Exploring the potential of self-monitoring kidney function after transplantation : from patient acceptance to replacing outpatient care

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CHAPTER 7

General discussion

In the last decade significant improvements in kidney transplant outcome have been achieved thanks to the availability of more effective immunosuppressive medications, and improved organ preservation, surgical techniques and antimicrobial prophylaxis [1].

However, patients continue to be at risk for acute rejection of their kidney graft, mainly in the first year after transplantation. The most important parameter for rejection is deterioration of renal function, measured by the concentration of serum level creatinine. As early detection of a rejection episode is mandatory to minimize permanent damage to the kidney graft[2-7], kidney transplant patients in the Netherlands visit the outpatient clinic about 20 times during the first year post-transplantation. Based on the experiences in other conditions where frequent monitoring is required, we expected that self-monitoring kidney function after transplantation has the potential to increase patient satisfaction[8-14], detect complications after transplantation early [15, 16] and reduce healthcare consumption[17-19] at the same time. With that, self-monitoring aligns seamlessly with the concept of value-based healthcare, a strategy that is increasingly being used to challenge the rising care expenditure and improve the quality of healthcare[20].

The general objective of this thesis was to investigate whether self-monitoring kidney function after transplantation supported by a self-management support system (SMSS) is well accepted and can replace part of regular care safely without loss of quality of care. Different studies have been performed to answer this question. The results of these studies will be discussed below, arranged by the main themes that have been described in the papers that are included in this thesis.

The acceptance of self-monitoring kidney function supported by an SMSS

Patient's readiness to self-monitor

The feasibility of self-monitoring is highly dependent on the readiness of kidney transplant patients to monitor at home. The willingness to participate in the study and the satisfaction of patients who engaged in self-monitoring are important indications for this readiness. The response rate in both the pilot study (94%, as described in chapter 2) and RCT (77%, as described in chapter 5) shows that kidney transplant patients seem very motivated to self-monitor kidney function. The difference between these two studies is not fully explained, but may be partly due to the inclusion of recipients of deceased donor kidneys in the RCT but not in the pilot study. As these patients could not be recruited beforehand, they were approached shortly after transplantation, when they may still have been too overwhelmed with the event of the transplantation to decide on study participation. Further, these

patients were on average older and in worse condition, which may have made self-monitoring kidney function supported by an online system less attractive to them.

High levels of satisfaction with self-monitoring kidney function after transplantation were expressed in both the pilot study (described in chapter 2) and RCT (described in chapter 5). The use of both the creatinine and blood pressure meter was considered pleasant and useful, despite level of trust in the accuracy of the creatinine device being relatively low. In the interviews with patients on their experience with self-monitoring kidney function after transplantation, patients were shown to be very positive taking into account the nearly unanimous (95%) recommendation of self-monitoring to other kidney transplant patients. Further, 75% of the interviewees said they would have liked to continue self-monitoring beyond the first year post-transplantation. The high levels of satisfaction with self-monitoring that we found in both studies aligns with what has been described before [9, 11, 13, 21, 22].

Factors related to patients' satisfaction with self-monitoring

The high response rates and levels of satisfaction that were found in both the pilot study and RCT suggest that many kidney transplant patients are eager to perform self-monitoring tasks. Still, eleven patients (18% of the intervention group) decided to quit self-monitoring. In all 7 cases with a known reason for quitting, the reason was study-related. Four patients indicated they had too little trust in the accuracy of the used creatinine device to continue using it. The importance of perceived reliability was also shown in the pilot study, where a positive relationship was found between level of satisfaction and level of trust in the accuracy of the creatinine device. This corresponds with existing literature, showing that patients' confidence in the accuracy and perceived reliability of devices is an important prerequisite to the acceptance of these devices[23, 24]. One patient did not want to continue self-monitoring as he experienced difficulties when trying to log on to the SMSS for the first time. Although extra support was offered, he seemed to have concluded that online registration of measurements would be too difficult. Difficulty being the main reason for not wanting to continue may refer to two other findings. It may underline the importance of self-efficacy that was found in the pilot study, where patients were more satisfied if they had a higher level of self-efficacy regarding their own self-monitoring skills. The correlation between level of self-efficacy and level of satisfaction has been described before[25, 26] suggesting that thoroughly instructing and supporting patients is important for successful and satisfactory self-monitoring. Difficulty in this case may also refer to the effort someone is willing to invest, which corresponds to our finding that the expected additional burden of self-monitoring was the main reason for not wanting to participate in the RCT.

