

## REVIEW

# eHealth in transplantation

Wiebke Duettmann<sup>1</sup>, Marcel G. Naik<sup>1</sup>, Bianca Zukunft<sup>1</sup>, Bilgin Osmonodja<sup>1</sup>, Friederike Bachmann<sup>1</sup> , Mira Choi<sup>1</sup> , Roland Roller<sup>2</sup>, Manuel Mayrdorfer<sup>1</sup>, Fabian Halleck<sup>1</sup>, Danilo Schmidt<sup>3</sup> & Klemens Budde<sup>1</sup> 

1 Department of Nephrology and Medical Intensive Care, Charité – Universitätsmedizin Berlin, Berlin, Germany

2 German Research Center for Artificial Intelligence, Berlin, Germany

3 Business Division IT, Department of Research and Teaching, Charité – Universitätsmedizin Berlin, Berlin, Germany

**Correspondence**

Wiebke Duettmann MD, Department of Nephrology and Medical Intensive Care, Charité – Universitätsmedizin Berlin, Campus Charité Mitte, Charitéplatz 1, 10117 Berlin, Germany.

Tel.: 030-450-614204;

fax: 030-450-7514927;

e-mail: wiebke.duettmann@charite.de

[Correction added on 28 January 2021, after first online publication: Klemens Budde was designated as corresponding author]

**SUMMARY**

eHealth (“electronic” Health) is a new field in medicine that has the potential to change medical care, increase efficiency, and reduce costs. In this review, we analyzed the current status of eHealth in transplantation by performing a PubMed search over the last 5 years with a focus on clinical studies for post-transplant care. We retrieved 463 manuscripts, of which 52 clinical reports and eight randomized controlled trials were identified. Most studies were on kidney ( $n = 19$ ), followed by liver ( $n = 10$ ), solid organ ( $n = 7$ ), bone-marrow ( $n = 6$ ), and lung transplantation ( $n = 6$ ). Eleven articles included adolescents/children. Investigated eHealth features covered the whole spectrum with mobile applications for patients ( $n = 24$ ) and video consultations ( $n = 18$ ) being most frequent. Prominent topics for patient apps were self-management ( $n = 16$ ), adherence ( $n = 14$ ), symptom-reporting (11), remote monitoring of vital signs ( $n = 8$ ), educational ( $n = 7$ ), and drug reminder ( $n = 7$ ). In this review, we discuss opportunities and strengths of such new eHealth solutions, the implications for successful implementation into the healthcare process, the human factor, data protection, and finally, the need for better evidence from prospective clinical trials in order to confirm the claims on better patient care, potential efficiency gains and cost savings.

*Transplant International* 2021; 34: 16–26

**Key words**

app, applications, eHealth, mHealth, telemedicine, transplantation

Received: 6 August 2020; Revision requested: 17 August 2020; Accepted: 23 October 2020;

Published online: 27 November 2020

**Introduction**

eHealth (“electronic” Health) is a new field in medicine, lacking a broadly accepted definition yet. It includes the use of electronic devices, modern electronic technologies, and any electronic applications to support the health of patients comprising electronic processes for data exchange and communication of healthcare professionals [1–3]. The field includes telemedicine and the exchange of home-measured medical information (e.g., self-assessments or vital signs). mHealth (“mobile” Health) as part of eHealth implicates the use of mobile

applications or devices such as smartphones, apps, and wearables in order to capture data from home, assist or provide information to the patient or doctor [4]. Other aspects of eHealth are robotic approaches, which will be not covered in this review. eHealth applications generate large amounts of data, which can be processed by big data techniques or methods of artificial intelligence (AI). Those methods are supposed to revolutionize medicine using high quality healthcare data. They help to gain more insights to understand complex disease processes, improve diagnosis, treatment, and thus help to prevent complications. Big data and AI applications

in medicine are beyond the scope of this review and will not be covered [5–8].

In general, eHealth has the potential to change all stages of transplantation: improve processes before transplantation, during the transplant processes itself, and after transplantation. In the pretransplant phase, novel electronic techniques can help to promote organ donation, for example, by sharing knowledge, personal experiences, and scientific literature. eHealth-based educational lessons about life-donor procedures are a useful tool for donor education, modern clinical decision support systems assist in living kidney donor assessment and such eHealth solutions may even increase the number of living donor transplantations [9–11]. Better software tools may improve waitlist management, data exchange, and communication with patients and doctors before transplantation. Remote monitoring to support peritoneal dialysis patients has already been implemented [12,13]. eHealth solutions may increase efficiency in the peri-transplant process, for example, by sharing radiology and pathology data [14,15] or the use of digital microscopy [16]. Electronic systems improve communication and data exchange between transplant centers and organ procurement organizations, for example, on organ imaging at retrieval to help centers make better decisions [17]. Transplantation was one of the first fields in the 90's to implement eHealth solutions—far before the term was created—in the allocation process of deceased donors routinely by using web-based electronic health records (EHR) and large databases for documentation of donors and recipients in order to run complex allocation algorithms [18]. Today, the development of better allocation systems is driven by data and risk prediction models, and smart algorithms search for the best suitable donor in paired kidney exchange programs [19].

Finally, eHealth may dramatically transform health care after transplantation. In this review, we focus on the current status of eHealth for treatment of transplanted patients and review the evidence for better patient care, patient empowerment, quality of life (QoL), adherence, and long-term outcomes. We also compare the impact of eHealth efficiency gains and the economic consequences. Other important aspects covered by this review are usability for patients and healthcare providers, as digital solutions can only change health care, if they are actually being used and are user friendly. In consequence, we have to look at the human factor: how to integrate eHealth solutions into workflows and healthcare processes to create efficiency gains and avoid clinically irrelevant time-consuming tasks.

Finally, we look at important data protection issues, as the European Union (EU) released the General Data Protection Regulation (GDPR) in 2018 with a major impact on all eHealth approaches [20]. In the United States, the Health Insurance Portability and Accountability Act (HIPAA) protects sensible health data from inadequate use. In summary, this review presents an overview about the most important aspects of eHealth in post-transplant care.

