

Acceleration of mobile health for monitoring post-transplant in the COVID-19 era: Applications for pediatric settings

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Funding information

National Institute of Diabetes and Digestive and Kidney Diseases, Grant/Award Number: U34 DK112661

[Correction added on 12th November, 2021, after first online publication: The 5th author surname has been corrected.]

Abstract

Background: Since the start of the COVID-19 pandemic and consequent lockdowns, the use of telehealth interventions has rapidly increased both in the general population and among transplant recipients. Among pediatric transplant recipients, this most frequently takes the form of interventions on mobile devices, or mHealth, such as remote visits via video chat or phone, phone-based monitoring, and mobile apps. Telehealth interventions may offer the opportunity to provide care that minimizes many of the barriers of in-person care.

Methods: The present review followed the PRISMA guidelines. Sources up until October 2020 were initially identified through searches of PsycInfo[®] and PubMed[®].

Results: We identified ten papers that reported findings from adult interventions and five studies based in pediatrics. Eight of the adult publications stemmed from the same two trials; within the pediatric subset, this was the case for two papers. Studies that have looked at mHealth interventions have found high acceptability rates over the short run, but there is a general lack of data on long-term use.

Conclusions: The literature surrounding pediatric trials specifically is sparse with all findings referencing interventions that are in early stages of development, ranging from field tests to small feasibility trials. The lack of research highlights the need for a multi-center RCT that utilizes robust measures of medication adherence and other outcome variables, with longer-term follow-up before telehealth interventions should be fully embraced.

KEYWORDS

mobile health, monitoring, pediatric transplantation, telehealth

1 | INTRODUCTION

Telehealth, also commonly referred to as eHealth, is defined by the World Health Organization as interventions that use communication and technology to improve health-related fields.¹ Specifically among pediatric transplant recipients, this most frequently takes

the form of interventions on mobile devices, or mHealth, such as remote visits via video chat or phone, phone-based monitoring, and mobile apps.² Since the start of the COVID-19 pandemic and consequent lockdowns, the use of telehealth interventions has rapidly increased both in the general population and among transplant recipients.³⁻⁵

Abbreviations: CAD, Canadian Dollars; EHR, electronic health record; mHealth, mobile Health; PRISMA, preferred reporting items for systematic reviews and meta-analyses; QoL, quality of life; RCT, randomized controlled trials; SD, standard deviation; SOC, standard of care; TRU-PBMT App, technology recordings to better understand pediatric blood and marrow transplant application; USD, United States Dollars.

The potential benefits of telehealth were rapidly accepted during the pandemic, but their scope may apply beyond the current public health crisis. Telehealth may serve as a convenient and feasible option for delivering post-transplant care to pediatric solid organ recipients and could offer many benefits over traditional in-person care beyond its necessity during the pandemic. It can fill accessibility gaps in rural areas and underserved communities where there may not be an adequate number of qualified providers⁶ and may reduce the burden of care on patients and their caregivers. Telehealth minimizes the need for transportation access, which disproportionately affects individuals of low socioeconomic status, and is quite relevant to the transplant context as access to centers may require long commutes. Individuals with accessibility barriers may not receive consistent care, which adversely affects health outcomes.

Telehealth also comes with its own set of barriers depending on the type of service utilized. A recent study of telehealth use during the COVID-19 pandemic found that patients over 65 years old had the lowest odds of utilizing telehealth services versus office or emergency room visits.⁷ This may be relevant for pediatric patients with caregivers who experience difficulties utilizing telehealth services for care. For video-conferencing, patients must have access to a stable internet connection, which may not be the case for many families. To this point, one survey found that among individuals making less than \$30 000 USD per year, 29% did not own a smartphone, and 44% did not have broadband services.⁸ Accessibility should therefore also be considered when evaluating the use of telehealth.