Further, 2 patients indicated they experienced too little benefit of self-monitoring creatinine post-transplantation, perhaps due to the limited number of outpatients that were actually replaced by telephone appointments. The remaining 4 patients did not provide a reason for quitting but did not perform or register any measurements and were therefore considered voluntary dropouts. If self-monitoring creatinine would become an integrative part of transplant aftercare, with the alternation of outpatient and telephone consults embedded in everyday practice, this would probably increase the perceived benefit of self-monitoring on the one hand and the perceived importance of patients to perform and register their measurements on the other. Considering this, the level of integration or implementation of procedures into care appears to be an important factor for patient satisfaction. This corresponds to one of our pilot study results, showing that a higher level of perceived autonomy support from physicians was related to a higher level of patient satisfaction. This finding also suggests that patients consider self-monitoring to be part of a care system in which their physicians keep playing an important role. It has indeed been shown before that patients consider self-monitoring a less attractive option if this automatically implies a substantial loss of human interaction with the clinical staff[23].

The importance of experienced self-efficacy, involvement of physicians and autonomy support corresponds to Self-Determination Theory[27], where competence, relatedness and autonomy are considered basic human needs. Taking this into account, the experience and result of self-monitoring kidney function can be optimized if patients feel competent to perform the required actions, experience a connection with their healthcare professionals and feel supported by them to play an important role in their own care.

Patients' acceptance of a self-monitoring support system

During the RCT (described in chapter 5), patients used a self-management support system (SMSS), that included the creatinine and blood pressure devices, eLearning, personal health record to register self-measured values and a feedback system that advised patients on their next action (continue regular schedule, measure again or contact the hospital). To study factors related to acceptance of the SMSS, we used a self-developed questionnaire that was based on the Technology Acceptance Model (TAM,[28]) and one of its' extensions, the Unified Theory of Acceptance and Use of Technology, (UTAUT, [29]). Both the TAM and UTAUT are well-known theories that explain people's acceptance of technology. In these theories, several factors are described to explain behavioural intention, the degree to which an individual intends to use a new system. Behavioural intention has been widely used to evaluate user acceptance of technology [28-32]. In TAM and UTAUT, effort expectancy is usually

considered as the main predictor of behavioural intention, whereas a less important factor is people's affective response towards the system. In our study, however, the behavioural intention to start or to continue using the SMSS was very strongly related to patients affect towards the SMSS[29], with affect being represented by items that asked patients whether they considered using the ADMIRE system to be pleasant and whether it gave them peace of mind. Our diverging finding may be explained by the fact that the expected additional burden of self-monitoring after kidney transplantation was the main reason for patients to decline participation in the first place. This is different to what happens when an entire organization implements a new technology that replaces the old one, a situation where the TAM and UTAUT have traditionally been used to study user acceptance. When people are 'free' to choose whether to use a system or not, their affect towards the pertaining system may become much more important. Comments made by patients in the interviews at the end of participation confirm the role of affect in behavioural intention, especially the feelings of being safe. The majority of interviewed patients (75%) indicated that, if possible, they would have liked to continue using the SMSS beyond the first year post-transplantation as it gave them a feeling of safety. We do, however, need to take into account that patients were asked to evaluate the SMSS as a whole, including the measurement devices, eLearning, online personal health record and feedback system, while patients might have held different attitudes and feelings towards the various components of the SMSS. This could have influenced our findings. For example, logging of eLearning usage showed that intervention patients made very little use of the eLearning modules. More than 50% of the intervention patients had never used the eLearning modules or spent less than one minute looking at it. As patients knew they would also receive a live instruction, they may have considered using the eLearning as too much effort, especially given the timing: recipients of a living donor kidney were requested to look at the eLearning modules in the week(s) prior to their transplantation when they may have been more occupied with their upcoming surgery than with preparing for self-monitoring. This may suggest that effort expectancy instead of affect was the main factor contributing to the intention (not) to use the eLearning. For future studies, it would therefore be interesting to study whether the role of affect, effort expectancy and other factors of TAM and UTAUT is different for the various components of an SMSS.

