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Review and Evaluation of mHealth Apps in Solid Organ Transplantation: Past, Present, and Future

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Background. With the rapid and widespread expansion of smartphone availability and usage, mobile health (mHealth) has become a viable multipurpose treatment medium for the US healthcare system. **Methods.** The purpose of this review is to identify posttransplant mHealth applications that support patient self-management or a patient–provider relationship and aim to improve clinical outcomes. The interventions were then analyzed and evaluated to identify current gaps and future needs of mHealth apps in solid organ transplantation. **Results.** The authors found a nearly universal dichotomy between perceived utility and sustained use, with most studies demonstrating significant attrition during the course of the intervention. In addition, interoperability continues to be a challenge. **Conclusions.** The authors present potential methods for mitigating the identified barriers and gaps in mHealth apps for solid organ transplant recipients.

(*Transplantation Direct* 2022;8: e1298; doi: 10.1097/TXD.0000000000001298).

Solid organ transplantation is the optimal treatment for patients with end-stage organ disease. However, organs are a limited resource, and current demand far outpaces supply. Although many aspects of the medical and surgical care of organ recipients have improved over the past few decades, the median time that a transplanted organ will function, the allograft half-life, has not substantially improved in any of the solid organ transplant populations. The prevailing causes of late allograft loss include nonadherence, antibody-mediated rejection, poor control of chronic comorbidities, or infectious disease and malignancies related to overimmunosuppression.[1-6]

Although tailoring immunosuppressive therapy may help mitigate graft loss and mortality from overimmunosuppression, challenges remain with complex medication regimens and competing chronic comorbidities, most appropriately categorized as medication-related problems. Oftentimes, medication-related problems are aggravated by the current complex and overwhelmed healthcare system. This is particularly true in countries without a universal healthcare system, such as the United States, where care fragmentation results in patients having multiple providers in different health systems. This fragmented care model limits shared and informed decision making and hinders patient-centered care, which can exacerbate issues with self-efficacy, self-management, and limited health literacy.

Over the past decade, mobile health (mHealth) has become a growing subcategory of telehealth, with vastly more accessibility and potential compared with traditional telemedicine. Although no standardized definition has been established for mHealth, the Global Observatory for eHealth has defined it as "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices."[7] The primary driver of patient accessibility through the mHealth medium has been the rapid proliferation of smartphones. As of early 2019, smartphones were owned by 81% of the US population, 76% in other advanced economies, and 45% in emerging economies, rapidly expanding from 35% in 2011.[8]

With the widespread expansion of smartphone availability and usage, mHealth has become a viable, multipurpose treatment medium for the US healthcare system. It has generated significant interest because of the confluence of

Received 22 September 2021. Revision received 14 December 2021.

Accepted 4 January 2022.

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The authors declare no funding or conflicts of interest.

J.N.F. participated in research design, performance of the research, and writing of the article. M.D.P., D.J.T., J.W.M., C.J.D., S.L.D., and E.T.C. participated in research design, writing of the article.

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ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001298

multiple movements: the need to address the overwhelming rise in chronic disease burden, advances in technology resulting in smaller and cheaper mobile electronics, and the increasingly patient-centric US healthcare model.[9] Additionally, the COVID-19 pandemic has accelerated telemedicine and highlighted the growing need of mHealth for rapid dissemination of information, understanding of patient needs, and more practical methods of delivering care.

Many barriers propagated by the current healthcare system could potentially be mitigated with a well-functioning and integrated mHealth program, including accessibility of the clinic (distance, parking, and transportation), wait times, appointment scheduling, affordability, inability to meet medical fees, delays in availability, and limited support of self-care practices.[10] These barriers substantially impact patient populations with sociodemographic challenges, further widening disparities in health outcomes. Furthermore, these barriers are even more formidable in specialty patient populations, such as solid organ transplant, where transplant centers and healthcare providers are frequently housed within metropolitan areas, necessitating significant travel for recipients that may live several hours away.

In addition to the physical barriers to accessing care, patients face individual challenges to sustain ongoing posttransplant self-management. Successfully managing complex medication regimens, long-term renal allograft health, and risk/comorbidity management (such as skin, cardiovascular, bone, and metabolic health) pretransplant and posttransplant requires patient engagement as well as partnering and communicating with providers to address concerns, questions, and needs. Patients who are more engaged in their care and self-management are more likely to successfully navigate complex medication regimens,[11,12] as they have a better understanding of benefits of the medications and risks of not adhering to their medication regimen.[13] Additionally, patients who have higher rates of medication adherence believe that they are responsible for the daily management of their condition and have confidence in their ability to follow their medication regimen and skills to address barriers that may arise.[14,15] Finally, patients who trust their providers and communicate collaboratively are better able to adhere to complex medication regimens.[16,17] By enhancing patient engagement and facilitating open communication between patients and their providers, barriers to medication adherence posttransplant can be mitigated. Given the complexity of the medication protocol posttransplant, patients have reported the need for open communication with their providers, such as through bidirectional communication facilitated through mHealth applications, so that the regimen can be tailored to their life circumstances so as to best address their challenges and support needs.[18,19]