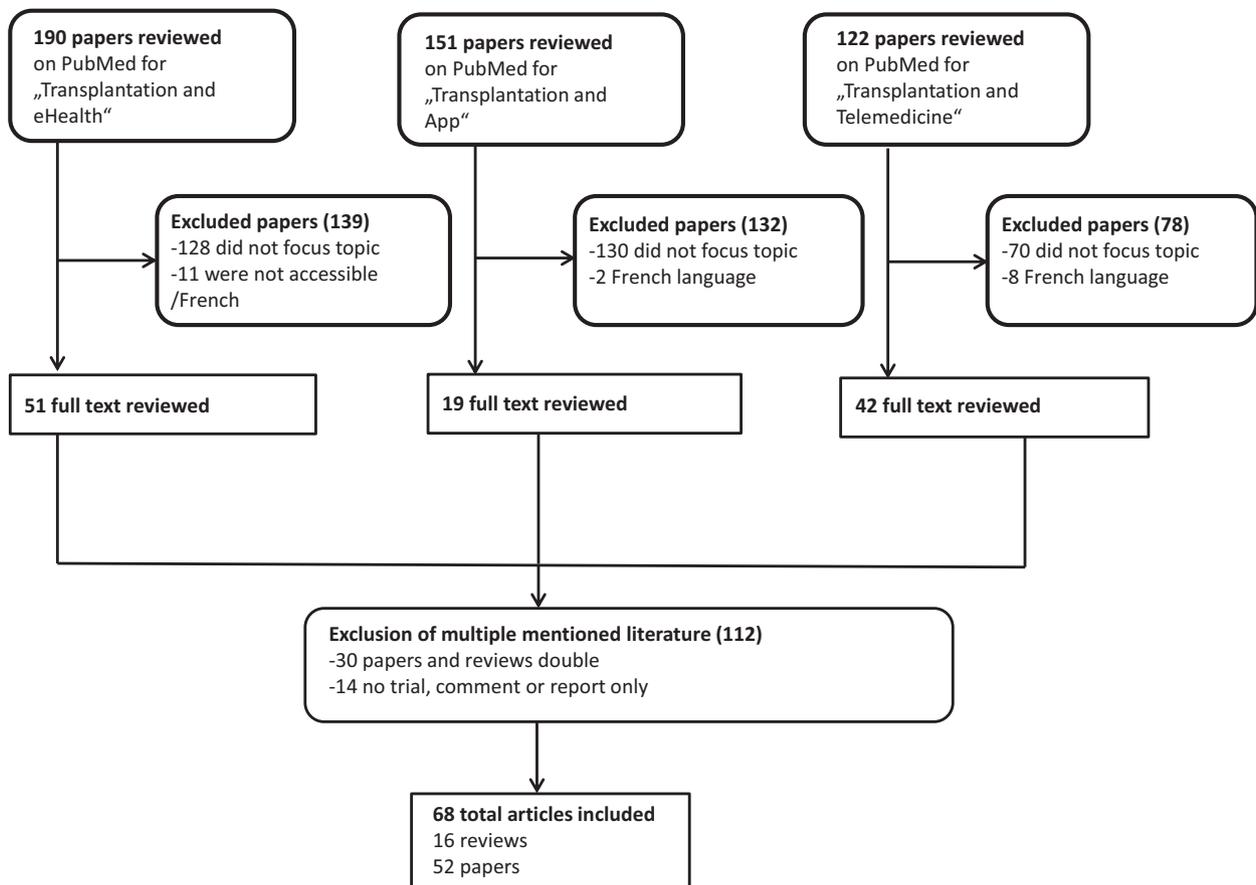
### Literature search

For an overview, we searched PubMed for the terms “Transplantation” in combination with “eHealth,” “telemedicine,” and “app.” We limited our search to the previous 5-year period (01.01.2015–31.12.2019) in English language. We focused on clinical reports on eHealth approaches in the care of patients after transplantation, irrespective of organ and age. We also included reviews to get a better overview of eHealth in the transplant setting. We excluded manuscripts describing eHealth in the pre- and peri-transplant process, as well as papers focusing on technologies such as big data, AI, machine learning, or natural language processing.

In summary (Fig. 1), we retrieved 68 publications: 16 reviews and 52 manuscripts with eHealth solutions for post-transplant care. There were 35 clinical studies (Table 1, Table S1) including eight randomized controlled trials (RCT), 13 descriptions of eHealth pilots without clinical results, and four articles covering various aspects (medical imaging, histopathology). Ten/35 clinical studies were prospective cohort studies, 4/35 retrospective studies, 7/35 cross-sectional investigations, and 4/35 described qualitative research. Most papers focused on adult transplant patients, and 13/52 publications investigated eHealth solutions for children/adolescents. Kidney transplantation ( $n = 19$ ) was most prevalent, followed by liver ( $n = 10$ ), solid organ ( $n = 7$ ), bone-marrow ( $n = 6$ ), lung ( $n = 6$ ), heart ( $n = 2$ ), cornea ( $n = 1$ ), and intestine ( $n = 1$ ). Most frequent eHealth features (Fig. 2) were mobile patient applications ( $n = 24$ ) and video consultations ( $n = 18$ ). Prominent topics for patient apps were help for self-management ( $n = 16$ ), adherence ( $n = 14$ ), symptom-reporting (11), remote monitoring of vital signs ( $n = 8$ ), educational ( $n = 7$ ), and drug reminder ( $n = 7$ ).

### Mobile applications (apps)

Smartphone apps can support the self-management of patients as they are constantly available and free of



**Figure 1** Review process of manuscripts. Flow chart is the disposition of manuscripts at the time of primary analysis, performed when the last manuscript has been read.

charge. Wearables may support monitoring on physical activity, are frequently used in the fitness sector, and may open completely new avenues for clinical research, as recently demonstrated [21,22] for the Apple watch in diagnosis of atrial fibrillation. However, limitations of this approach are many false-negative or false-positive results [23]. Until now, only few data are available on the utility of wearables for chronically ill or transplanted patients and acceptance for users varies largely [24]. A RCT showed that patients using wearables were more active compared to controls after kidney/liver transplantation [25].

In the general population, the use of apps increased over time [26] and the willingness for the use of mobile applications is generally high in transplanted patients [26,27]. The use of health apps is also influenced by the smartphone penetration, which describes the rate of smartphone users among a population and can range from 16% to 83% in 2019 [28]. The smartphone penetration varies dramatically by country and age group, and lack of access to modern technology

can be a barrier to socioeconomic groups that are most at risk of poor outcomes such as graft loss and poor medication adherence. Particularly, younger patients (<50 years) and those with better education are more likely to use smartphones and are interested in new technologies. In contrast, the use of health apps is less appreciated in elderly (>60 years) male transplant patients with lower education and poor cognitive performances [29]. One general problem of mobile applications is the rapid and high attrition rate. The 30-day retention rate for apps is just 42%, and the 90-day retention rate is only 25% [30]. A RCT in transplanted patients [31] failed because of low engagement with the app as only 47% used the app after 1 month dropping to 11.5% after 6 months. Chronically ill patients, however, are expected to use the app for years on a regular basis. It has been shown that gender, income, education, and regular use of technology, as well as the length of stay in a hospital predict the adherence to an eHealth tool [32]. Other studies confirm these findings with varying details [33–36].