The ADMIRE project was a cooperation between the Leiden University Medical Centre, the Technical University of Delft and TNO. Supported by the expertise of the TU Delft and TNO, different studies have been performed to investigate patients preferences for the interface design to optimize the acceptance of future SMSSs[33]. The results of these studies suggest that a patients' preference is influenced by his level of experience with being a transplant patient (i.e. time since transplantation)

and the content of feedback (i.e. green, orange or red traffic light with corresponding advice). More experienced patients seem to prefer a factual interface, showing only measurement history, medical information and the current advice, over a guided style, that provides more support for interpretation and an avatar showing empathy to address emotional needs. This preference became especially apparent in case of a green traffic light, indicating that a patients' condition was stable. Apart from these general findings, much diversity in preferences was observed. This argues for an interface design that can be tailored to the preferences of an individual patient. However, as these studies also showed that patients often do not use the option to adapt the interface, a default setting based on level of experience and potentially even content of feedback is recommended[33].

The effect of self-monitoring on experienced empowerment and self-efficacy

Self-monitoring has previously been shown to result in an increased sense of the ability to care for oneself, often termed patient empowerment and self-efficacy [9, 13, 34]. The World Health Organization defines empowerment as 'a process through which people gain greater control over decisions and actions affecting their health'[35]. Self-efficacy is defined as 'one's belief in one's ability to succeed in specific situations or accomplish a task' [36]. During the RCT (described in chapter 5), the Partners in Health questionnaire was used to measure level of self-management behavior, including items that reflect both empowerment and self-efficacy. We expected self-management behaviour to increase more in the self-monitoring population, but both the intervention and control group had high levels of self-management behaviour at baseline already which further increased over time. Although this finding is not in line with our hypothesis, it does make sense that the level of self-management behaviour increased in both groups. Patients in the control group did not have access to the creatinine measurements, but they did engage in self-monitoring blood pressure, which is part of standard care after kidney transplantation.

Doctors' acceptance of the SMSS

For a successful implementation of a new SMSS, it is also highly important that the concerning system is accepted by the other users: the doctors. During the RCT, 70% of the doctors (n=15) treating kidney transplant patients had logged on to the SMSS in less than half of their total number of appointments. Three doctors had never visited the SMSS although having had multiple (telephonic) consults. Results from the interviews with pilot participants that were held in an early phase of the project (described in chapter 2) also indicated that doctors generally paid little attention to the self-measured creatinine data. These findings do, however, need to be placed within the right perspective. The pilot study took

place in 2010 and early 2011, the RCT started early 2012. Considering the speed of technological developments and digitalization of our society, the finding that several doctors were somewhat hesitant towards using the SMSS system will probably no longer be representative anno 2018, as doctors are now more used to delivering part of their care in a digital way. Besides the lack of experience with eHealth at that time, some other potential causes for the limited SMSS use can be distinguished. First, some of our doctors were critical about the accuracy of the creatinine device that was used. It has been concluded before that doctors need to feel confident in order to be able to share some of the control with patients[37] and that diagnostic confidence is key to incorporating remote monitoring into the transplant clinic[38]. In addition, as many patients brought a handwritten note with their recent measurement results to the consultation, most doctors might have considered discussing the paper print as being less time-consuming than logging on to the SMSS. Although access to the SMSS was integrated into the hospital information system, actually obtaining the data required an additional step. Both routine and time have been shown to be important factors in the adoption of new ways of delivering care[37, 39, 40]. Third, during the kick-off meeting for this study, many doctors stated that 'there is more to outpatient care of kidney transplant patients than checking creatinine and blood pressure'. Doctors generally feel highly responsible for ensuring that high-quality care is achieved[37, 40, 41] and using patient acquired creatinine and blood pressure only may have clashed with their perception of professional responsibility.