mHealth offers an opportunity to gather large volumes of patient-level data in near real time, allowing medical providers to identify problems earlier before they lead to irreparable harm and deleterious outcomes. Furthermore, mHealth technology allows greater connectivity between patient and provider and creates a more patient-centered medical environment. However, mHealth apps themselves face many barriers to success that have prevented their widespread adoption.[20] The purpose of this review is to identify posttransplant mHealth applications that support patient self-management or a patient–provider relationship and aim to improve clinical outcomes. The interventions were then analyzed and evaluated to identify current gaps and future needs of mHealth apps in solid organ transplantation.

MATERIALS AND METHODS

Although this was not meant to be a systematic review, we performed a literature search to ensure that all applicable articles were taken into consideration for our assessment. The protocol for the literature search was designed with the primary purpose in mind: detailing mHealth research focused on patient and clinical outcomes within the field of solid organ transplant and identifying current barriers to progress. This study was exempt from institutional review board approval.

Literature Search

A literature search of PubMed was performed on June 30, 2021. The search terms used were "technology AND transplant" OR "app AND transplant" OR "mobile health AND transplant" OR "mobile AND transplant" OR "adherence AND transplant." Titles and abstracts were screened by J.N.F., followed by screening of the full text focusing on posttransplant solid organ transplant populations. Studies were excluded if they were written in a non–English language; were review articles, case reports, nontransplant research; or did not describe a mobile technology that focused on patient-related or clinical outcomes. Included studies were divided into major foci, including "education and adherence," "control of chronic conditions," and "medication safety and adverse drug events." From each included study, we explored the following subjects: (1) study design, (2) population studied, (3) the mHealth intervention, and (4) reported outcomes. We also reviewed the components of each mHealth intervention, assessing their ability to meet the needs of patients and caregivers to promote digital retention within both populations. To fully assess the mHealth interventions in the literature, we included published protocols for studies including mHealth interventions in a separate analysis.

RESULTS

A total of 4871 publications were identified using the aforementioned search criteria. After applying the inclusion and exclusion criteria, as mentioned previously in the literature search, 28 full-text English-language publications were identified that described a mobile technology used posttransplant that focused on patient self-management or the patient–provider relationship (Tables 1 and 2). The articles were divided into 3 general topic areas: education and adherence, control of chronic conditions, and medication safety and adverse effects.

Posttransplant mHealth Utilization

Education and Adherence

Posttransplant medication nonadherence is a significant problem in transplantation and is an important predictor of poor long-term allograft survival. It is evident from the number of articles, as well as published protocols on the topic, that education and adherence to medications or medical recommendations is a prominent driver of technological solution development (Tables 1 and 2). Based on previous reviews, it seems clear that simple text messaging is unlikely to produce

TABLE 1.

