparable mental HRQOL one or two years after kidney transplantation. Our findings reinforce the benefits of kidney transplantation in terms of HRQOL and indicate room to further improve HRQOL after kidney transplantation via identifying risk factors for suboptimal HRQOL.

In **Chapter 5**, using data from the ongoing multi-center cohort study in the Netherlands – the Patient-reported OutcomeS In kidney Transplant recipients: Input of Valuable Endpoints (POSITIVE) study –, we investigated whether patients' symptom experience had an impact on HRQOL in KTRs as a risk factor and whether this impact was mediated by illness perceptions. We found a large number of symptoms with a moderate level of burden in KTRs at transplantation. KTRs shortly after transplantation had similar mental HRQOL but significantly lower physical HRQOL in comparison to the Dutch general population. The number of symptoms experienced at transplantation had a significant impact on HRQOL shortly after transplantation, while the symptom burden had a minor impact. Furthermore, our analysis indicated a mediation effect of this impact via illness perceptions. These results emphasize the importance of active symptom management in KTRs and the potential to improve KTRs' HRQOL via modifying unhelpful negative illness perceptions into more positive helpful perceptions, especially in case there is an absence of effective medical treatment for the symptoms experienced by patients.

Finally, **Chapter 6** presents a narrative review to promote the clinical implementation of patient-reported outcomes measures (PROMs) in kidney transplant care. In this review, we introduced the concepts of patient-reported outcomes (PROs) and PROMs, described the potential benefit of implementing PROMs in kidney transplant care, and summarized a number of PROMs recommended by different international initiatives to measure relevant PROs (e.g. HRQOL and symptom burden). Furthermore, we shared our first steps in the implementation of PROMs in Dutch kidney transplant care and addressed the challenge of PROMs implementation based on our experience in both dialysis care and kidney transplant care. In conclusion, PROMs can be a valuable addition to the current standard care and provide a great opportunity to improve the quality of healthcare for KTRs. Several PROMs that are primarily used in research can be used in routine care, and the decision to select PROMs in practice should be made depending on the purpose and the population at hand. To facilitate successful PROMs implementation, adequate preparation and strategies to encourage patient and healthcare provider engagement are necessary.

Clinical implications of the main findings

In summary, the findings of this dissertation indicate the need to improve patient-relevant outcomes under study and suggest several pathways to achieve this. The clinical implications of each study have been discussed in the corresponding chapters (**Chapter 2-6**). In this chapter, the clinical implications of each study will be discussed using a more general approach, also in the light of findings from other studies in this dissertation.

Tackle medication non-adherence to immunosuppressants, a risk factor for graft loss

Medication adherence to immunosuppressive treatment is crucial in KTRs in order to maintain graft function, which requires patients to take their immunosuppressants in the right dose and at the prescribed times on a daily basis[1]. However, the high prevalence of medication non-adherence to immunosuppressants, reported by previous studies [2, 3] and by our study in **Chapter 2,** leaves considerable room to improve this important self-management behavior in KTRs. Optimizing medication adherence requires healthcare professionals to identify medication non-adherence timely and provide adequate support for patients to achieve better adherence. Methods to detect medication non-adherence to immunosuppressants can be both direct and indirect[4]. The direct methods include supervised medication-taking by healthcare professionals, monitoring biological markers in the blood (e.g. the concentration of therapeutic drugs), and adoption of more advanced technology (e.g. using an ingestible sensor system embedded in pills to monitor medication-taking)[4-6]. The indirect methods include pill counting, refill monitoring, evaluating self-reported medication adherence regularly, and using smart medication containers which register when pills are extracted from the container [4, 7, 8]. Notably, self-reported medication adherence can be measured routinely via implementing PROMs in clinical practice. An example of a PROM that can be used to detect and discuss medication non-adherence is the brief, commonly used and validated Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS© Written)[9]. The latter is also discussed in **Chapter 6**.