An important but often neglected aspect of telehealth is a dearth of findings demonstrating its comparability to standard care. As in any new approach to care, embracing new technologies without appropriate testing could lead, in the long run, to provision of more expensive and less efficient care—the exact opposite of the intended outcomes. Other interventions that seemed on the surface conducive to streamlining care have yielded mixed findings. One example of this is related to the premature embrace of the EHR. Without any appropriate pre-vetting or research, EHRs were touted as a vehicle to increase efficiency of care, reduce costs, and reduce medication errors. Yet, the wide embrace of EHR did not lead to any of those hoped-for outcomes, and EHRs are now routinely cited as one of the top factors associated with physician burnout.^{9,10} More specifically in transplant medicine, although many electronic and automated interfaces have been suggested and promoted to increase and facilitate engagement with patients and families, almost none of those have been rigorously studied. At the same time, it is important to acknowledge the potential of these types of interventions and our aim is to synthesize available literature to date in order to better understand the applicability of telehealth to pediatric transplant.

The present review focuses on the use of telehealth in monitoring of post-transplant outcomes including, but not limited to, self-reported adherence, QoL, patient self-reported symptoms, and medical outcomes, and explore how it may apply it to the pediatric population. The purpose of this paper is to provide an empirical, nuanced examination of the potential benefits and drawbacks to telehealth established by prior work as well as important future directions to guide clinicians on its delivery.

2 | METHODS

The present synthesis was based on a systematic review following the PRISMA guidelines.¹¹ The procedures that were followed are described below and outlined in Figure 1.

2.1 | Eligibility criteria

We aimed to cast a wide net to exhaustively canvas studies investigating monitoring in transplant patients. Therefore, all empirical research designs were included such as RCTs, controlled trials (not randomized), cohort studies, observational cohort studies, pre-post comparisons, and retrospective chart reviews. Articles were excluded if they did not report on an intervention or monitoring (e.g., only adherence was discussed).

2.2 | Information sources

Sources up until October 2020 were initially identified through searches of PsycInfo[®] and PubMed[®]. We used only information provided in the published articles and did not use any other external sources (i.e., we did not look at grant proposals or registration materials and did not contact the authors for details that were not presented in published manuscripts).

2.3 | Search

Sample electronic database search strategy: PubMed title/abstract: “Telehealth” AND “transplant,” filters activated: Humans, English.

2.4 | Study selection

Three authors (BRC, RT, and RAA) separately screened article titles produced by the search strategy described above. First, article titles were reviewed, and abstracts were then examined for articles that did not meet the exclusion criteria based on the title and content. Full-text articles were reviewed for studies that appeared to meet eligibility criteria based on the abstract. One author (RAA) independently reviewed the selected studies to confirm eligibility.

2.5 | Data extraction

The following data were collected from each article that reported on an intervention approach: sample size, demographic data, study design, intervention description, and the results.

2.6 | Assessment of bias

The inclusion of only published results can result in loss of negative or neutral findings. We also found that on multiple occasions, the