Fourth, the (potential) benefits of self-monitoring kidney function at home are less obvious for doctors than for patients. In a recent paper describing the development of a conceptual model for the design and evaluation of eHealth interventions in chronic disease, it was stated that it is important to emphasize the role that eHealth can play to support healthcare providers[42]. In the current study, some doctors requested for prolonged use of the creatinine device in case a transplant patients' condition was unstable or requested the use of the creatinine device for non-transplant kidney patients for whom increased kidney function monitoring was required. In these cases, self-monitoring made it easier for doctors to keep closer track of their patients' condition without having to increase the number of laboratory analyses and outpatient visits. Especially indicative for the importance of perceived usefulness is the finding that one of the doctors who was more critical of self-monitoring and had never logged on to the SMSS asked for the use of the creatinine device for a non-transplant patient. This may illustrate that healthcare professionals' perception that self-monitoring is really supportive to their care is indeed important for their readiness to use patient generated data.

The safety of self-monitoring

The accuracy of the creatinine device

One of the most important prerequisites for safe self-monitoring is the use of reliable measurement devices. When evaluating the performance of a measurement device, it is important to take the purpose of the measurement into consideration [43]. For measuring kidney function, one can distinguish diagnostic and monitoring purposes. A diagnostic purpose of measurement refers to the necessity to give an accurate indication of the current kidney function directly, for example before administering iodinated contrast media. In people with a decreased kidney function, iodinated contrast media can lead to contrast-induced nephropathy, one of the major causes of hospital-acquired acute kidney injury[44]. The accuracy of a single measurement is less important for a monitoring purpose, as one is interested in how kidney function develops over time. As the suitability of the StatSensor® for kidney transplant follow up had never been studied, we investigated whether the StatSensor® can be used both for detecting current renal function with a single creatinine measurement and for kidney function monitoring purposes. In chapter 4, we first evaluated the suitability of the StatSensor® to detect current renal function with a single measurement. Therefore, the traceability and exchangeability of StatSensor® results was compared to an isotope-dilution mass spectrometry (IDMS) traceable laboratory method, which is the gold standard for creatinine assays[45]. Our results showed that the StatSensor® creatinine device does not fulfil desirable nor minimum analytical performance criteria, which suggests that the StatSensor® is not suitable for detecting current renal function of kidney transplant patients with a single creatinine measurement. These findings are in agreement with previous studies that showed insufficient analytical validity of the StatSensor® in other populations [46, 47] compared to an IDMS traceable laboratory method. Improving the analytical performance of the StatSensor® would improve the potential for using the StatSensor® for diagnostic purposes.

As detection of rejection episodes after kidney transplantation mainly reflects a monitoring purpose, it is important to investigate whether a device is able to detect trends in sequential measurements. The reliability of a single test results is less critical for monitoring over time. For recently transplanted patients, clinicians are especially interested in sudden increases in serum creatinine of >10% as this requires further analysis or intensified follow-up. We investigated whether a >10% change in serum creatinine (as measured by the central IDMS-traceable laboratory method) can also be detected when using StatSensor® for trend monitoring. A reasonable correlation (R = 0.77) between changes detected by the central laboratory and the StatSensor® was found. The StatSensor® correctly identified an

increase of 10% (true positive) in 70% of all cases and a decrease of 10% (true negative) in 67% of all cases. These results were obtained in a laboratory setting. For self-monitoring to be a safe alternative to regular transplant follow-up, it is important to know whether the creatinine device is also sufficiently able to detect deteriorations in kidney function when used by patients. For the detection of clinically relevant increases in creatinine (>10%), we even found a higher level of agreement when self-monitoring was conducted in a real-life setting by patients themselves: in 78% of all relevant cases a similar trend for home-based and laboratory-based creatinine levels was observed (described in chapter 5). The higher level of similarity between home-based and laboratory-based creatinine trends first suggests that patients are able to correctly perform the creatinine measurements at home. Second, it suggests that the accuracy of the creatinine device and test strips has improved over time. The test strips that were used during the laboratory study came from a batch that was manufactured at least 2 years before the batches of strips that were used during the RCT. With the test strips being constantly improved, this could possibly explain the increase of 10% in similarity between home and laboratory measurements and it may indicate that the ability of the StatSensor® to detect changes in kidney function is improving.