mHealth clinical outcomes studies

Authors	Study design	Population	Intervention	Outcomes
Education and Adherence				
McGillicuddy et al[21]	Prospective, randomized pilot study	Kidney transplant recipients identified as nonadherent based on screening using electronic medication tray	Electronic medication tray with reminders, Bluetooth BP monitor, smartphone for transmitting data and send reminders to check BP (SMASK System)	Nineteen subjects enrolled. Medication adherence improved progressively. SBP decreased from 138 to 122 mm Hg in mHealth vs 135 to 138 mm Hg ($P < 0.05$ at month 3). High overall satisfaction with mHealth system (4.8/5 Likert scale)
DeVito Dabbs et al[22]	Prospective randomized trial	Adult lung transplant recipients immediately after transplant	Self-monitoring days, adherence to medical regimen, reporting of critical health indicators, admissions, hospitalization days, death	Two hundred one patients enrolled between intervention (n = 99) and usual care (n = 102). mHealth group performed more self-monitoring than controls (OR, 5.11; 95% CI, 2.95-8.87; $P < 0.001$) and were more likely to be adherent to the regimen at 12 mo of follow-up (OR, 1.64; 95% CI, 1.01-2.66; $P = 0.046$). mHealth group reported more critical values (OR, 3.1; 95% CI, 1.37-7.01; $P = 0.007$). No differences in readmissions, hospitalization days, or death
Reese et al[23]	Single-center, randomized controlled trial	Kidney transplant recipients	Two intervention groups: customized reminders (alarms, texts, telephone calls and emails); customized reminders plus provider notification (every 2 wk, providers were notified if adherence was <90%) in addition to the usual care group	One hundred twenty subjects enrolled. Adherence (measured using wireless pill bottles) was significantly better for both intervention groups compared with controls (78% [reminders], 88% [reminders plus notification], 55% [control], $P < 0.001$ in comparison of each group with control); no difference in mean or median tacrolimus levels, CV of tacrolimus levels, or percentage of tacrolimus measurements in the target range
Jiang et al[24]	Cross-sectional correlational study	Adult lung transplant recipients currently using Pocket PATH for daily self-monitoring	Pocket PATH generated a feedback message any time a critical value was entered detailing the information that should be reported to their coordinator	Of 96 subjects, 53 had at least 1 critical message generated. Most (90%) responded to the message, whereas 62% followed decision support. Moderate users of Pocket PATH (vs high and low utilizers), patients with lower income, and those with longer hospital stays were less likely to follow decision support
Geramita et al[25]	Long-term follow-up of a randomized controlled trial	Post–lung transplant recipients	Pocket PATH app, including reminders for medication taking and appointments, patient-entered results for health indicators established by transplant programs	One hundred five LTRs (75% of survivors) were assessed (M = 3.9 y posttransplant, SD = 0.8). Nonadherence rates in the past month were 23%–81% for self-care and lifestyle requirements (diet, exercise, BP monitoring, spirometry), 13%–23% for immunosuppressants and other medications, and 4% for tobacco use, with 31% clinic appointment nonadherence in the past year. In multivariable analysis, the Pocket PATH group showed lower risk of nonadherence to lifestyle requirements (diet/exercise) than the usual care group ($P < 0.05$)
Korus et al[26]	Randomized controlled trial	Twelve- to 17-y-old kidney or liver transplant recipients	Comprehensive online educational program, including interactive animations, on waitlist and posttransplant topics determined by a multidisciplinary team	Forty-two patients enrolled. Patients enjoyed learning about other teen experiences but reported barriers to accessing the site because of being too busy, computer being too slow, and inability to access it on their mobile device. Time spent on the site was low. No differences in health-related outcomes between groups
Torabi et al[27]	Single-center, prospective, randomized trial	Kidney transplant recipients	Use of Transplant Hero, a commercial app	Patients were randomized into app users (n = 18) and nonusers (n = 49). Tacrolimus CV was significantly lower in app users vs nonusers at 1 mo (27.7 vs 37.0, $P = 0.014$) but not at 3 mo (33.6 vs 35.4, $P = 0.63$)
Zanetti-Yabur et al[28]	Single-center, prospective, self-selected trial	Kidney or liver transplant recipients	Use of Transplant Hero, a commercial app	Patients self-selected into app users (n = 21) vs nonusers (n = 53). No significant difference in BMQ scores, MMAS-8, or IAT survey. No difference between mean serum tacrolimus levels or serum creatinine
Foster et al[29]	Multicenter parallel-arm randomized trial	Kidney transplant recipients aged 11–4 y and ≥3 mo posttransplant	TAKE-IT intervention: patient choice of text message, email, visual cue dose reminders in addition to meeting with coach at 3-mo intervals; adherence monitored with electronic pillbox	Three hundred eighty-eight patients screened, 277 eligible, and 172 enrolled: 81 subjects were enrolled in the intervention, whereas 88 were enrolled in the control group. Participants in the intervention group had significantly greater odds of taking their prescribed medications (OR, 1.66; 95% CI, 1.15-2.39) and taking their medications at or near the prescribed time (OR, 1.74; 95% CI, 1.21-2.50)
Han et al[30]	Single-center prospective, randomized, controlled trial	Kidney transplant recipients	Adhere4U app (audible and visual reminders, personal tracking of administration times, medication adherence report, detailed medication information, educational video, and patient laboratory test results) with electronic adherence monitoring	One hundred thirty-eight transplants randomized to mobile intervention (n = 71) or control (n = 67). No difference in change in nonadherence over time, assessed by BAASIS and VAS. Low patient engagement with high attrition (app use 47.6% at 28 d, 33.9% at 90 d, 11.5% at 180 d)