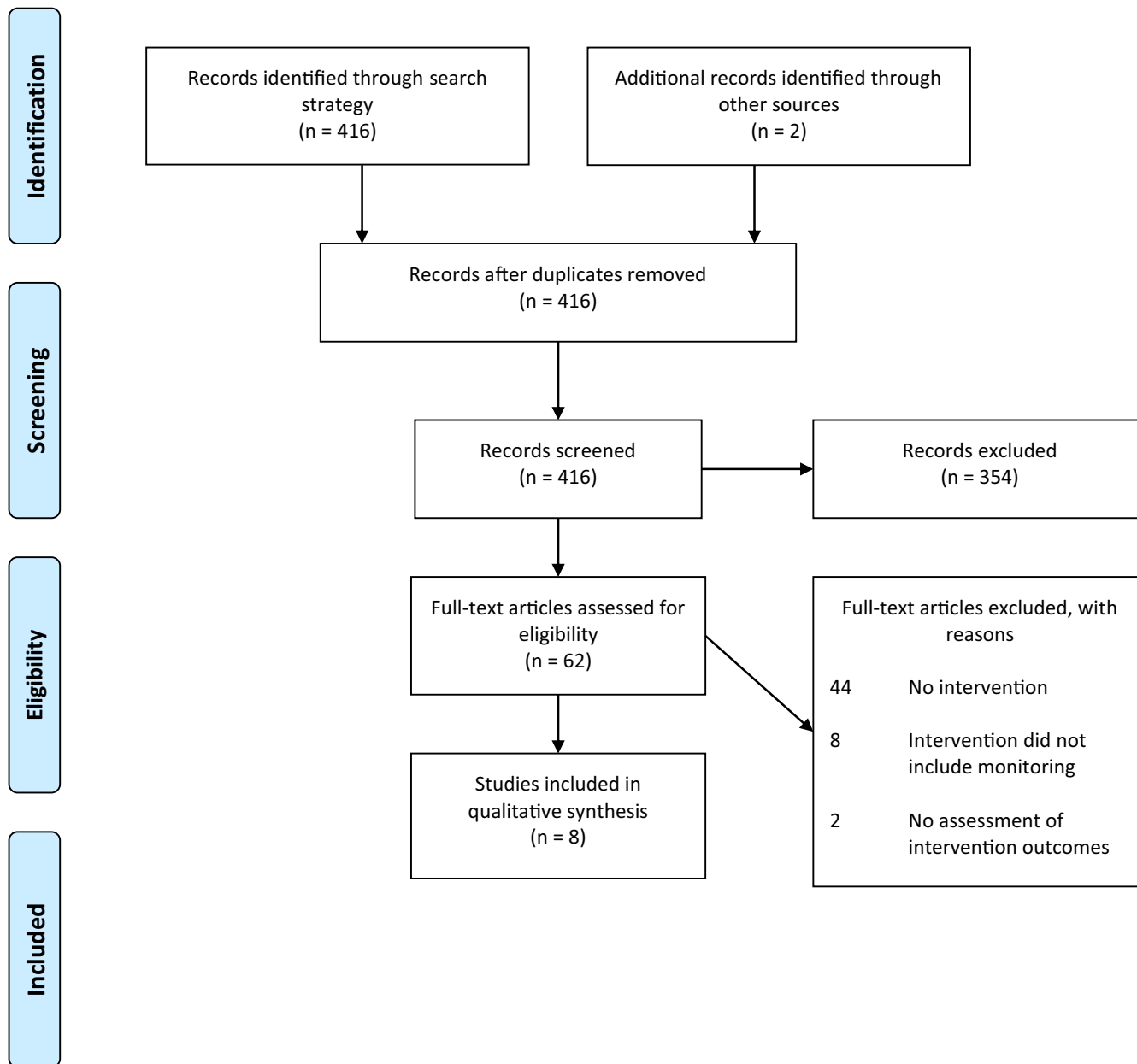


FIGURE 1 PRISMA diagram

same study was described in multiple papers. In order to minimize bias, we have consolidated results and also captured a wide range of design choices to provide a more nuanced summary in terms of generalizability.

3 | RESULTS

3.1 | Overall of findings in transplantation

Our first step was to examine the utility of telehealth for monitoring generally in transplantation. We identified ten papers that reported findings from adult interventions and five studies based in pediatrics. Of note, eight of the adult publications stemmed from the same

two trials; within the pediatric subset, this was the case for two papers. Findings are summarized in Table 1.

3.2 | Monitoring in adult transplant settings

Lee et al.¹² conducted a RCT of 100 liver transplant recipients who received either SOC alone or SOC with remote home monitoring. The SOC component consisted of interdisciplinary patient information post-discharge, including a “Home Monitoring Paper Log.” In addition to SOC, the intervention group received a tablet and peripheral equipment for monitoring vital signs, blood sugar, and weight. These devices offered the opportunity to communicate with the transplant team as well as reminders and relevant patient information. Data