To address the medication non-adherence if detected, healthcare professionals need to have knowledge of the underlying causes and corresponding intervention strategies. The findings of our study in **Chapter 2** indicate the potential to improve medication adherence via providing support for patients to shape negative illness perceptions into more helpful perceptions. In particular, patients who believe to a lesser extent that they understand their illness and who believe to a greater extent that their illness causes them more symptoms and greater worries are at a higher risk of being nonadherent to their immunosuppressants. Such unhelpful illness perceptions are modifiable by means of psycho-educational interventions[10, 11]. Medication non-adherence can also happen when the complexity of immunosuppressive treatment exceeds the patients' capability to handle the medication regimen, when patients have inaccurate beliefs regarding their treatment (e.g. 'I would not become ill if I do not take my medication'), and when patients are financially challenged[12]. Under such circumstances, healthcare professionals may consider simplifying the dosing (e.g. taking all immunosuppressants at one moment instead spread across two moments a day), helping patients sort their pills using proper tools (e.g. pillbox), enhancing patient education regarding the necessity and benefits of their immunosuppressive treatment, and involving social workers to help patients with their medication-taking and seek for financial support[12-15]. Finally, increasing awareness of the screening methods and potential treatment strategies for medication non-adherence to immunosuppressants among healthcare professionals is necessary[12].

Reduce hospital readmission, an indicator for disease burden for KTRs

Our study in **Chapter 3,** as well as previous studies, revealed a high prevalence of hospital readmission in patients within 3 months after kidney transplantation[16, 17]. According to previous research, hospital readmissions are costly and can lower patients' HRQOL[16, 18]. Of note, our results from **Chapter 4** and **Chapter 5** underscored the need to improve HRQOL after kidney transplantation. Taken together, these findings suggest a potential benefit of reducing hospital readmission in terms of multiple outcomes (i.e. disease burden *and* HRQOL). Furthermore, donor type was identified as a risk factor for hospital readmission after kidney transplantation in **Chapter 3**, knowledge which can be used to screen for high-risk patients along with other risk factors reported by previous studies[16]. For example: previous studies reported a predictive value of symptom clusters and HRQOL for hospital readmission[19, 20], suggesting the use of PROMs in clinical practice to identify high-risk patients and enable timely intervention. Interventions to reduce hospital readmission have been described in the discussion of **Chapter 3**, and include, for example, patient education about post-transplant medication and discharge planning. Furthermore, it is important to take into account the delicate balance between the burden and necessity of hospital readmission in clinical practice. In general, patients do not think of hospital admissions as a positive experience[21]. However, some patients may perceive it as positive as they have more confidence in specialists or hospital care compared to primary care[22]. In recent years, hospital readmissions and length of hospital stays have emerged as quality metrics: fewer hospital readmissions and shorter hospital stays are encouraged as they are considered indicators for better healthcare[23]. However, hospital readmissions due to health conditions and other concerns (e.g. some patients may require more time to understand changes in treatment without family support) are believed to be beneficial for KTRs[24]. Moreover, previous research found an association between a longer hospital stay and a lower risk of subsequent hospital readmission, suggesting a conflict between the two indicators[23]. Taken together, efforts from healthcare professionals and policy-makers should be made to avoid unnecessary hospital readmission or hospital readmission resulting from modifiable causes and, at the same time, enable efficient treatment via hospital readmissions if necessary.