**Table 1.** Characteristics clinical studies.

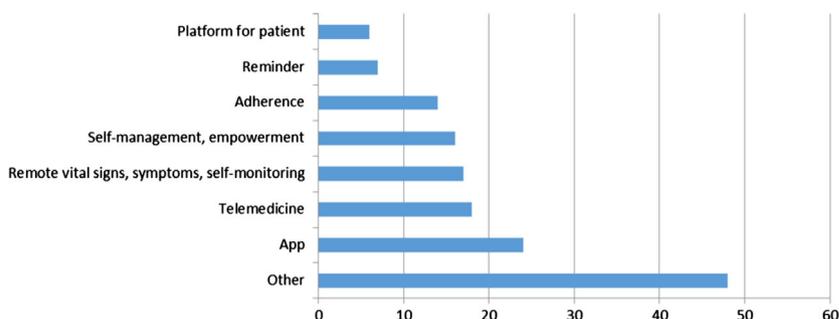
	Results
Observation period	01.01.2013–12.31.2019
Participant number	
Mean (median)	27.7 (10)
Min.–max.	2–144
Data protection	
HIPAA-conformity mentioned	2
GDPR-conformity mentioned	2
Security features mentioned	9
Questionable conformity	4
Not mentioned	8
No data exchange	10
Articles per continent—no.	
United States of Amerika	20
European Union	10
Australia	3
Asia	2
Primary outcomes—no.	
Characteristics for eHealth usability	11
Adherence	11
Behavioral change with eHealth product	3
Comparison of telemedicine vs. standard care	3
Mortality and complications	3
Cost balance	3
Comparison of methods	1

In a survey on patients after hematopoietic stem cell transplantation (HSCT), only 20.9% (92/441) of patients reported a preference for follow-up that included a telehealth facility [35]. A cross-sectional survey from Germany investigated the reasons for rejecting telemedicine: Main arguments were distrust in using EHR (53%), apps (53%), e-mails to report symptoms (57%), and a profound skepticism on the use of teleconference tools (64%). The older and the less educated a participant, the higher the level of discomfort [37] (6). Nevertheless, patients with a low socioeconomic

background had better participation if the telemedicine service included smartphone apps as an option [4].

Therefore, it is of utmost importance that an app and its features meet the needs and expectations of their users to facilitate long-term use [38]. Unfortunately, useful apps are scarce [39]. A systematic evaluation found that only 23/378 health apps (6%;  $n = 5$  both Android and iOS,  $n = 12$  only Android,  $n = 11$  only iOS) were address the needs of patients with kidney diseases and were able to support because of useful features [36]. Therefore, medical experts or patients themselves should be integrated into the developing process of an app from the beginning to adapt to specific needs [40,41]. Today, start-up companies and publicly funded projects from medical experts develop flexible eHealth tools tailored to the requirements of patient groups and healthcare providers [31,32,35,41–50]. Ideally, apps are connectable to the hospital's EHR [41,44], as standalone software limits accessibility and data transfer. Many healthcare IT solutions are outdated for today's requirements lacking interoperability, flexibility, and are not designed for healthcare professionals. Updating software is expensive limiting flexibility and adaptation to the needs of patients/physicians, resulting in frustration and high dropout rates [51].

Key factors for successful implementation of eHealth solutions are Internet access, possession of devices, and their technical level. In addition, patients may have individual preferences for certain technical devices (e.g., for smartphone, tablet, or computer/laptop), which is important for the acceptance of eHealth solutions [35,52]. Studies found that some patient groups favor Internet-based platforms on their desktop computer and are hesitant to use smartphone-based solutions [41,52]. Smartphones are harder to operate for some patient groups such as elderly patients with impaired vision or reduced tactile abilities. Others prefer their smartphone, and some do not have a computer at home. If both, the combination of a web-based

**Figure 2** Commonness of digital features.

platform for computers or laptops and an app for smartphones or tablets, are available, the preferences of patients would be addressed best [27,53]. Many patients consider flexible access to their data as important [33], for example, in order to print reports. Wang *et al.* [49] pointed out that for implementation of eHealth into the lives of transplanted patients, the attention to the unique experiences and special needs around the transplantation process itself is crucial in order to have high acceptance among transplant recipients.

### Apps to support adherence

As apps for smartphones allow permanent availability, they are an obvious solution for interventions, which aim to strengthen adherence. O'Brien *et al.* [33] observed that 69/164 kidney transplant patients used smartphone alarms as medication reminder. Adhering to therapeutic protocols such as regular medication intake, regular measurements of vital signs, and documenting this information is an important part of post-transplant care and fundamental for long-term success of organ transplantation. Recent recommendations even emphasize to capture adherence regularly as the “fifth vital sign” [54]. A combination of different interventions is recommended to enhance patient self-management and adherence. It is known that the level of adherence significantly declines over time after lung transplantation, for example, transmission of remote vital signs [38]. The slightest change in daily routine may result in neglect of medication intake in patients with poor knowledge and average adherence [55]. A study on sun protection behavior in adolescents showed that educational sessions improved knowledge, but had only a minor impact on behavioral changes [47]. For patients, the only significant factor to use a self-management app for longer than 4 months was the “affect” (in sense of feeling) toward the app [49].

Monitoring regular and long-term medication intake is difficult [50]. Doctors rely on self-reporting, clinical judgement, laboratory values such as drug levels and clinical outcomes. Kelly *et al.* [56] compared tacrolimus levels before and after online sessions on medical adherence but did not find differences. The use of digital pharmaceuticals with an ingestible sensor is a novel approach [57] to directly measure drug adherence. After ingestion together with medication, the sensor is activated in the stomach and transmits a signal to the smartphone via a patch on the skin [58]. This system has a detection accuracy of 100%. Unfortunately, the skin patch is not well tolerated causing high dropout

rates in children and adults after transplantation. The system needs improvement before it can be recommended for routine assessment of adherence. [59] Wireless pill bottles with customized reminders and physician notifications were used in a RCT to increase adherence for tacrolimus. The group with reminders and notifications had highest adherence (88%), followed by reminders only (78%), compared to controls (55%) demonstrating high impact of this eHealth approach on adherence. Such systems are of interest particularly for adolescents, who are at highest risk for nonadherence and have a high affinity to mobile apps [60]. Several factors (such as interest for the app/topic, satisfaction with app training, age, level of distress physical functioning) had a positive impact on the long-term use of an app, although acceptance of an app does not automatically mean that the use is satisfying [61]. An important aspect is the willingness of patients to implement apps or eHealth solutions into their lives, independent of the usability, whereby the general acceptance for medical adherence apps is high [31,52,55]. The integration of social backing systems such as friends and family as well as patient priorities (daily schedule, sports, work) is important to support adherence to an app [62]. The use of a self-managing app can improve the systolic blood pressure over time only by better self-awareness [45]. On the other hand, further studies observed only small effects of apps regarding medical adherence [50]. For example, Han *et al.* [31] could not find self-reported differences in adherence between patients with or without an app, most likely because of high dropout rates.