TABLE 1 Summary of interventions on monitoring in transplant settings

Citation	Population	Design	Telehealth (eHealth) approach	Findings
Lee et al, 2019 ¹²	N = 100 adult recent liver transplant recipients	RCT, single center	Remote home monitoring versus standard care	Lower readmission rate and better QoL in eHealth group
Schmid et al, 2017 ¹³	N = 46 adult recent renal transplant recipients	RCT, single center	Telemedical case management versus standard care	Lower rates of acute care and costs as well as better adherence and QoL in the eHealth group
McGillcuddy et al, 2013 ¹⁴	N = 21 adult recent renal transplant recipients	RCT, single center	mHealth system for monitoring post-transplant hypertension and adherence versus standard care	More adjustments to medications and lower blood pressure readings in clinic as well as better adherence in the eHealth group
Devito Dobbs et al, 2016 ¹⁵	N = 201 adult lung transplant recipients	RCT, single center	Pocket PATH [®] versus standard care	No change in clinical outcomes; positive impact on self-monitoring and adherence
Shellmer et al, 2016 ¹⁶	N = 7 adolescent liver, heart, and lung transplant recipients	Field test of mHealth application prototype	Teen Pocket PATH [®]	Suggests usability; users found Teen Pocket Path easy to use and effective in promoting medication adherence
Triplett et al, 2019 ¹⁷	N = 33 pediatric liver or kidney transplant recipients and their respective caregivers	Cohort study, single center	Proteus Discover [®] -medication embedded with a digestible sensor, a sensor skin patch, a mobile application, and an electronic portal	Suggests ease of use and positive self-reports of medication adherence; challenges included reluctance to participate and patch wearability difficulties
Vaughn et al, 2018 ¹⁸	N = 10 pediatric blood marrow transplant recipients	Longitudinal cohort study, single center	mHealth smartphone application to collect symptom data, and a wearable tracking device to collect physiological data	Suggests potential acceptability and feasibility
Kelly et al, 2019 ¹⁹	N = 33 adolescent heart, kidney, and lung transplant recipients	Longitudinal cohort study, single center	Home-based telehealth group adherence intervention	Group was generally feasible, acceptable and engaging; suggests an increase in medication adherence; high levels of patient satisfaction reported

were collected on the acceptability of technology as well as usage. Overall, the intervention group displayed significantly lower readmission rates 90 days post-discharge (28% vs. 58%) as well as better QoL in the domains of physical functioning and general health than those receiving SOC only.

In Germany, a similar approach has been successfully conducted as well.¹³ Schmid and colleagues randomized 46 renal transplant recipients to SOC versus a telemedically supported case management group. The latter included reception of equipment for monitoring as well as remote case management services. Results showed that the intervention group had lower rates of acute care, coupled with a significant reduction in costs (comprehensive cost information about the intervention was provided as well). Secondary findings also showed better adherence and QoL indices.

A small RCT among kidney transplant recipients ($N = 21$) with uncontrolled hypertension compared standard care to a mHealth platform that monitored blood pressure readings, medication adherence, and provided feedback to patients.¹⁴ Results were promising in that the mHealth group demonstrated reductions in blood pressure ratings taken in clinic, better adherence, and increased adjustments to antihypertensive medications. Finally, the Pocket PATH[®] study compared usual care to a mHealth application, delivered via smartphone, among a sample of 201 lung transplant recipients in a RCT.¹⁵ One of the main auspices of Pocket PATH[®] is to facilitate improved self-management, and this includes consistent monitoring. Results suggested better self-management in the intervention group, but there were no differences in the clinical outcomes assessed.

3.3 | Monitoring in pediatric transplant settings

Despite the recent emergence of mHealth technologies for the management of pediatric chronic medical conditions,²⁰⁻²² few studies have explored the use of mHealth in the pediatric transplant population. One study described the development and testing of an mHealth application, Teen Pocket PATH[®], an iteration of the Pocket PATH[®] application tailored to adolescents.¹⁶ The authors suggest preliminary usability and efficacy in prompting adolescents to adhere to their medications. Another study utilized a mHealth application in conjunction with other forms of digital medicine: a wearable patch and an ingestible sensor pill that relayed health information to the app and care team.¹⁷ The study showed promise in terms of positive patient satisfaction with the intervention and positive self-reports of medication adherence. However, there were extremely high levels of attrition for a multitude of reasons, including irritability from the skin patch.¹⁷ Another intervention developed is the TRU-PBMT App, which is used in conjunction with an apple watch in order to monitor patient symptoms.¹⁸ The TRU-PBMT intervention is currently being studied for feasibility, acceptability, and usability.^{23,24} Thus, the development of mHealth interventions for the pediatric transplant population is in its early stages.