However, to make the StatSensor® a more reliable tool for self-monitoring, the further improvement of its analytical performance remains very important as this will automatically improve its' clinical performance (both for diagnostic and monitoring purposes). Awaiting the improvement of the analytical performance of the StatSensor®, two manoeuvres could offer a provisional solution. First, it is desirable that the number of false negatives is decreased, as it leads to delayed detection of rejection, which is dangerous and should not or hardly occur. If applied to the StatSensor®, one could choose a cut-off percentage that is lower for StatSensor® results than for laboratory measurements. For example, by lowering the StatSensor® cut-off percentage to ≥5%, the number of correctly identified relevant increases in level of creatinine (≥10% as determined by the central laboratory method) would have increased from 70% to 82%. A drawback of this approach is that it would result in an increased number of false positives and, consequently, additional diagnostic interventions. Second, the clinical performance regarding monitoring will improve when the number of measurements is increased. With increasing the frequency of StatSensor® measurements, a more reliable trend will be obtained. As patients perform the measurements themselves, we could advise patients to increase their measurement frequency. With lowering the cut-off and a guideline to measure in a higher frequency, the chances of detecting rejection are increased and theoretically, the number of outpatient visits can be safely reduced.

There are, however, two reasons why the percentage of similar trends found in the RCT could actually even be an underestimation of the real similarity between home-based and laboratory-based creatinine measurements. First, level of agreement was based on a comparison between laboratory-based creatinine trends and self-measured values that were registered in the SMSS, not on values that were stored in the creatinine device. As in about 10% of registrations the registered value did not correspond to the actually measured one, it is expected that level of correspondence between laboratory-based and home-based creatinine trends will be higher if values from the devices' memory are used. Second, level of agreement between self-measured and laboratory-based creatinine trends could have been higher if the protocol was followed more strictly. When determining the protocol, we assumed that every other face to face visit would be replaced by a telephonic consult resulting in a lower frequency of laboratory analyses. We used a 1:7 ratio for determining the required measurement frequency, meaning that ideally patients performed seven creatinine measurements to replace one outpatient visit with laboratory assessment. As less outpatient visits were replaced by a telephonic consult than expected (causing the frequency of laboratory analysis to be higher than expected), the number of self-monitored values in between two laboratory assessments was lower. It is possible that the correspondence between home- and laboratory-based creatinine trends would have been even better if more home measurements in between two laboratory assessments would have been available, because a higher number of measurements results in a more reliable trend.

Non-inferiority to regular care

To investigate whether self-monitoring kidney function supported by a SMSS can indeed lead to a reduction in number of outpatient visits in the first year post-transplantation without compromising on quality of care, a randomized controlled trial was performed (described in chapter 5). Self-monitoring led to a significant decrease in number of outpatient visits and total number of reimbursable minutes spent per patient. This achievement was made without compromising on quality of care, indicated by the absence of differences between intervention and control patients regarding kidney function, blood pressure, quality of life and general satisfaction at one-year follow-up. Five self-monitoring patients experienced a rejection episode during their participation in the RCT. In three of these cases, the emerging rejection was detected earlier (i.e. in between two consults) due to the creatinine measurements performed at home, while none appeared to be missed.

The actual difference in number of face-to-face visits between the intervention and control group was, however, smaller than expected. Following our protocol exactly (i.e. replacing half of the face to face visits by a telephonic one from week eight after transplantation onwards), the expected difference in

number of visits between intervention and control patients would have been six. The actual difference between intervention and control group was, however, 2.3 visits. If more patients had responded to the SMSS feedback to contact the hospital (see chapter 5), the difference in number of visits would have been even smaller as these patients would probably have had to come to the hospital for further investigation. Other studies have also reported that reductions in regular care using eHealth were lower than expected [38, 48]. The hesitance of healthcare professionals to use eHealth equipment is suggested as an important factor contributing to the results falling short of expectation [38], which corresponds to the seemingly limited acceptance of the SMSS by the healthcare professionals during the RCT.