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TABLE 1. (Continued)

mHealth clinical outcomes studies

Authors	Study design	Population	Intervention	Outcomes
Tsapepas et al[31]	Single-center, retrospective description	Kidney transplant recipients early posttransplant	MRxEd app: medication collection and selection, video streaming with local clinician education modules, dynamic questioning, real-time notifications, and robust data reporting	Two hundred eighty-two patients described; 90% able to correctly answer questions about drug indications; however, 61% had trouble tying adverse events to specific medication; 92% of patients rated the education process as 4 or 5 on a Likert scale
Levine et al[32]	Single-center, prospective cohort	Kidney, SPK, CLKTx	Transplant Hero, medication reminders, and educational content, with or without a Pebble Smart Watch	One hundred eight patients enrolled, 19% with app and smartwatch, 35% app alone, 46% with no intervention. No significant differences between groups for tacrolimus CV at 1 or 3 mo
Gomis-Pastor et al[33]	Single-center, prospective cohort	Heart transplants within 1.5 y of transplant	mHeart: bidirectional interface that uses ePROM to detect medication nonadherence, report to healthcare professionals, and use text reminders to take medications, with self-reported dose administration tracking	Thirty-one patients enrolled, 42% were unaware of nonadherence consequences, and 39% were self-reportedly nonadherent; according to self-reported responses, intervention improved nonadherence by 16%–26% ($P<0.05$)
McGillicuddy et al[34]	Post hoc analysis of 6-mo prospective, parallel-arm, randomized controlled clinical trial	Kidney transplant recipients identified as nonadherent based on screening using electronic medication tray	Electronic medication tray with reminders, Bluetooth BP monitor, smartphone for transmitting data and send reminders to check BP (SMASK System)	Baseline tacrolimus CV was similar between arms (37% vs 37%, $P=0.894$). Patients randomized to the intervention had significant reduction in mean 12-mo tacrolimus CVs ($P=0.046$) and a significant improvement in the proportion achieving low tacrolimus CV <40% ($P=0.001$)
Fleming et al[35]	Secondary planned analysis of 12-mo, parallel, 2-arm, semi-blind, 1:1 randomized controlled trial	One hundred thirty-six participants randomized to mHealth-based, pharmacist-led intervention vs usual posttransplant care	TRANSAFE Rx app: mobile app with real-time medication lists from transplant center EMR, medication reminders and patient-reported tracking, Bluetooth-enabled BP and BG monitors, adverse event tracking, tacrolimus CV tracking, and clinic visit adherence tracking	The intervention arm demonstrated statistically significant decrease in tacrolimus IPV over time compared with control arm ($P=0.0133$). Significantly more patients in intervention group met goal of IPV <30% at 12 mo ($P=0.033$), despite groups being comparable at baseline
Control of chronic conditions				
Aberger et al[36]	Retrospective cohort	Kidney transplant recipients referred to a pharmacist for BP management (within 1 y of transplant or >3 y from transplant)	Home-based monitoring of BP with automated feedback messages to reinforce or prompt home BP monitoring. BP managed by a pharmacist	The 66 patients enrolled had a significant decrease in systolic (6 mm Hg) and diastolic (3 mm Hg) blood pressures ($P<0.01$) from baseline
McGillicuddy et al[37]	Retrospective review of long-term results after prospective, randomized pilot study	Kidney transplant recipients studied for 3 mo using mHealth system (9) and BP control 9 mo after trial ended	mHealth from month 0 to 3 listed in previous study and usual care from month 3 to 12	Of 18 subjects assessed, prior mHealth group sustained lower BP at 12 mo compared with the usual care group (131 vs 155 mm Hg, $P=0.004$)
Rosenberger et al[38]	Long-term follow-up of a prospective, randomized trial	Adult lung transplant recipients from previous study who survived to 12 mo posttransplant	Pocket PATH app: records daily health indicators, provides graphical displays of trends, advises patients to notify coordinator if health indicators outside of preestablished parameters	Eighty-eight intervention patients were compared with 94 usual care patients. No effect on outcomes. Self-monitoring (regardless of study group) reduced mortality risk (HR, 0.45; 95% CI, 0.22-0.91; $P=0.027$). Reporting of critical health indicators was associated with reduced mortality risk (HR, 0.15; 95% CI, 0.04-0.65; $P=0.011$) and BOS (HR, 0.27; 95% CI, 0.08-0.86; $P=0.026$)
Singer et al[39]	Single-center, prospective before-and-after study	Lung transplant recipients	In-person assessment and training followed by home-based exercise phase using a mobile education and tracking app with real-time provider monitoring and interface (Aidcube), and weekly coordinator check-ins	Fifteen participants enrolled out of 45 screened; 13 completed follow-up; 89% of subjects had a lack of access to traditional pulmonary rehabilitation. Participants had moderate adherence (60%) with high perceived utility ratings. SPPB frailty scores improved in 7 (54%) and FFP frailty scores improved in 8 (62%). No at-home safety events