Optimize HRQOL, a valuable outcome after kidney transplantation

HRQOL has been identified as an important outcome after kidney transplantation next to patient survival and graft survival[25]. Our findings in **Chapter 4** showed improved HRQOL in KTRs compared to themselves before transplantation and patients on dialysis with or without being on a waiting list. However, when compared to the general population or healthy controls, the results underline that there is still room for further improvement of HRQOL in KTRs. Risk factors for suboptimal HRQOL after kidney transplantation can be sociodemographic (e.g. unemployment and living alone), biomedical (e.g. side effects from the treatment and comorbidities), and psychosocial (e.g. depression and negative illness perceptions), which are described in the discussion of **Chapter 4**. Furthermore, our study in **Chapter 5** suggested that KTRs with worse symptom experience could develop unhelpful illness perceptions which then leads to suboptimal HRQOL. Given the wide range of risk factors for HRQOL in KTRs and the interplay between risk factors (i.e. symptoms and illness perceptions), a holistic approach that acknowledges patients' physical, psychological and social needs is necessary to achieve better HRQOL[26]. Such holistic management is also endorsed by results from a previous study in patients with cancer, showing an association between suboptimal HRQOL and unmet needs in their healthcare[27]. Notably, PROMs that measure HRQOL, symptom experience and other psychosocial aspects can serve as a powerful tool to reveal unmet needs in the healthcare delivery process and, consequently, guide (adjustment to) treatment in close collaboration with patients for better health outcomes, including HRQOL[28-30]. The 36-item Short-Form Health Survey (SF-36), the RAND 36-item Health Survey and a combination of the Patient-Reported Outcomes Measurement Information System–Global Health and the 29-item PROMIS are recommended by the International Consortium for Health Outcomes Measurement CKD working group to measure HRQOL in nephrology and kidney transplant care[25]. A consensus meeting organized by European Renal Association (ERA) also proposed the preferred PROMs to measure HRQOL for different purposes: the 12-item Short-Form Health Survey (SF-12) for generic HRQOL, the 36-item Kidney Disease Quality of Life Survey for disease-specific HRQOL and the EuroQol 5-Dimension to measure HRQOL for health economic evaluations[31]. Several PROMs are also available for symptom screening in KTRs, including the Modified Transplant Symptom Occurrence and Symptom Distress Scale–59 Items Revised (MTSOSD-59r), the Gastrointestinal Rating Scale, the revised version of the Edmonton Symptom Assessment System and PROMs for specific symptoms (e.g. depression and anxiety)[9, 32-34]. More detailed information about these PROMs (i.e. target population, domain coverage, number of items, and estimated time to fill in the PROMs) are summarized in **Chapter 6**. In our POSITIVE study to implement PROMs into Dutch kidney transplant care, the SF-12 and a symptom checklist including both CKD-specific symptoms (the Dialysis Symptom Index) and immunosuppressive treatment-specific symptoms (the MTSOSD-59r) are used.

Implement PROMs, a promising pathway to better healthcare for KTRs

PROMs are developed to structurally capture PROs[35]. In addition to measuring outcomes (e.g. HRQOL and symptom burden), PROMs can, in the broad sense, also be employed to measure psycho-behavioral factors (e.g. illness perceptions and medication adherence)[36, 37]. As an addition to the current standard care, PROMs implementation provides an opportunity to enhance healthcare that emphasizes biological, psychological, and social aspects of patients' health[38]. Our narrative review in **Chapter 6** summarized the potential benefits of PROMs implementation in improving patient management, enhancing patient engagement, and informing decision- and policy-making. Findings from **Chapter 2-5** in this dissertation also, directly and indirectly, support using PROMs to monitor PROs (i.e. HRQOL, symptom experience, medication non-adherence, and patients' illness perceptions) in KTRs to ensure better health outcomes. An essential step to systematically implement PROMs in clinical practice is to select the proper PROMs.[39] Currently, international working groups have recommended PROMs to measure HRQOL in KTRs[25, 31]. However, recommendations for other outcomes are not yet available. An integrated approach to select PROMs for clinical practice has been described in detail elsewhere[39], including establishing a representative PROMs selection committee, identifying PROs to be measured, collecting 'candidate' PROMs, appraising collected PROMs, evaluating measurement properties of selected PROMs (e.g. reliability and validity), selecting the PROMs and conducting a pilot test of the selected PROMs in the target population. Also, effective measures to facilitate PROMs administration and enhance its uptake are essential for systematic PROMs implementation. Potential measures to this end will be discussed later in this chapter (e.g. establish a patient- and healthcare professional- friendly PROMs administration system and increase the perceived values of PROMs). Examples of PROMs implementation in routine healthcare for dialysis patients[40, 41], solid organ transplant recipients[42] and KTRs (i.e. the POSITIVE study) are available in current literature, which endorse the feasibility of PROMs implementation and provide practical information for upcoming attempts.