### Telemedicine

Telemedicine is defined as “remote delivery of health-care services over the telecommunication infrastructure.” Patients can be examined, symptoms evaluated, diagnosed, and treated via remote consultations with personal technology [63]. Transplant centers have a large catchment area resulting in long travel distances for patients. Therefore, telemedicine concepts with web-based platforms [40,41], mobile smartphone apps [29,44,61,64], videoconferencing [43,62,65,66], chat [42,61,67], remote vital sign monitoring [32,38,48,61], or various of those combinations [68,69] are well suited for transplantation follow-up. However, the added benefit of new telemedicine concepts compared to standard care after transplantation must be demonstrated in order to justify the use of additional costs.

Patients with additional telemedicine support through smart tablets had significantly lower readmission rates within the first 90 days after liver transplant compared to standard of care [44]. The comprehensive platform consists of remote vital sign monitoring through Bluetooth devices, drug reminder, regular self-assessments, access to educational sessions as well as text messaging, and video conferencing tools. Patients within the telemedicine group reported better QoL, better physical function, and general health. Adherence with telemedicine was excellent (86%) for basic health sessions (vital sign recording), but only 45% for using messaging or videoconferencing. In fact, patients and staff preferred regular phone calls. Le *et al.* [43] compared standard aftercare of liver transplant recipients to a telemedicine group with video calls. Patient satisfaction was similar without compromising the valuable patient-physician relationship as 19/21 (90%) patients opted to use this service again. As expected, waiting and travel time was significantly less suggesting improved clinical workflows, reduced costs, and protects environment protection. A large RCT in lung transplant recipients [64] could not show benefits for additional telemedicine aftercare with the comprehensive Pocket PATH app on survival or hospitalization rate. However, highly significant effects on adherence, self-monitoring, and reporting of abnormal health behavior were observed. Pocket PATH was designed to support self-monitoring and adherence by providing a smartphone with customized programs for recording and displaying vital signs, symptoms, and laboratory values. In addition, it contains reminder systems, note-keeping functions, and generates automatic feedback messages for decision support. High initial acceptance was not associated with use [46]. As expected, use decreased over time. Patients, who used the app extensively for self-monitoring, had lower mortality and less bronchiolitis obliterans syndrome compared to patients with low engagement. However, results have to be interpreted with caution as the use of apps is associated with potential confounding factors, such as younger age, better health and education, ability to use an app, attitudes toward treatment, health and adherence as well as socioeconomic status. The app users generally may show more therapeutic adherence and, therefore, may have developed fewer complications by sticking tighter to therapeutic recommendations. Nevertheless, regular reinforcement seems to be important as an app can only help, when being used.

Other studies observed benefits through telemedicine strategies in young adults, especially, if face-to-face videoconferencing is used or gamification techniques

were deployed [66,70]. Another study addressed caretakers of young transplant recipients and described an improved post-transplant care by an app supported discharge program enabling better communication [67]. Advantages of video consultations are close contact irrespective of the distance and less commuting [65,66].

New eHealth pharmacy services have the potential to change the care of transplanted patients. This may include online educational sessions, drug interaction checks, or eReceipt (“electronic” Receipt). Information about drugs, and frequent co-morbidities/complications, and sharing of patient information with pharmacies will optimize drug prescription and might reduce complications [34]. Ultimately, the patient is empowered for better self-management and by this means adherence is supported. Interestingly, 25% of patients needed medication plan adjustments already 5 days after discharge demonstrating the potential of telemedicine to improve healthcare delivery. However, patients take appointments for video consultations less serious than physical appointments, as “no shows” for pharmacy telemedicine visits occurred in 55%. This number could be reduced to 7% after implementing automatic visit entries into the calendar and appointment reminders [34]. This demonstrates the need to engage patients constantly and to refine eHealth solutions continuously.

### Telemedicine in the COVID-19 pandemic

The Novel Coronavirus Disease 2019 (COVID-19) pandemic highlights the need for telemedicine solutions to protect patients and medical staff against the virus and as a consequence the use of technology for remote consultations has increased dramatically. As immunosuppressed transplanted patients have higher risks of a critical course of the disease [71], self-isolation at home with strict reduction of face-to-face appointments were suggested as protective measures [72]. As a consequence, many transplant centers changed their regular practice and telemedicine solutions were promoted [73]. Although video consultations and remote monitoring of vital signs or symptoms are useful to bridge patient care during the pandemic, this concept holds also some inherent limitations. Except for the fact that not every patient wants to—or is able to—perform telemedicine, not all aspects of patient care can be adequately covered by telemedicine. Main obstacle is that good clinical practice includes physical examinations and the regular control of laboratory values (e.g., blood level of immunosuppressant, graft function) and, in case of symptoms or even infection, oropharyngeal swabs for

diagnosis of COVID-19 together with laboratory assessments are needed for differential diagnosis. Thus, telemedicine approaches are a valuable additional tool in the pandemic and are perfect to support the care of transplanted patients (e.g., screening for symptoms or problems, spacing out visits, providing advice). Nevertheless, regular outpatient visits remain necessary in some time intervals or for symptomatic patients. In summary, the global pandemic has accelerated the implementation of eHealth solutions to deliver additional and alternative care options for transplanted patients and to reduce travel and hospital footfall for this vulnerable population.