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TABLE 1. (Continued)

mHealth clinical outcomes studies

Authors	Study design	Population	Intervention	Outcomes
Moayedi et al[40]	Single-center, prospective pilot study	Heart transplant recipients, postdischarge for the first 30 d of follow-up	Remote monitoring of health status using 5 wirelesses within digital devices, including smart watch, scale, BP cuff, thermometer, sleep tracker	Five consecutive male transplant patients were enrolled. Two patients were readmitted within 30 d of transplant discharge. Biometric data were available 70%–80% of the time for step count, heart rate, and BP during the 4-wk study period. Temperature was available between 60% and 80% of follow-up days. Weight measurements decreased significantly over time, from 75% of days in week 1 to 10% of days in week 4. Time in tacrolimus therapeutic range was 30%; no patients had rejection. Descriptive results of improved workflow efficiency, favorable use feelings toward educational videos, but frustration that there was no 2-way communication to personalize the experience, in addition to a feeling of notification burnout
Schenkel et al[41]	Single-center, prospective, observational pilot study	Lung transplant recipients after discharge, followed up for 2 y and compared with matched controls	Bluetooth-enabled devices including BP, heart rate, weight, BG, oxygen saturation, pulmonary function, and activity levels; incentive badges and humorous memes for high compliance, encouraging messages for poor compliance	Patients enrolled in program experienced lower incidence of readmission (IRR, 0.56; 95% CI, 0.41-0.76; $P<0.001$), which remained significant in multivariate analysis (IRR, 0.38; 95% CI, 0.23-0.63; $P<0.001$), along with Black race. There were also significantly decreased readmission days and hospital readmission charges
Medication errors				
Jandovitz et al[42]	Single-center, retrospective description	Post–kidney transplant recipients with access to technology with webcam capabilities	Virtual visit with outpatient transplant pharmacist via American Well HIPAA-compliant video interface platform	Half (52%) of the 46 patients who registered for a virtual visit completed 1. An average of 1.2 ± 0.4 medication changes were updated in the medical records
Taber et al[43]	Single-center, prospective, interventional trial	Kidney transplant recipients at least 1 y posttransplant with stable allograft function	Bluetooth-enabled Home-based monitoring for BP and BG with app and web-based portal. Monthly face-to-face encounters with pharmacists focusing on reducing barriers for CVD risk factor control, medication nonadherence, medication errors, self-efficacy, and lifestyle choices	Sixty patients enrolled, 51 completed follow-up. Improved BP control (50 vs 68%, $P=0.054$), HgA1c control (33 vs 47%, $P=0.061$). Medication errors reduced from 3.0 ± 2.7 to 0.14 ± 0.44 (–0.71 errors per month, $P<0.001$). Patient-reported adherence improved from 59.6% to 89.5% (increased odds of reporting high medication adherence per month: OR, 1.34; 95% CI, 1.10-1.64; $P=0.004$)
Gonzales et al[44]	Single-center, prospective, randomized controlled interventional trial	Adult kidney transplants between 6 and 36 mo posttransplant	Bluetooth-enabled home-based monitoring for BP and BG, patient-reported adherence and side effects, risk-guided televisits	One hundred thirty-six patients enrolled, 68 in each arm. Participants in the intervention arm experienced a significant reduction in medication errors (61% reduction; incident risk ratio, 0.39; 95% CI, 0.28-0.55; $P<0.001$) and a significantly lower incidence risk of grade 3 or higher adverse events (IRR, 0.55; 95% CI, 0.30-0.99; $P=0.05$). For the secondary outcome of hospitalizations, the intervention arm demonstrated significantly lower rates vs the control arm (IRR, 0.46, 95% CI, 0.27-0.77; $P=0.005$)

app, application; BAASIS, Basel Assessment of Adherence to Immunosuppressive Medication Scale; BG, blood glucose, BMQ, Brief Medication Questionnaire; BOS, bronchiolitis obliterans syndrome; BP, blood pressure; CI, confidence interval; CLKTx, combined liver kidney transplant; CV, coefficient of variability; CVD, cardiovascular disease; EMR, Electronic Medical Record; ePROM, electronic patient-reported measures; FFP, Fried Frailty Phenotype; HIPAA, Health Information Portability and Accountability Act; HR, hazard ratio; IAT, Implicit Association Test; IPV, intrapatient variability; IRR, incident risk ratio; LTR, lung transplant recipients; M, mean; mHealth, mobile health; MMAS-8, Moriskey Medication Adherence Scale - 8 Question; OR, odds ratio; SBP, systolic blood pressure; SD, standard of deviation; SMASK, Smartphone Medication Adherence Saves Kidneys; SPK, simultaneous pancreas kidney transplant; SPPB, Short Physical Performance Battery; TAKE-IT, Teen Adherence in Kidney transplant Effectiveness of Intervention Trial; VAS, Visual Analog Scale.