To date, only two other studies have utilized telehealth in the pediatric transplant population without the use of mHealth apps.

The first implemented a home-based telehealth group adherence intervention for adolescent transplant recipients, which demonstrated acceptability and feasibility.¹⁹ The second study, which is underway now, is evaluating the use of a telemedical case management model for post-kidney transplants. This model includes the use of video consultations, psychological adherence assessments, home-based exercise training programs, case management, and internet-based case files with the goal of improved care and reduced healthcare costs.²⁵

3.4 | Patient perspectives

Overall, findings indicate positive patient attitudes toward using telehealth for transplantation follow-up care.^{14,26-28} In a comparison of patient satisfaction between a group using telehealth and a group using traditional in-person office visits, there was no difference in satisfaction levels, suggesting that telehealth is a helpful and viable alternative to face-to-face care.²⁷ McGillicuddy and colleagues¹⁴ found that 81% of patients felt that this approach would be helpful for transplantation follow-up care and 79% of patients would use the system if instructed to do so and provided with access free of cost. Similarly, in a population of solid organ transplant patients, over 75% rated their willingness to use interactive health technology as high. Patients who held negative attitudes toward using telehealth or remote monitoring systems typically had less confidence in using technology or did not have access to such technology, such as a smartphone.^{14,28,29}

A benefit consistently noted throughout previous studies is decreased travel time to appointments and less time waiting for the appointment to begin.^{26,27} In a study of 19 liver transplant patients, patients felt telehealth lessened the burden of travel, especially considering the number of appointments they had to attend. The most important benefit attributed to telehealth was saved travel time. Relatedly, telehealth reduced the cost of their post-transplant care because it eliminated taking time off from work and/or securing childcare.²⁷ In a study examining the follow-up care of transplant patients, patients reported feeling like the telehealth app and access to their own patient data through the app improved focus in video chats with doctors,³⁰ which may too reflect the lessening of time constraints.

In creating telehealth systems, patient access to technology and their ability to use such technologies must be considered. A study by Vanhoof et al.²⁸ of older adult patients with an average age of 55.38 (SD = 13.4) attempted to use a "human centered design approach" in the development of a telehealth system in order to increase positive attitude and utilization. The study found that a lack of prior technology use was correlated with a lower overall willingness to use telehealth, although there was no difference in willingness across gender, employment, type of transplant, or age. In addition, it was found that most had a positive attitude toward features that facilitated greater accessibility, such as automatic data transfer to their clinics and the inclusion of visual aids. In this

study, the use of websites was preferred over a smartphone application, though at the time of completion, few of the participants owned smartphones. Similar findings were found in a 2018 study whose sample had a mean age of 51.8 (SD = 14.2 years).²⁹ The authors argued that younger individuals could potentially benefit from telehealth more than older individuals due to their higher affinity toward technology. These aspects of telehealth may be especially relevant for older caretakers who may be less likely to utilize technology.

3.5 | Acceptability

Reports generally show that patients do use mHealth interfaces—at least for a brief period of time. While long-term use remains unexplored, the shorter-term studies have reported high rates of acceptability.³¹ In one study, 75% of the participants approached to join the study agreed to participate.¹⁴ Kelly et al.¹⁹ found that among adolescents who were part of a group-based telehealth intervention aiming to increase medication adherence, 85.7% of participants were satisfied with the use of technology, 78.6% would use telehealth in the future, and 85.7% would recommend using telehealth to a friend. A study of adults, with an average age of 57 (SD = 14), found that 80% of participants rated highly the perceived usefulness of mobile apps.³² Other studies have reported similar findings.^{14,24,33} Patients may, thus, be willing to use telehealth monitoring and interventions post-transplant, but persistence in using such apps/devices or interventions, beyond the initial novelty, has yet to be established.