### Future telemedicine concepts

Currently, personal visits in the outpatient clinic are inevitable to perform physical examinations or laboratory tests. While physical examinations always will require the visit in a doctors office and personal conversation on certain aspects can not be replaced by video conferences, laboratory tests may be partly replaced by modern point-of-care (POC) testing to avoid the need for travel and hospital visits. Today, patients can be advised to perform only simple tests like measurement of vital signs, weight, blood sugar (for diabetic patients), and INR (for patients on anticoagulant therapy). The utility of urine self-determinations by the patient with dipsticks for early detection of urinary tract infection or albuminuria was already investigated in several studies [74–77] and could lead to a more timely detection of urinary tract infections, one of the most frequent complication following kidney transplantation. Novel POC systems such as dried blood spot sampling (reference) or microsampling devices [78–81] may allow for the determination of immunosuppressive blood levels, renal function, or other important laboratory parameters. Such innovative POC devices may be an ideal way to further complement telemedicine programs in the future. While visits in real clinics remain the basis of patient care, such visits will be supplemented by virtual clinic visits by experienced medical experts (doctors as well as nurses), health trackers, and novel POC systems. By analyzing all incoming data, critical situations may be highlighted to the transplant team by AI-driven decision support systems. In addition, modern eHealth platforms can provide tailored information to the patient, for example, on medication, diet, and physical activity. An important aspect of future care is to keep in closer contact with the patient in order to detect problems early and strengthen adherence. In summary, future

telemedicine concepts need to be patient-centered and will be embedded in established and well-functioning outpatient care concepts, but should not aim to replace them.

### The human factor

Despite all fancy features and rapid software innovations, the engagement of patients, nurses, and doctors remains key for successful implementation of eHealth projects. In the past, user experience was forgotten repeatedly resulting in poor acceptance, distraction from patient care, and additional workload. Recruitment, training, and communication with patients rely on the medical staff and their willingness, enthusiasm, and time. Technical problems might occur because of hardware or software issues, and user errors are observed [44,56]. The need for additional help at home for hookup and function was observed in 32% of patients, despite extensive teaching in the hospital. Someone must answer questions, fix technical problems, and take medical action, if necessary [41,53,65]. Experienced medical experts (doctors and nurses) are needed to respond to dangerous and critical situations. Face-to-face video conferences with medical experts have higher impact on behavioral changes and adherence as sole education (literature, videos) or regular eLearning (“electronic” Learning) sessions [42]. Through a close relationship of patients with the telemedicine team, adherence is strengthened, and complications are detected earlier [44,64,67,82]. Thus, the team who operates behind the technique is crucial for success.

Even the smartest eHealth solution will fail, if additional workload or costs are not compensated. Ideally, software creates efficiency gains, for example, by automatic data exchange or reducing phone calls and paperwork. Software must be integrated into the workflow and be interoperable, as standalone solutions without connection to the EHR may increase workload (several logins, difficult knowledge extraction), confusion, and reduce acceptance. Instead, a software solution should provide obvious and clear benefits for users.

### Financial consequences

eHealth has not only to prove its clinical benefits, but also its potential to reduce costs, since healthcare provider ask for cost reductions, software developers need to be paid, dedicated personnel costs money, and companies must earn money. Similar to drug development, financial consequences need to be analyzed and ideally

skim off some profit for the stakeholder [83]. Cost reduction can be achieved by less travel costs, which also may result in better quality of life (QoL) because of less travel time. The care of transplanted patients is more challenging in countries with extraordinary long travel distances. Therefore, Australia has pushed the development of digital care in order to facilitate care for transplant patients from far distances [84]. Telemedicine in Australia may have saved in 2016 approximately 203 202 km, 2771 h, and 31 048.00 AU\$ for petrol [66,84]. The evaluation of pediatric kidney transplant recipients showed higher patient safety because of better availability of professional health services with close cooperation between home pediatrician and kidney transplant specialist. There was a cost reduction because of lower travel costs and more days at work with cost savings of 31 837AU\$ (505AU\$ saved per consultation) [85]. A telemedicine concept for living donor recipients in Germany accounted for highly significant cost savings of 3417€ per patient in the first year after transplantation [65]. A telemedicine approach for post-transplant care after intestine transplantation resulted in better QoL but could not demonstrate significant cost savings in Great Britain, eventually because of the low number of participants ( $n = 19$ ). It is estimated that nonadherence is associated with around 20% of kidney allograft losses (Ref. 53) with the need for costly dialysis or retransplantation [63]. Side effects or complications may result in nonadherence, which might be captured by apps [32,46,64] or by a comprehensive telemedicine concept [44,82]. Addressing problems early and proactively may not only increase adherence but may also reduce costly hospitalizations [85]. The demonstration of cost savings and better QoL is also crucial for reimbursement, as governments and statutory health insurances need solid evidence for the efficacy before paying for eHealth innovations.

Reimbursement of novel eHealth products is challenging in most healthcare systems. For example, the reimbursement of virtual visits is difficult or unclear in most countries. For sustainable eHealth systems, the reimbursement must cover all costs including costs for staff, training, maintenance, and technology. For a realistic cost estimate also subpopulations (e.g., elderly patients) are to be included, as subpopulations may need more support and training. At the end, reimbursement may require clinical studies demonstrating efficacy for the target population across age groups, thereby questions on usability, training etc. have to be addressed upfront for the whole population. It may also necessary to cover costs for technology such as smartphones or

tablets in order to provide patients directly with adequate current technology, which might offer even certain benefits, for example, with regard to data protection, training, and acceptance. While a few countries are more open to the new opportunities of eHealth, most countries are more conservative and in reimbursement changes in health systems are generally slow. Given the general underfunding of the health systems worldwide, inertia of health systems, and the young age of eHealth and telemedicine, it becomes immediately clear that there are many challenges ahead for innovative eHealth solutions to get adequate reimbursement.

### Data protection, legal aspects, and certification of eHealth products

Aspects of data protection and security of data transfer were mentioned in most publications, but the exact data protection concepts were not outlined in greater detail (Table 1). There are numerous steps involved in building a secure app or platform including secure encryption, transmission, and data storage. Thus, it is questionable whether all eHealth solutions are fully compliant with GDPR or HIPAA. Studies even frankly describe the use of Facebook for patient recruitment, e-mails or standard messenger for communication, non-encrypted short messages for remote vital sign monitoring, or Skype sessions for video consultations. None of these features allow sufficient data protection of sensible health data and consequently would not be approved in many countries, because fundamental personal rights are neglected. Another frequently neglected aspect of eHealth products is certification according to the medical device regulation (MDR) with an updated classification for medical software in Europe [86]. The European GDPR and MDR establish clear rules and will transform eHealth toward more reliable and secure data protection concepts in healthcare systems. Certification and strong data protection will reduce fear for misuse by this means increase acceptance. Besides data protection and certification other aspects of eHealth solutions may give rise to legal concerns, for example, liability issues. Therefore, legal obstacles may add another layer of complexity for the introduction of eHealth products.