TABLE 2.

Published mHealth research protocols

Authors	Study design	Population	Intervention	Primary endpoints
McGillicuddy et al[45]	Protocol for randomized controlled trial	Eighty kidney transplant recipients	Multilevel mobile intervention: automated reminders from electronic medication tray, tailored text messages and motivational feedback guided by self-determination theory, automated summary reports for providers	Medication adherence (>90% opening medication tray) and BP control
Jung et al[46]	Protocol for randomized controlled trial	One hundred fourteen kidney transplant recipients, age 8 or older, at least 1 mo posttransplant	Smart pill box equipped with a personal identification system (fingerprint); home monitoring system to save, monitor, and transmit data	Medication adherence
Pase et al[47]	Protocol for a randomized controlled trial	One hundred twenty-eight adolescent (13–21 y) kidney transplant recipients randomized to 2 groups	Three-month educational platform housed within a secret group on Facebook, allowing interaction between patients and the multidisciplinary team	Impact of the intervention on knowledge, self-esteem, and satisfaction
Fleming et al[48]	Protocol for a randomized controlled trial	One hundred thirty-six participants randomized to mHealth-based, pharmacist-led intervention vs usual posttransplant care	TRANSAFE Rx app: mobile app with real-time medication lists from transplant center EMR, medication reminders and patient-reported tracking, Bluetooth-enabled BP and BG monitors, adverse event tracking, tacrolimus CV tracking, and clinic visit adherence tracking	Incidence and severity of medication errors and adverse drug events

app, application; BG, blood glucose, BP, blood pressure; CI, confidence interval; CV, coefficient of variability; EMR, electronic medical record; mHealth, mobile health; OR, odds ratio.

a durable impact on adherence, from laboratory monitoring to healthcare visits and self-care.[49] Our review indicates that most researchers favor study methods that incorporate multimodal mHealth interventions. Most interventions leveraged the multiple notification methods available in the current technological era, whereas others coupled patient-level notifications with active feedback and tailoring to individual patients.

For heart transplantation, in a small prospective cohort study from Spain, Gomis-Pastor et al demonstrated improvement in self-reported nonadherence with a bidirectional validated questionnaire and text message reminders to take medications in heart transplant patients within 18 mo of transplant. It is notable that 42% of patients did not report knowledge of the detrimental impact of nonadherence at baseline, so both education and reminders likely played a role in producing the described outcomes. The study did not fully describe the level of provider interaction delivered during the intervention, because their bidirectional interface allowed reporting of patient results within the electronic medical chart.[33] Reese et al[23] demonstrated improved medication adherence using either a customized reminder plan (78%) or a reminder plan plus active provider feedback (88%), compared with usual care (58%, $P<0.001$ versus either intervention group).

Within the lung transplant population, DeVito Dabbs et al developed and studied the Pocket PATH app. This app includes mobile reminders for medications and self-monitoring, in addition to decision-support tools such as automated messaging if health indicator values fell outside of an established range and required clinical attention.[22] Their original prospective, randomized trial demonstrated improved self-monitoring (odds ratio [OR], 5.11 [95% confidence interval (CI), 2.95-8.87]; $P<0.001$) and adherence (OR, 1.64 [95% CI, 1.01-2.66]; $P=0.046$). On long-term follow-up with the absence of decision-support tools, there was no association with app use on clinical outcomes; however, improved self-monitoring was significantly correlated with improved clinical outcomes, regardless of the original randomization grouping.[25]

In kidney transplantation, McGillicuddy et al assessed the impact of a comprehensive mHealth system (Smartphone Medication Adherence Saves Kidneys), targeting patients who had previously demonstrated nonadherence through electronic monitoring. Their mHealth intervention included a wireless medication tray with alert capabilities, a Bluetooth-enabled blood pressure (BP) monitor, a smartphone, a series of device-, patient-, and coordinator-level alerts, and a tailored weekly physician report. During a 3-mo intervention period, there was 91% patient retention, and the intervention demonstrated significant improvements in medication adherence and BP measures.[21] From these preliminary data, the authors developed and are currently testing a larger randomized control trial with the addition of text messages and motivational feedback for patients, which will be instrumental in determining if retention rates remain high over a longer time period (Table 2).[45] Additionally, Reese et al[23] demonstrated improved medication adherence using either a customized reminder plan (78%) or a reminder plan plus active provider feedback (88%), compared with usual care (58%, $P<0.001$ versus either intervention group). Foster et al tested a lower-tech intervention that used the pairing of adherence reminders with targeted coaching based on the self-management model. The authors of this trial demonstrated that this intervention mechanism produced increased medication adherence, both in terms of how often medications were taken and the timing with regard to when the medication was supposed to be taken.[29]