Perspectives on future research directions

Maximizing the value of medical treatment is of great interest for individual patients and the healthcare system, which is especially true in the context of kidney transplantation due to the organ shortage in the present and in the foreseeable future. In the era of patient-centered and value-based healthcare, the role of patients in their healthcare has been continuously emphasized, and the value of kidney transplantation should depend on outcomes relevant to patients, including but not limited to patient and graft survival[25, 43]. As a result, more and more studies over the past decade have explored PROs and patient self-management after kidney transplantation. Below, the remaining knowledge gaps and challenges in advancing research about these two topics in KTRs will be further discussed to inform future studies.

Currently, data with regard to PROs after kidney transplantation with a structural follow-up more than 5 years are still lacking. Even studies with a follow-up of 2 to 3 years are scarce. As a consequence, little is known about the trajectory of such outcomes and their interventional targets to ensure further improvement of these outcomes. Routinely collected PROs data via incorporating PROMs into standard care and into kidney registries provides an opportunity for future research to narrow this knowledge gap. A disease registry refers to an organized system that aims to collect uniform data continuously and systematically about a certain disease in a defined population[44]. Ideally, such registries ensure the sustainability and generalizability of the collected data[45]. However, this opportunity comes along with challenges. Our experience and existing literature[40, 46] have found a suboptimal response rate with a downtrend to PROMs over time in cohort and registry-based studies. Evidently, a low response rate poses a threat to the generalizability of the collected PROs data[46, 47]. Furthermore, it can lead to potential selection bias and influence the accuracy of estimates when PROs are used to identify potential risk factors or evaluate interventions[46, 48]. To examine the influence of non-response in research, patient characteristics of responders are often tabulated and compared with non-responders or the target population [49]. However, data about non-responders and the target population is not always (sufficiently) available. Statistical formula and external knowledge of the non-response mechanisms have also been used in previous studies to evaluate the direction of potential selection bias, but the frequently-encountered heterogeneity of the non-response mechanisms can complicate this evaluation (e.g. both low and high HRQOL could lead to non-response)[47, 50]. A fundamental solution to minimize the influence of non-response is to prevent it in the first place[51]. The potential causes for the high non-response to clinically implemented PROMs and their implications for future research will be discussed hereafter.

First, non-response to PROMs can happen when patients and health professionals are not aware of the potential benefits of their use in clinical practice. A large body of qualitative research in nephrology care and beyond have shown that patients and healthcare professionals have a positive attitude towards the clinical implementation of PROMs[52-56]. Results from randomized controlled trials and cohort studies in cancer patients have also demonstrated positive impacts of routinely using PROMs in clinical practice, showing: 1) reassessment and treatment adjustment triggered by a symptom alert, 2) more referral for unmet needs and less emergency room visits , and 3) less symptoms, reduced symptom burden and improved HRQOL in patients receiving PROMs regularly in their healthcare than those with standard healthcare[57-60]. However, there is a lack of quantitative research investigating the impact of PROMs implementation on health outcomes and healthcare quality indicators in CKD patients, including KTRs. Therefore, additional quantitative research in kidney transplant care is necessary to enhance the current evidence-basis for PROMs implementation and to improve its perceived value in clinical practice, thereby potentially also increasing the uptake and response to PROMs.