Patient's adherence to a self-monitoring protocol

Adherence to a measurement protocol is important for all patients who engage in self-monitoring, but especially for kidney transplant patients. As most patients who develop graft rejection are asymptomatic and present with an increased serum creatinine only, frequent measuring is essential to make the difference between treatment in time and damage to or even loss of the kidney transplant. Based on data that was derived from the RCT, we concluded in chapter 6 that level of adherence to self-monitoring creatinine was generally good. Well above 90% of all patients performed the requested number of measurements during month 2-4 after transplantation. Adherence was somewhat lower during the first month (75%) when a high measurement frequency was requested, and at the longer term during months 5-12 after transplantation (85%). Two studies reporting on level of adherence to monitoring vital signs after lung transplantation found similar percentages of adherence being above 80% for the entire study period[49, 50]. For self-monitoring blood pressure, patients with uncontrolled hypertension were shown to be adherent for about 73% of the entire study period[51, 52]. In both studies, level of adherence was highest in the first few weeks and declined gradually over time. The level of adherence that has been found in the current study therefore corresponds to percentages that have previously been reported. In contrast, we did not find the highest levels of adherence in the first period. This may have been due to a strenuous measurement protocol: patients had to measure every day in the first month. In these first weeks when patients have to recover and have to get used to life post-transplantation, performing measurements in such a high frequency might be too burdensome. Further, in this first period face-to-face visits were not yet replaced by telephonic consults and patients therefore visited the hospital at least weekly to monitor early signs of graft failure. Due to this high frequency of visits, patients may have felt a reduced need to perform measurements at home, as they did not have to rely on these measurements. The latter may also be an explanation for non-adherence

during the whole study period. Although the number of face-to-face visits was significantly lower for our intervention group, the reduction in number of visits was less than anticipated. Patients therefore continued to visit the outpatient clinic relatively often, potentially resulting in a lower perceived need to perform (all requested) measurements.

The reliability of patient-reported data

For self-measured values to be clinically useful, they need to be reported accurately. In chapter 6, we showed that approximately 90% of both creatinine and blood pressure measurements was registered correctly in the SMSS. This percentage corresponds to what has previously been described for patient-reported blood pressure[51, 53] and anticoagulation[54], but is much higher than has been observed for patient-reported levels of blood glucose[55-57]. In case of non-correspondence between measured and actually registered values, the values that were registered in the SMSS were significantly lower than those actually measured. This suggests that patients select, alter or add values in such a way that their creatinine profile looks more positive. This corresponds to what has been found in a population of patients self-monitoring International Normalized Ratio (INR), where the measurements that fell within the desired range were significantly higher when using patient-reported data compared to data stored in the device[35]. For patients with diabetes or hypertension, it was found that inaccurate reporting increased with increasing levels of blood glucose[56] or blood pressure[53]. Why patients report values that look better than the values they actually measured or add non-existent measurements has not yet been fully clarified. For diabetes, it has been suggested that patients report false glucose levels due to a feeling of guilt for not having achieved glycaemic goals[57] or add phantoms values in an attempt to fill up logbooks and satisfy their healthcare providers[55]. Both situations seem to represent an attempt to be a 'good' patient. However, altering and selecting data that is not representative of the actual clinical situation or adding phantom values in any case may be dangerous. This can lead to suboptimal treatment and, eventually, to worsened patient outcomes[53, 55]. Kendrick and colleagues have indeed shown that women with pregnancy-derived diabetes received suboptimal treatment due to a large difference between their reported glucose values and what they had actually measured[57]. It also seems to work the other way around: diabetic patients who were more reliable in their reporting had a significantly better glycaemic control[55]. This is probably due to a clinicians' ability to adjust therapy more precisely if measurements are reported accurately. To rule out the possibility of incorrect reporting, other authors have already recommended the use of devices that can transfer data automatically [54-56, 58].