Finally, a unique measurement that has been associated with medication nonadherence is the tacrolimus coefficient of variation (CV). Two separate mHealth studies assessed the impact of their interventions on tacrolimus CV in a post hoc and secondary planned analysis, respectively.[34,35] Both McGillicuddy's (described previously, Smartphone Medication Adherence Saves Kidneys System) and Fleming's (TRANSAFE Rx System, described next) interventions were multimodal, including smartphones and Bluetooth devices, along with reminder alerts, and both demonstrated significantly improved tacrolimus CV over the course of the study, as well as proportionately more patients in the intervention groups meeting tacrolimus CV goals of <40% and <30%, respectively.[34,35]

It was evident that the desire for mHealth interventions that impact patient adherence has found traction in the commercial domain. Three of the recently published studies have used a commercially available app, Transplant Hero.[27,28,32] Although these analyses did not demonstrate improved adherence, it is reassuring to see a commercial entity committed to advancing the science of adherence with an eye toward improving clinical outcomes.

Control of Chronic Conditions

Another focus of mHealth interventions includes improving the prevention and management of the chronic conditions that are frequent in transplant recipients, with or without adherence monitoring (Table 1). Hypertension (HTN) is one of the most common chronic conditions posttransplant. Aberger et al demonstrated that the addition of home-based BP monitoring and web-based collaborative care to pharmacist-managed HTN was able to significantly improve BP in kidney transplant recipients within 30 d.[36] McGillicuddy et al demonstrated sustained improvements in BP control for 12 mo after the conclusion of their previously described 3-mo intervention, suggesting improved patient engagement and the durable impact of mHealth interventions.[37]

Frailty, another chronic condition that is highly associated with deleterious outcomes posttransplant, was targeted in a single-center prospective study of lung transplant recipients. Singer et al used a combination of in-person training with home-based exercise education, tracking, and real-time monitoring, leading to improved frailty scores in over half of the cohort, with no at-home safety events. This occurred in a population that lacked access to traditional pulmonary rehabilitation; however, the study had very low enrollment compared with the number screened, and so this intervention may only represent an option for a small and specific underserved population.[39]

Two recent articles in the cardiothoracic populations described multimodal mHealth systems designed for whole health and allograft monitoring in the posttransplant period. In the heart transplant population, Moayedi et al reported on a pilot program using 5 digital devices, including a smartwatch, scale, BP cuff, thermometer, and sleep tracker. They described perceptions of improved workflow efficiency from staff and favorable feelings toward educational videos from patients. Participants reported frustration from patients that there was no 2-way communication and a feeling of notification burnout.[40] In a single-center pilot study in lung transplant recipients with 2-y follow-up, Schenkel et al reported on a mHealth system, which monitored BP, hazard ratio, weight, blood glucose (BG), oxygen saturation, pulmonary function, and activity levels. This study provided positive reinforcement for patients with high adherence, as well as messages of encouragement for patients with poor adherence to the mHealth system. They found significantly lower readmission rates (incident risk ratio [IRR], 0.56) compared with matched controls.[41]

Medication Safety and Adverse Drug Events

Current immunosuppression regimens are highly effective but carry considerable toxicities and complexity. This, coupled with the fractionated care received within the US healthcare system, places transplant patients at high risk of developing adverse drug events and medication errors (MEs).

Jandovitz et al connected patients with pharmacists using a Health Information Portability and Accountability Act-compliant video interface platform compatible with any mobile device having webcam capabilities. Approximately half of the patients who registered for a virtual visit completed 1, and an average of 1.2 ± 0.4 medication corrections were made within the medical record.[42] Subsequently, Taber et al combined mobile home-based monitoring for BP and BG with monthly face-to-face meetings with a pharmacist. Although they were able to demonstrate trends in improved BP and BG control, the most significant finding of their study was a decrease in MEs from 3.0 ± 2.7 at baseline to 0.14 ± 0.44 at the end of follow-up, a reduction of 0.71 errors per month ($P < 0.001$). Subjects also had a higher odds of reporting high medication adherence for each month that they were in the study (OR, 1.34 [95% CI, 1.10-1.64]; $P = 0.004$).[43] This research group recently completed a single-center, prospective, randomized trial examining a pharmacist-led mHealth program, focused on reducing the incidence and severity of MEs and adverse drug events (TRANSAFE Rx) (Table 2).[48] They used a Bluetooth-enabled home-based monitoring system for BP and BG, patient-reported adherence, side effects, and risk-guided televisits with a transplant pharmacist. They were able to show significant reductions in MEs (IRR, 0.39), a lower risk of grade 3 adverse event (IRR, 0.55), and significantly lower hospitalization rates (IRR, 0.46) in the intervention arm compared with the control group.[44]