### Conclusion

In our review, we performed a literature search and give a comprehensive overview on eHealth in post-transplant care. We observed that eHealth solutions can support

patient health after transplantation in many ways. First clinical studies show that apps and web-based platforms have the potential to strengthen adherence and may help to empower patients. The acceptance of eHealth products is the key for success, which is influenced by many factors but usability and training by medical professionals seems to be most important. Especially, comprehensive eHealth interventions with a dedicated team may have a strong impact on adherence and other key outcomes. Recent studies could demonstrate cost savings, mainly through reduced hospitalisations. To date, rigorous data protection is not yet implemented in many eHealth solutions, especially older applications are not built by the concept of “privacy by design.” In summary, eHealth is a rapidly growing field in transplantation, but more clinical data are needed to prove its utility.

## Funding

EU Lighthouse project H2020 BigMedilytics, Smart Service World 1 + 2, BMWi.

## Conflict of interest

The authors have no relevant disclosures to make.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Table S1.** Core information on clinical studies.

## REFERENCES

- Iwaya LH, Gomes MAL, Simplício MA, et al. Mobile health in emerging countries: a survey of research initiatives in Brazil. *Int J Med Inform* 2013; **82**: 283.
- World Health Organization. *mHealth: New Horizons for Health through Mobile Technologies*, Geneva: . World Health Organization, 2011.
- <https://en.wikipedia.org/wiki/EHealth>.
- Abaza H, Marscholke M. mHealth application areas and technology combinations\*. A comparison of literature from high and low/middle income countries. *Methods Inf Med* 2017; **56**: e105.
- Rajkomar A, Oren E, Chen K, et al. Scalable and accurate deep learning with electronic health records. *NPJ Digit Med* 2018; **1**: 18.
- Miotto R, Li L, Kidd BA, Dudley JT. Deep patient: an unsupervised representation to predict the future of patients from the electronic health records. *Sci Rep* 2016; **6**: 26094.
- LeCun Y, Bengio Y, Hinton G. Deep learning. *Nature* 2015; **521**: 436.
- Tomašev N, Glorot X, Rae JW, et al. A clinically applicable approach to continuous prediction of future acute kidney injury. *Nature* 2019; **572**: 116.
- Axelrod DA, Kynard-Amerson CS, Wojciechowski D, et al. Cultural competency of a mobile, customized patient education tool for improving potential kidney transplant recipients' knowledge and decision-making. *Clin Transplant* 2017; **31**: e12944.
- Gordon EJ, Feinglass J, Carney P, et al. A website intervention to increase knowledge about living kidney donation and transplantation among Hispanic/Latino dialysis patients. *Prog Transplant* 2016; **26**: 82.
- Knight SR, Cao KN, South M, Hayward N, Hunter JP, Fox J. Development of a clinical decision support system for living kidney donor assessment based on national guidelines. *Transplantation* 2018; **102**: e447.
- Milan Manani S, Rosner MH, Virzi GM, et al. Longitudinal experience with remote monitoring for automated peritoneal dialysis patients. *Nephron* 2019; **142**: 1.
- Makhija D, Alscher MD, Becker S, et al. Remote monitoring of automated peritoneal dialysis patients: assessing clinical and economic value. *Telemed J E Health* 2018; **24**: 315.
- Zarca K, Dupont J-CK, Jacoud L, et al. Effectiveness and efficiency of teleimaging in the transplantation process: a mixed method protocol. *BMC Health Serv Res* 2019; **19**: 672.
- Bath NM, Wang X, Bledsoe JR, et al. The use of smartphone for liver graft biopsy assessment at the time of procurement. *Transplantation* 2018; **102**: e459.
- Eccher A, Neil D, Ciangherotti A, et al. Digital reporting of whole-slide images is safe and suitable for assessing organ quality in preimplantation renal biopsies. *Hum Pathol* 2016; **47**: 115.
- Reddy MS, Bhati C, Neil D, Mirza DF, Manas DM. National organ retrieval imaging system: results of the pilot study. *Transpl Int* 2008; **21**: 1036.
- De Meester J, Persijn GG, Smits J, Vanrenterghem Y. The new Eurotransplant kidney allocation system: a justified balance between equity and utility? *Transpl Int* 1999; **12**: 299.
- Muster H, Steffens E, Kim SJ, Kasiske BL, Israni AK. Donor exchange programs in kidney transplantation: rationale and operational details from the north central donor exchange cooperative. *Am J Kidney Dis* 2011; **57**: 152.
- commission, E. [https://ec.europa.eu/info/law/law-topic/data-protection/data-protection-eu\\_de](https://ec.europa.eu/info/law/law-topic/data-protection/data-protection-eu_de), 2016.
- Turakhia MP, Desai M, Hedlin H, et al. Rationale and design of a large-scale, app-based study to identify cardiac arrhythmias using a smartwatch: the Apple Heart Study. *Am Heart J* 2019; **207**: 66.
- Perez MV, Mahaffey KW, Hedlin H, et al. Large-scale assessment of a smartwatch to identify atrial fibrillation. *N Engl J Med* 2019; **381**: 1909.
- Turakhia MP, Desai M, Perez MV, Apple Heart Study Investigators. A smartwatch to identify atrial fibrillation. Reply. *N Engl J Med* 2020; **382**: 975.
- Fiordelli M, Rivas H, Concepcion W, Wac K. "I must try harder": design