Timely registration of measurements

To make optimal use of the feedback system that was incorporated into the SMSS, measurement results had to be registered as soon as possible after the measurement was performed. Many patients, however, saved up their measurements over several days or even weeks to register them all at once (chapter 6). This probably occurred because logging on to the SMSS took time and registering multiple measurements at once was therefore considered more efficient. However, when measurements are registered retrospectively, the advice given by the SMSS is no longer up to date. One can imagine patients saving up measurements in case of a stable creatinine trend, but patients seemed to have postponed registration regardless of the stability of their kidney function. This is alarming as frequent monitoring and taking immediate action in case of early signs of graft failure is vital to prevent or diminish damage to the kidney transplant. Postponed registration appeared to be the main reason why patients had not followed up the advices that were generated by the SMSS. For example, the advice to contact the hospital (which only appeared when creatinine had increased by >15%) was given 24 and followed 14 times (58%). In the remaining 10 cases (concerning 10 individual patients) measurements were registered with several days delay. If only cases with registration on the day of measurement were taken into account, adherence to contacting the hospital was 100%. Postponed registration of measurements will no longer be an issue in case a device is used that can automatically transfer data, combined with a system that can send the automatic feedback to a patients' mobile phone directly.

Clinical implications and directions for future research

The results as described in this thesis show that self-monitoring kidney function after transplantation seems attractive to kidney transplant patients and can lead to a significant decrease in number of outpatient visits without compromising on quality of care. Further, self-monitoring offers a convenient solution to increase monitoring frequency, which could probably lead to earlier detection and treatment of complications and, consequently, improved clinical outcomes. However, the results as described in this thesis also indicate there is some room for improvement. For example, although the readiness of kidney transplant patients to self-monitor was high considering the high response rate in both the pilot study and randomized controlled trial, a few patients quit their participation voluntarily. The main reason for quitting was because of problems related to the creatinine device. Further, some patients indicated they experienced too little benefit of self-monitoring creatinine post-transplantation. The fact that the reduction in number of outpatient visits was smaller than expected might have contributed to the limited benefit these patients experienced. Summarizing, self-

monitoring is well accepted among patients and has the potential to improve health care after kidney transplantation. To further increase the potential of self-monitoring kidney function after transplantation to replace part of regular outpatient care, we suggest that the following three points need careful consideration.

The accuracy of measurement devices

The use of a creatinine device that is less accurate than what both healthcare professionals and patients are used to may have played an important role in the limited reduction of outpatient visits. As a transplanted kidney is a valuable asset, it is understandable that both healthcare professionals and patients are careful when considering new methods of monitoring kidney function. Patients could turn to the SMSS for interpretation of their creatinine value, but many patients saved up their measurements over several days before registering them online. This suggests that patients interpreted their measurements themselves before registering them in the SMSS. However, the fluctuations in level of self-measured creatinine (even in relatively stable situation) made it difficult for patients to put a single value in the correct perspective, which may have hampered their trust in the creatinine device.

Although we had shown that the self-monitored creatinine values can be used for trend-analysis, using the creatinine device may have clashed with what healthcare professionals perceive to be their professional responsibility. It has been concluded before that for doctors to feel (more) confident about sharing control with their patients, the biomedical aspects of care need to be well addressed [37]. This is an important prerequisite to create doctors' support for new interventions. If we had used a creatinine device with a more continuous level of accuracy, doctors would probably have felt more at ease with replacing outpatient visits with a telephonic consult. Dried blood spot analysis may offer an alternative to patients self-monitoring creatinine in case reduction of outpatient visits is the main objective, as dried blood spots have been shown to give reliable creatinine results[59, 60]. However, with dried blood spot analyses there is a delay between blood drawing and test results of at least two days, as the dried blood spots first have to be sent to a laboratory before they can be analysed and linked back to the patient. This is not a problem when a regular outpatient visit is being replaced and the patients' condition is stable, but hampers direct treatment if this is necessary. Moreover, dried blood spot analysis becomes cumbersome in case an increased monitoring frequency is required. And finally, using dried blood spot analyses does not seem to increase patient involvement and autonomy regarding their own treatment. Patients perform the blood collection themselves, but are usually dependent upon the laboratory and their doctor for analysis and interpretation. In conclusion,

improving the accuracy of the point of care creatinine device as used in the RCT is desirable for at least two reasons. First, the device can analyse a drop of blood within seconds, accelerating the detection of a deteriorating kidney function and the start of treatment. Second, it enables patients to become full-fledged partners in their own care, as they perform the full cycle of blood drawing, interpretation of test result (whether or not supported by a feedback system) and acting (i.e. contacting their doctor) in case the results give cause for concern.