DISCUSSION

Although many mHealth interventions have demonstrated effectiveness, a nearly universal observation is a dichotomy between perceived utility by the user and sustained use. Previous long-term studies have demonstrated very high attrition rates over time, even in the face of high patient acceptance, perceived usefulness, and ease of use ratings. As an example, the Pocket PATH app demonstrated 48% daily use within the first 2 mo among lung transplant recipients, further decreasing to 19% in month 6 through 12.[24] Additionally, only 33% of the Pocket PATH intervention patients performed self-monitoring on at least half the days they were expected to.[22] A recent prospective, randomized trial using the Adhere4U app in a South Korean kidney transplant population also documented poor patient engagement and high attrition.[30]

Although most mHealth interventions reviewed in this article appear to offer high ratings for ease of use and perceived utility, there does not appear to be sufficient positive reinforcement to foster durable engagement and long-term use. The only exception to this observation was the TRANSAFE Rx mHealth system, with a 97% retention rate over the course of a year study.[44] There could be multiple reasons for this attrition, and issues of patient and provider fatigue cannot be dismissed. Designers of mHealth interventions should consider tailored intervention and feedback options to improve engagement across the spectrum of ages and sociodemographic groups. Individualization can occur through active patient feedback, allowing for tailoring to the patient's engagement style and need for more or less intensive interaction based on their adherence, risk factor control, and chronicity posttransplant. Although some patients may prefer less feedback and be content with monthly visuals demonstrating positive health and lifestyle changes, others may be better engaged by individualized coaching within the app.

Gamification, the application of game-design elements and principles in nongame contexts, is another promising strategy to mitigate attrition. It can be tailored to be age appropriate across multiple age groups, as a more rapid and dynamic positive feedback mechanism to keep patients engaged long enough to realize long-term improvement in their chronic conditions.[50] mHealth intervention designers should consider both provider and patient involvement in the design of the mHealth tool and possibly the conduct of the study. The use of human factors experts in the development of the platform and usability testing to ensure it meets the user experience standards may also be helpful.

Another major challenge for mHealth is interoperability. For patients and healthcare providers to see a benefit from mHealth systems without adding unnecessary work or mundane tasks, standardized integration within the electronic health records (EHRs) is necessary. Providing similar structure and standardization to data will be critical for merging data from mHealth devices into EHRs, as well as for analyzing the impact of the mHealth intervention. As most mHealth systems described in the literature are small scale and individually built to work within each researchers' unique healthcare environment, they are not universally deployable. An app must be able to communicate with various EHRs to provide usable information for patients, concurrently allowing healthcare providers to monitor patients via prespecified alerts or tailored portals. It is evident that third-party industry participation will be necessary to mitigate these interoperability gaps; however, to what degree and how private companies can be aligned toward this goal remain to be seen.

Although at first glance, it may seem that there is a surplus of commercially available apps that address most chronic health conditions, in reality, there is a fragmented environment with a range that is continuously being updated, created, or abandoned.[51,52] Convergence of all technology options paired with individualized mHealth interventions may lead to an increase in perceived utility while minimizing alert and technology fatigue. A mHealth system should be able to provide a platform for monitoring and tracking any chronic condition that has measurable physiological parameters, which can be tailored for each patient. For example, if a post–kidney transplant patient does not have HTN but is struggling with anemia, a mHealth system that can be individualized to track and alert on anemia-related parameters and medication administration, yet be silenced on issues surrounding BP would best serve the patient and clinicians. It should also have the ability to alert on the basis of concerning trends in physiological parameters or laboratory values, such as immunosuppressant level variability or missed clinic visits, to focus clinicians' attention on patients at risk for events.[53-56]

The challenges of producing a mHealth system that would be acceptable to patients, healthcare providers, and hospital systems have been described in detail elsewhere.[9,20]

Although smartphones have permeated throughout society, patients and providers have various levels of technology functionality. To maintain high patient utilization, a mHealth system must produce durable behavioral changes that improve self-management. Technology support may be necessary to help train patients on the app and functionality and to address technological problems; many may need support to use the apps effectively. From the provider side, a dedicated healthcare practitioner, such as a pharmacist or nurse, tracking patients and data, preprogrammed alerts for alarming singular values and trends, or both may be beneficial for sustained physician acceptance and use of the technology for their patients.

In conclusion, mHealth systems show promise in improving patient engagement and self-management in solid organ transplantation. To gain acceptance from the health system and society as a whole, an app must be cost-effective, save time, improve chronic condition management, and reduce MEs. Future studies should incorporate gamification, coaching, user/provider technology support, and standardized incorporation into the EHRs.

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