3.6 | Costs

The economic cost of telehealth may be much less than that of traditional in-person care.^{34,35} One study compared the cost of telehealth to in-person postoperative visits which included the cost of travel, accommodations, meals, and missed work.³⁴ For patients who lived at least 1635 miles away round trip, telehealth visits had a cost savings of \$1501 per visit. For patients who lived closer to providers and did not need accommodations, savings totaled \$256 per visit. Another study of lung transplant recipients in Canada found that the average cost of telehealth visits was CAD \$30 (USD \$25) versus CAD \$263 (USD \$216) for in-person visits.³⁵

Telehealth may also be effective at reducing cost for health systems when it is adjacent to in-person visits rather than a replacement for visits.³⁶ One study in kidney transplant recipients compared the cost of standard care versus standard care with the addition of telehealth supported case management in 46 patients during the first year post-transplant.³⁶ The authors found that the addition of the telehealth component yielded a non-statistically significant savings of €1944 (USD \$2352) per patient for hospitals due to a reduction in care utilization. The authors estimated that this would amount to € 791 033 (USD \$957 071) if implemented in the 12 German hospitals

doing more than 20 transplants a year. Thus, telehealth may present cost-savings for multiple stakeholders.

3.7 | Shifts in transplant care due to COVID-19

The COVID-19 outbreak has caused major shifts in routine health-care delivery with drastic consequences for transplant centers. Due to the heightened risks for immunocompromised patients, the limited resources, and the lack of Intensive Care Unit beds available for transplant recipients, many pediatric transplant centers around the world performed only urgent transplants around the height of the pandemic's first wave in March 2020.³⁷ Another particularly significant change was the authorization of providers to bill for telehealth visits through Medicare beneficiaries at costs comparable to in-person visits, eliminating deductibles, and waiving penalties for non-HIPAA compliant communication.³⁸ These shifts served as catalysts for both patient willingness to try telehealth and insurance coverage, two prior barriers to the utilization of telehealth.⁵

While some transplant clinics had implemented the use of telehealth prior to COVID-19 pandemic, COVID-19 has accelerated the use of telehealth for transplant, as a way to mitigate barriers to standard care. An April 2020 survey reported that 98% of Liver and Intestinal Transplant sites in the USA now utilize telehealth, a stark contrast to the 16% utilization reported in a 2019 survey.⁴ Another clinic reports that their kidney transplant program converted 98% of its transplant clinic into telehealth sessions successfully in response to the COVID-19 pandemic.⁵

Recent studies have suggested that the use of telehealth appointments was feasible for transplant recipients during the COVID-19 pandemic.^{5,39-42} This modality was well received by patients, as it curbs risk of infection and removes the hassles of transportation, parking, and wait times.^{40,43} One study also suggested that accessing care from home was more comfortable for patients.⁴³ Transplant clinics have also uncovered unexpected benefits from the use of telehealth, such as the ability to frequently check-in on patients with acute medical and surgical issues and the ability to reinforce education as needed.⁴⁴ One clinic has even incorporated telehealth robots for in-person appointments to minimize the spread of COVID-19 among liver transplant patients, and reports confidence in this approach.⁴⁵ Telehealth could thus offer a range of benefits for the transplant community, particularly via the reduction of transmission rates, patient burden, and cost. Given these potential benefits and the promising feasibility of telehealth, it is possible that these shifts precipitated by the COVID-19 pandemic will be everlasting for the transplant community.

4 | DISCUSSION

Although telehealth has burgeoned in the COVID-19 era, there are still very few empirical studies to support its usage for monitoring

and key methodological issues germane to adherence research have not been well covered. However, there are promising findings to draw from. Shorter-term monitoring studies have yielded positive outcomes, utilizing mobile phone apps, telehealth-based case management, and group-based cognitive behavioral therapy interventions.^{12,13,15} Also promising, given the context of the COVID-19 pandemic, one study found that those who participated in telehealth visits versus in-person visits did not have significantly different outcomes.⁴⁶

Telehealth interventions may offer the opportunity to provide care that minimizes many of the barriers of in-person care. Monitoring that includes additional resources may also be more successful in improving outcomes. For example, a German study that included telehealth case management found positive results in reducing critical care costs.¹³ However, to date, no interventions have been compared or have demonstrated long-term effects. A notable exception is the app called Pocket PATH[®], which was tested over the course of several years by a particularly persistent and rigorous group of investigators. The device failed to improve re-admissions and other transplant outcomes in the original study,¹⁵ but the authors continued to study it, thinking that there were some indications of potential long-term efficacy, and even pilot-tested a teen version.¹⁶ But over the long term, the app continued to show no efficacy in improving transplant outcomes.^{31,47} The Pocket PATH[®] experience may well be true for many other apps that do not have the benefit of a dedicated group of investigators willing and able to rigorously study such applications.