A multidisciplinary approach in developing and implementing eHealth

A second point that should be taken into account is that the developmental process of the ADMIRE system may not have been optimal. Many eHealth interventions for chronic conditions have been shown to struggle with engaging both patients and healthcare professionals, with low uptake and high dropout rates[42]. It has been stated that many of the approaches that are being used to develop eHealth technologies are not productive enough to create technologies that are meaningful, manageable and sustainable[61]. According to the World Health Organization, a mismatch between context and technology is the main reason why up to three quarters of the implementation of new medical devices fails[62]. This mismatch could be due to the fact that practice can't keep up with the ongoing technological developments. It takes years to fully implement a new procedure, and by then the 'new' procedure will probably be outdated already. However, there are also other factors that can contribute to the mismatch between context and technology. The Normalization Process Theory (NPT) [63] states that for a successful implementation of new health technologies, it is important that there is a (shared and individual) understanding of the benefits of a new technology and a general expectation that the concerning technology makes people's life or work easier[64]. So, the implementation of new services is expected to run more smoothly if all parties involved see the added value of a new technology. In the ADMIRE project, we especially focused on the experiences of patients with self-monitoring. In cooperation with the technical university of Delft, different studies have been performed in parallel to the RCT to learn more about patients' acceptance of our SMSS and their preferences for, for example, feedback style[33, 65]. The results of these studies gave us the tools to explain some of our study findings and to give recommendations for implementation to enable future use of SMSSs in kidney transplant patients. However, the opinion of the other group of end users, the healthcare professionals, has probably not been sufficiently taken into account. For example, the first time we found out that the medical staff considered it unrealistic to start replacing face to face visits with telephonic consults directly from discharge after transplantation was during the kick-off meeting of the RCT. This point would probably have come up much earlier if more healthcare professionals had

been consulted. More extensive qualitative research during the development of the SMSS and ADMIRE logistic protocol may have guaranteed that concerns could be addressed earlier, for example by also listening carefully to physicians that were more critical of self-monitoring.

Study design

Third, a traditional randomized controlled trial (RCT) design may not have been the best choice in the current situation. According to Van der Meijden and colleagues[66], the evaluation of eHealth is often aimed at measuring the effects of the eHealth intervention while the value of evaluations to improve a technology during development and implementation is neglected. Unlike in evaluating drugs, users' opinions of or reactions to computer systems decide whether or not a system will have an effect[67]. It is needed to understand what differences eHealth technologies can make in healthcare, why eHealth technologies make these differences, and why eHealth technologies may not have the expected impact[68]. To answer these questions, it is important to take the conditions for implementation into account right from the start, by performing formative evaluations to test design assumptions and prototypes throughout the entire process [69]. We used process variables (i.e. number of logons to the SMSS, number of outpatient visits) as a proxy for acceptance, but we did not gather more in-depth information about why the current eHealth technology worked very well for patients but did not succeed in gaining an optimal effect. For example, if we had taken a more practical approach and performed formative evaluations during the RCT, we would have observed that less outpatient appointments were replaced than anticipated. By discussing these findings openly with both healthcare professionals and patients we could have tried to figure out the reasons for not scheduling telephonic instead of outpatient appointments and, if possible, have made changes to the protocol accordingly to optimize the possible effectiveness. The advantage of such a flexible approach is that one can deliver a protocol that has shown to be 'the best practice' (within the boundaries of available time and money) instead of having to stick to the more rigid procedures that are concomitant to an RCT.

General conclusion

Self-monitoring kidney function after transplantation is highly appreciated by patients and can improve the detection of complications while leading to a reduction in healthcare consumption at the same time. To increase the potential of self-monitoring kidney function to replace part of standard outpatient care, it is recommended to use accurate measurement devices and design the protocol with the help of a multidisciplinary and representative project group. For future eHealth-related studies, it

is recommended to choose a study design that includes formative evaluations. To get the most out of a study, it is important to notice shortcomings that reveal itself during a study and be able to act directly upon them, requiring a more process- rather than outcome-oriented study design.

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