- implications for mobile apps and wearables contributing to self-efficacy of patients with chronic conditions. *Front Psychol* 2019; **10**: 2388.
25. Serper M, Barankay I, Chadha S, *et al.* A randomized, controlled, behavioral intervention to promote walking after abdominal organ transplantation: results from the LIFT study. *Transpl Int* 2020; **33**: 632.
  26. Browning RB, McGillicuddy JW, Treiber FA, Taber DJ. Kidney transplant recipients' attitudes about using mobile health technology for managing and monitoring medication therapy. *J Am Pharm Assoc* 2003; **2016**: 450.
  27. Treiber F, McGillicuddy J, Gebregziabher M, Taber DJ. Improving transplant medication safety through a pharmacist-empowered, patient-centered, mHealth-based intervention: TRANSafe Rx Study Protocol. *JMIR Res Protoc* 2018; **7**: e59.
  28. Wikipedia. [https://en.wikipedia.org/wiki/List\\_of\\_countries\\_by\\_smartphone\\_penetration](https://en.wikipedia.org/wiki/List_of_countries_by_smartphone_penetration).
  29. Reber S, Scheel J, Stoessel L, *et al.* Mobile technology affinity in renal transplant recipients. *Transplant Proc* 2018; **50**: 92.
  30. <https://www.geckoboard.com/best-practice/kpi-examples/retentionrate/#:~:text=Although%20exact%20benchmarks%20vary%20by,is%2032%25%20to%2066%25.2020>.
  31. Han A, Min S-I, Ahn S, *et al.* Mobile medication manager application to improve adherence with immunosuppressive therapy in renal transplant recipients: a randomized controlled trial. *PLoS One* 2019; **14**: e0224595.
  32. Jiang Y, Sereika SM, DeVito Dabbs A, Handler SM, Schlenk EA. Using mobile health technology to deliver decision support for self-monitoring after lung transplantation. *Int J Med Inform* 2016; **94**: 164.
  33. O'Brien T, Russell CL, Tan A, Washington M, Hathaway D. An exploratory correlational study in the use of mobile technology among adult kidney transplant recipients. *Prog Transplant* 2018; **28**: 368.
  34. Jandovitz N, *et al.* Telemedicine pharmacy services implementation in organ transplantation at a metropolitan academic medical center. *Digit Health* 2018; **4**: 2055207618789322.
  35. Dyer G, Gilroy N, Brown L, *et al.* Erratum to: "What They Want: Inclusion of Blood and Marrow Transplantation Survivor Preference in the Development of Models of Care for Long-Term Health in Sydney, Australia" [Biol Blood Marrow Transplant 2016;22:731–743]. *Biol Blood Marrow Transplant* 2016; **22**: 1537.
  36. Serper M, Reese PP, Patzer RR, Levitsky J, Wolf MS. The prevalence, risk factors, and outcomes of medication trade-offs in kidney and liver transplant recipients: a pilot study. *Transpl Int* 2018; **31**: 870.
  37. Paslakis G, Fischer-Jacobs J, Pape L, *et al.* Assessment of use and preferences regarding internet-based health care delivery: cross-sectional questionnaire study. *J Med Internet Res* 2019; **21**: e12416.
  38. Fadaizadeh L, Najafzadeh K, Shajareh E, Shafaghi S, Hosseini M, Heydari G. Home spirometry: assessment of patient compliance and satisfaction and its impact on early diagnosis of pulmonary symptoms in post-lung transplantation patients. *J Telemed Telecare* 2016; **22**: 127.
  39. Singh K, Diamantidis CJ, Ramani S, *et al.* Patients' and nephrologists' evaluation of patient-facing smartphone apps for CKD. *Clin J Am Soc Nephrol* 2019; **14**: 523.
  40. Massierer D, Sapir-Pichhadze R, Bouchard V, *et al.* Web-based self-management guide for kidney transplant recipients (the getting on with your life with a transplanted kidney study): protocol for development and preliminary testing. *JMIR Res Protoc* 2019; **8**: e13420.
  41. Nielsen C, Agerskov H, Bistrup C, Clemensen J. User involvement in the development of a telehealth solution to improve the kidney transplantation process: a participatory design study. *Health Informatics J* 2020; **26**: 1237.
  42. Böttcher S, Buck C, Zeeb H, *et al.* Randomised controlled trial to evaluate the influence of mHealth and eHealth skin cancer prevention education among young organ transplant recipients: the HIPPOlino intervention study. *BMJ Open* 2019; **9**: e028842.
  43. Le LB, Rahal HK, Viramontes MR, *et al.* Patient satisfaction and healthcare utilization using telemedicine in liver transplant recipients. *Dig Dis Sci* 2019; **64**: 1150.
  44. Lee TC, Kaiser TE, Alloway R, Woodle ES, Edwards MJ, Shah SA. Telemedicine based remote home monitoring after liver transplantation: results of a randomized prospective trial. *Ann Surg* 2019; **270**: 564.
  45. McGillicuddy JW, Taber DJ, Mueller M, *et al.* Sustainability of improvements in medication adherence through a mobile health intervention. *Prog Transplant* 2015; **25**: 217.
  46. Rosenberger EM, DeVito Dabbs AJ, DiMartini AF, Landsittel DP, Pilewski JM, Dew MA. Long-term follow-up of a randomized controlled trial evaluating a mobile health intervention for self-management in lung transplant recipients. *Am J Transplant* 2017; **17**: 1286.
  47. Robinson JK, Friedewald JJ, Desai A, Gordon EJ. A randomized controlled trial of a mobile medical app for kidney transplant recipients. *Transplant Direct* 2016; **2**: e51.
  48. Shellmer DA, *et al.* Development and field testing of Teen Pocket PATH ((R)), a mobile health application to improve medication adherence in adolescent solid organ recipients. *Pediatr Transplant* 2016; **20**: 130.
  49. Wang W, van Lint CL, Brinkman WP, *et al.* Renal transplant patient acceptance of a self-management support system. *BMC Med Inform Decis Mak* 2017; **17**: 58.
  50. Zanetti-Yabur A, Rizzo A, Hayde N, Watkins AC, Rocca JP, Graham JA. Exploring the usage of a mobile phone application in transplanted patients to encourage medication compliance and education. *Am J Surg* 2017; **214**: 743.
  51. Jeffs E, Vollam S, Young JD, Horsington L, Lynch B, Watkinson PJ. Wearable monitors for patients following discharge from an intensive care unit: practical lessons learnt from an observational study. *J Adv Nurs* 2016; **72**: 1851.
  52. Vanhoof JMM, Vandenberghe B, Geerts D, *et al.* Technology experience of solid organ transplant patients and their overall willingness to use interactive health technology. *J Nurs Scholarsh* 2018; **50**: 151.
  53. Taber DJ, Pilch NA, McGillicuddy JW, Mardis C, Treiber F, Fleming JN. Using informatics and mobile health to improve medication safety monitoring in kidney transplant recipients. *Am J Health Syst Pharm* 2019; **76**: 1143.
  54. Neuberger JM, Bechstein WO, Kuypers DRJ, *et al.* Practical recommendations for long-term management of modifiable risks in kidney and liver transplant recipients: a guidance report and clinical checklist by the Consensus on Managing Modifiable Risk in Transplantation (COMMIT) Group. *Transplantation* 2017; **101**(4S Suppl 2): S1.
  55. Israni A, Dean C, Kasel B, Berndt L, Wildebush W, Wang CJ. Why do patients forget to take immunosuppression medications and