Second, a lack of knowledge among healthcare professionals to correctly interpret PROs and properly intervene can lead to a suboptimal response to PROMs because, without sufficient feedback during consultations, patients may feel that their needs are not adequately addressed [61]. PROs can be interpreted intuitively. Healthcare professionals can use PROs as a starting point for their discussion with patients to identify neglected health problems and unmet (para)medical needs (e.g. a much lower mental HRQOL than the population norm may suggest psychological problems that are not regularly screened in patients)[62]. Previous research has also explored concepts and cut-offs to facilitate a quantitative interpretation of changes in PROs. The two most relevant concepts are the minimal detectable change and the minimal clinically important change[63]. A minimal detectable change refers to the smallest change in PROs that is not due to random variations or measurement errors, and a minimal clinically important change refers to the smallest change that is perceived as important by patients[63]. A previous study in patients with stage 5 CKD receiving conservative care showed a minimal detectable change of 4.2 and 7.0 for physical and mental HRQOL measured by the 36-item Short-form Health Survey, indicating that changes larger than such cut-offs could be considered a real change[64]. The same study also found a minimal clinically important change of 6.3 and 8.7 for physical and mental HRQOL[64]. To our knowledge, such investigation to interpret HRQOL is still lacking in KTRs and limited in general. In addition, one should also be aware that whether a change is important or not should be determined by patients individually as it may vary among patients. It is worth noting that the interpretability differs across PROs, and some PROs may be easier to interpret. For example, healthcare professionals can immediately know the occurrence of symptoms and how burdensome they are to patients based on results from a symptom checklist[9]. However, without relevant knowledge concerning those PROs, healthcare professionals may still find it difficult to initiate proper treatments[12, 41]. This is especially the case in kidney transplantation when patients experience side effects from certain immunosuppressants, and a switch to other immunosuppressants is not feasible. Nevertheless, symptom-specific treatment and holistic management can still be initiated under such circumstances to alleviate the symptom burden[65]. Taken together, sufficient training is necessary to inform healthcare professionals about the broad spectrum of PROs, how to interpret PROM results, how to discuss PROMs results with patients (e.g. addressing sensitive topics such as emotional or sexual problems) and the available treatment options. To this end, future studies combining efforts from patients, healthcare professionals, and researchers are necessary to establish a guideline for PROMs interpretation and develop toolboxes to effectively discuss and treat health problems identified by PROMs.

Finally, suboptimal response to PROMs can happen in the absence of an effective PROMs administration system that is user-friendly to patients and healthcare professionals. Previous studies showed positive results in increasing response from patients by measures to accommodate their preference in terms of the language and formats (i.e. digital and in paper) of PROMs and to facilitate timely response (e.g. sending reminders and collecting PROMs during their clinical visit)[40, 46]. However, the cost does increase with more efforts made to increase response[49], suggesting potential financial considerations during the development of a PROMs administration system. For healthcare professionals, a major barrier to use PROMs in clinical practice is the heavy workload and limited consultation time for each patient in outpatient clinics, although existing evidence suggests that discussing PROMs results does not necessarily prolong consultation time when the results are shared with healthcare professionals in advance[41, 66]. This divergence between the current evidence and the perceived burden to use PROMs by healthcare professionals emphasizes the importance of PROMs training but also a PROMs administration system that is incorporated into their standard workflow with easy accessibility[41, 66, 67]. Findings in dialysis and oncology care also highlighted the importance of incorporating an easily interpretable PROMs report with simple configuration and actionable treatment aids to alleviate potential health problems into the system to improve uptake of PROMs by healthcare professionals and, consequently, increase response from patients[41, 57]. In addition to optimizing response to PROMs, an efficient PROMs system should enable high completeness of PROMs. Digital PROMs and the flexibility to allow patients to fill in PROMs beyond their clinical visit have been found associated with better completeness[68, 69]. In recent years, attempts to implement PROMs in nephrology care have emerged, including our POSITIVE study in KTRs[40, 54]. Such ongoing efforts will provide more information on refinements to develop a cost-effective PROMs administration system that tackles barriers from both patients’ and healthcare professionals’ perspectives for kidney transplant care in the future.

Current healthcare models, such as patient-centered healthcare and value-based healthcare, emphasize patient-centeredness and provide a set of prescriptions for healthcare professionals to guide practice[70, 71]. However, to maximize the value of healthcare, adequate self-management by the patients is essential, especially for those with chronic conditions[71]. The Common-Sense Model of Self-regulation has been used to explain patients’ coping (including self-management) behaviors since it was proposed by Leventhal four decades ago[72, 73]. According to this model, patients form illness perceptions in the presence of health threats which then influences their self-management behaviors. Findings of our study in **Chapter 2** and **5** and existing evidence support this model, showing an association between more helpful illness perceptions and better self-management behaviors or health outcomes in KTRs and patients with other chronic diseases, as well as a mediation effect of illness perceptions between health threats and outcomes[74-76]. To further facilitate the translation of this model into clinical practice for KTRs, future studies may expand our current understanding in the following aspects.