Accordingly, specific to app-based interventions and monitoring, studies that only measure short-term outcomes are severely limited in generalizability. Improvements in adherence achieved in the first year of app use were not sustained, and given current results, it is quite possible that app-based interventions may not be engaging over a long period. A meta-analysis of app-based interventions for various chronic illnesses found a pooled dropout rate of 43%.⁴⁸ The short-term benefits of telehealth for monitoring may not be sustainable if the intervention or monitoring protocol is unable to facilitate ongoing participation.

Studies have found high acceptability rates over the short run, but findings to date are drawn from a handful of studies that may not generalize well given design considerations and short follow-up or, reliance on self-report measures rather than actual use metrics. In both adult and pediatric trials, findings were reported in the context of small sample sizes^{13,14,17,19,24} and a lack of long-term outcomes.^{12-14,16,17,24} Additionally, almost all trials were single-center trials, which may result in patient homogeneity in terms of race and socioeconomic status and consequently a lack of generalizability. Many of these studies, both adult and pediatric trials, made use of self-report and collateral measures,^{12,15,16} which tend to inflate adherence.⁴⁹

The literature surrounding pediatric trials specifically is sparse with all findings referencing interventions that are in early stages of development, ranging from field tests to small

feasibility trials. The majority of these studies used cohort (uncontrolled) designs,^{17,19,24} therefore lacking robust evidence for efficacy. Of note, there were a number of publications on proposed studies without the inclusion of data. There is an evident lack of sufficient data and published findings as well as holistic presentations of the use of telehealth for post-transplant monitoring at this time, and this is especially true for pediatric populations. The mixed findings of the adult literature offer pediatrics an unclear roadmap of what effective telehealth interventions might look like. However, this research does highlight the potential cost savings' benefits and the feasibility of implementation.

The previously mentioned limitations of this field highlight the need for a multi-center RCT that utilizes robust measures of medication adherence and other outcome variables, with longer-term follow-up. It is expected that the use of telehealth for post-transplant monitoring will continue to grow as a result of COVID-19 as many clinics are shifting to virtual appointments when possible. Telehealth could offer a wide range of benefits, but both history and current findings should give some pause to anyone who is willing to embrace new technology without scrutiny. We owe it to our patients to study promising technologies before they are implemented, and our reading of the literature is that whenever telehealth interventions were rigorously tested (which is not often), they failed to show the intended (hopeful) outcome and fell quite short of initial expectations. Perhaps one way to move forward, until more data are available, is to reduce expectations. Rather than looking at telehealth applications as a new panacea for improved care, we suggest framing these approaches as potential additions, yet unproven, to post-transplant care, that may offer some circumscribed benefits at a relatively acceptable cost.

AUTHOR CONTRIBUTIONS

BRC: Concept/design, data collection, data analysis/interpretation, drafting article, critical revision of article, approval of article; RT: Concept/design, data collection, data analysis/interpretation, drafting article, critical revision of article, approval of article; KS: Data analysis/interpretation, drafting article, critical revision of article, approval of article; JF: Data analysis/interpretation, drafting article, critical revision of article, approval of article; GH: Concept/design, critical revision of article, approval of article; ES: Funding secured by, concept/design, data analysis/interpretation, drafting article, critical revision of article, approval of article; RAA: Concept/design, data collection, data analysis/interpretation, drafting article, critical revision of article, approval of article.

DATA AVAILABILITY STATEMENT

No original data were collected for the present review.

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How to cite this article: Campagna BR, Tutino R, Stevanovic K, et al. Acceleration of mobile health for monitoring post-transplant in the COVID-19 era: Applications for pediatric settings. *Pediatr Transplant*. 2022;26:e14152. <https://doi.org/10.1111/petr.14152>