- miss appointments: can a mobile phone app help? *JMIR Public Health Surveill* 2016; **2**: e15.
56. Kelly SL, Steinberg EA, Suplee A, et al. Implementing a home-based telehealth group adherence intervention with adolescent transplant recipients. *Telemed J E Health* 2019; **25**: 1040.
  57. Triplett KN, El-Behadli AF, Masood SS, Sullivan S, Desai DM. Digital medicine program with pediatric solid organ transplant patients: perceived benefits and challenges. *Pediatr Transplant* 2019; **23**: e13555.
  58. Eisenberger U, Wüthrich RP, Bock A, et al. Medication adherence assessment: high accuracy of the new ingestible sensor system in kidney transplants. *Transplantation* 2013; **96**: 245.
  59. Reese PP, Bloom RD, Trofe-Clark J, et al. Automated reminders and physician notification to promote immunosuppression adherence among kidney transplant recipients: a randomized trial. *Am J Kidney Dis* 2017; **69**: 400.
  60. Lefkowitz DS, Fitzgerald CJ. Mobile health technology for adolescent transplant recipients: what's h'app'ening in adherence promotion? *Pediatr Transplant* 2016; **20**: 11.
  61. Jiang Y, Sereika S, DeVito Dabbs A, Handler S, Schlenk E. Acceptance and use of mobile technology for health self-monitoring in lung transplant recipients during the first year post-transplantation. *Appl Clin Inform* 2016; **7**: 430.
  62. Barnett A, Campbell KL, Mayr HL, Keating SE, Macdonald GA, Hickman IJ. Liver transplant recipients' experiences and perspectives of a telehealth-delivered lifestyle programme: a qualitative study. *J Telemed Telecare* 2020; **1357633X19900459**.
  63. <https://searchhealthit.techtarget.com/definition/telemedicine>.
  64. DeVito Dabbs A, Song MK, Myers BA, et al. A randomized controlled trial of a mobile health intervention to promote self-management after lung transplantation. *Am J Transplant* 2016; **16**: 2172.
  65. Gerlach UA, Vrakas G, Holdaway L, et al. Skype clinics after intestinal transplantation – follow-up beyond post codes. *Clin Transplant* 2016; **30**: 760.
  66. Trnka P, White MM, Renton WD, McTaggart SJ, Burke JR, Smith AC. A retrospective review of telehealth services for children referred to a paediatric nephrologist. *BMC Nephrol* 2015; **16**: 125.
  67. Lerret SM. Using MHealth to improve outcomes for children following solid organ transplant. *J Pediatr Nurs* 2019; **46**: 134.
  68. Flodgren G, Rachas A, Farmer AJ, Inzitari M, Shepperd S. Interactive telemedicine: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2015; (9): CD002098.
  69. Nerini E, Bruno F, Citterio F, Schena FP. Nonadherence to immunosuppressive therapy in kidney transplant recipients: can technology help? *J Nephrol* 2016; **29**: 627.
  70. Tark R, Metelitsa M, Akkermann K, Saks K, Mikkel S, Haljas K. Usability, acceptability, feasibility, and effectiveness of a gamified mobile health intervention (Triumpf) for pediatric patients: qualitative study. *JMIR Serious Games* 2019; **7**: e13776.
  71. Johnson KM, Belfer JJ, Peterson GR, Boelkins MR, Dumkow LE. Managing COVID-19 in renal transplant recipients: a review of recent literature and case supporting corticosteroid-sparing immunosuppression. *Pharmacotherapy* 2020; **40**: 517.
  72. Prevention, C.-C.f.D.C.a. If You Are Immunocompromised, Protect Yourself From COVID-19. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/immunocompromised.html>, 2020.
  73. Picard C, Le Pavec J, Tissot A, Groupe Transplantation Pulmonaire de la Société de Pneumologie de Langue Française SPLF. Impact of the Covid-19 pandemic and lung transplantation program in France. *Respir Med Res* 2020; **78**: 100758.
  74. Chavez JA, Chavez JM, Kuprasertkul A, et al. Prospective evaluation of daily and weekly urine pH variations along with diet intake in postmenopausal women with recurrent urinary tract infections. *Female Pelvic Med Reconstr Surg* 2020.
  75. Woodburn EV, Long KD, Cunningham BT. Analysis of paper-based colorimetric assays with a smartphone spectrometer. *IEEE Sens J* 2019; **19**: 508.
  76. Wang CS, Escoffery C, Patzer RE, et al. A dual efficacy-implementation trial of a novel mobile application for childhood nephrotic syndrome management: the UrApp for childhood nephrotic syndrome management pilot study protocol (UrApp pilot study). *BMC Nephrol* 2020; **21**: 125.
  77. Panuccio V, Pizzini P, Parlongo G, et al. Urine chloride self-measurement to monitor sodium chloride intake in patients with chronic kidney disease. *Clin Chem Lab Med* 2019; **57**: 1162.
  78. Marshall DJ, Kim JJ, Brand S, Bryne C, Keevil BG. Assessment of tacrolimus and creatinine concentration collected using Mitra microsampling devices. *Ann Clin Biochem* 2020; **57**: 389.
  79. Veenhof H, Boven JFM, Voort A, Berger SP, Bakker SJL, Touw DJ. Effects, costs and implementation of monitoring kidney transplant patients' tacrolimus levels with dried blood spot sampling: A randomized controlled hybrid implementation trial. *Br J Clin Pharmacol* 2020; **86**: 1357.
  80. Zwart TC, Gokoel SRM, van der Boog PJM, et al. Therapeutic drug monitoring of tacrolimus and mycophenolic acid in outpatient renal transplant recipients using a volumetric dried blood spot sampling device. *Br J Clin Pharmacol* 2018; **84**: 2889.
  81. Leino AD, King EC, Jiang W, et al. Assessment of tacrolimus inpatient variability in stable adherent transplant recipients: Establishing baseline values. *Am J Transplant* 2019; **19**: 1410.
  82. Schmid A, Hils S, Kramer-Zucker A, et al. Telemedically supported case management of living-donor renal transplant recipients to optimize routine evidence-based aftercare: a single-center randomized controlled trial. *Am J Transplant* 2017; **17**: 1594.
  83. Brophy PD. Overview on the challenges and benefits of using telehealth tools in a pediatric population. *Adv Chronic Kidney Dis* 2017; **24**: 17.
  84. Andrew N, Barraclough KA, Long K, et al. Telehealth model of care for routine follow up of renal transplant recipients in a tertiary centre: a case study. *J Telemed Telecare* 2020; **26**: 232.
  85. Kaier K, Hils S, Fetzer S, et al. Results of a randomized controlled trial analyzing telemedically supported case management in the first year after living donor kidney transplantation – a budget impact analysis from the healthcare perspective. *Health Econ Rev* 2017; **7**: 1.
  86. Informationen zu den Auswirkungen der Medizinprodukteverordnung (MDR). [https://www.spectaris.de/fileadmin/Infothek/Medizintechnik/Positionen/20190830\\_SPECTARIS\\_Informationen\\_zu\\_den\\_Auswirkungen\\_der\\_MDR\\_final.pdf](https://www.spectaris.de/fileadmin/Infothek/Medizintechnik/Positionen/20190830_SPECTARIS_Informationen_zu_den_Auswirkungen_der_MDR_final.pdf), 2019.