First, more studies are needed to explore risk factors for unhelpful illness perceptions to reveal treatment targets and identify high-risk patients who may develop unhelpful illness perceptions after kidney transplantation for timely intervention. Ford et al. found that illness perceptions in critically ill patients were influenced by their race, religion, and HRQOL before their illness[77]. However, current knowledge about risk factors of unhelpful illness perceptions in other disease populations, including KTRs, is limited. Second, illness perceptions refer to multiple beliefs that patients hold with regard to their illness. For example, one of the most widely-used questionnaires, the Brief Illness Perception

Questionnaire, consists of eight illness perceptions[78]. Therefore, future studies may investigate the impact of interventional strategies for individual illness perceptions to provide KTRs with a tailored treatment (e.g. focussing on the perceived lack of knowledge or the great deal of worry). Third, KTRs need adequate self-management to achieve better health outcomes, including, but not limited to, medication adherence. Other important but rarely studied self-management behaviors in KTRs are rejection and infection monitoring (e.g. paying attention to changes in urine output, weight, and body temperature), infection prevention (e.g. frequently washing hands and avoiding epidemiologic exposures), and regular exercise[79-81]. An ongoing study has shed light on nurse-led interventions to promote self-management beyond medication adherence in patients with organ transplantation[82]. However, more studies are needed to provide adequate information about self-management behaviors in KTRs and explore to what extent they can be modified by different intervention strategies targeting potential risk factors (e.g. unhelpful illness perceptions). Such knowledge can be used to enhance self-management in KTRs and consequently improve health outcomes which, in turn, could positively impact patients' illness perceptions[73]. Finally, studies with longitudinal design and temporal considerations are needed to capture the dynamic nature of this model to inform practice in kidney transplant care (e.g. conducting measurements in the following order to investigate the impact of illness perceptions on graft function: illness perceptions – medication adherence – graft function). In summary: efforts to modify multiple interventional targets of the Common Sense Model should be made to shape a positive psycho-behavioral loop and encourage efficient self-management in KTRs for better health outcomes[71].

Main conclusion

In conclusion, studies presented in this dissertation indicate room and possibilities to improve different patient-relevant outcomes after kidney transplantation (i.e. treatment-specific, disease burden-related, and patient-reported outcomes).

In particular, we have found a high proportion of KTRs who are not adherent to their immunosuppressive treatment, which suggests an opportunity to further improve graft function and survival. Our findings indicate that modifying unhelpful illness perceptions can be a potential strategy to improve medication adherence and subsequent outcomes. We also found a high prevalence of short-term hospital readmission in KTRs, suggesting a high burden of disease after kidney transplantation. Our results have shown a lower risk of being readmitted in KTRs with living donors than those with deceased donors and a similar risk between KTRs with donation after cardiac death and brain death. Therefore, donor type and other known risk factors for hospital readmission can be used to identify high-risk patients so that healthcare professionals can deliver tailored healthcare to reduce unnecessary hospital readmission. Finally, results from our systematic review show that KTRs have better HRQOL compared to themselves before kidney transplantation or patients on dialysis but lower HRQOL compared to the general population or healthy controls. These results support the benefits of kidney transplantation and imply room for further improvement in terms of HRQOL. According to our findings in a longitudinal study, KTRs experience a large number of symptoms and moderate symptom burden. Their symptom experience poses a negative impact on their HRQOL, which is mediated by their illness perceptions. That is to say, patients can develop more unhelpful illness perceptions as a result of worse symptom experiences which then lead to lower HRQOL. Therefore, active symptom management and support to modify unhelpful illness perceptions into more helpful ones are potentially effective pathways to help KTRs further improve HRQOL. This finding also reinforces the potential value of illness perceptions as an interventional target for better outcomes. In addition to exploring patient-relevant outcomes and their risk factors, this dissertation addresses the possibility of improving outcomes after kidney transplantation via implementing PROMs in clinical practice. Given the potential benefits of PROMs (e.g. enhancing clinical management, empowering patient engagement, and informing shared decision-making), future investigations aiming to improve the uptake of PROMs among KTRs and healthcare professionals are of great value and necessity.

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