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Digital directly observed therapy to monitor adherence to medications: A scoping review

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Abstract

Background: Technology-based directly observed therapy (DOT) is more cost-effective and efficient compared with in-person monitoring visits for medication adherence. While some evidence shows these technologies are feasible and acceptable, there is limited evidence collating information across medical conditions or in the context of HIV prevention, care, and treatment.

Objectives: We conducted a scoping review to understand the current evidence on the acceptability, feasibility, and efficacy of digital DOT to improve medication adherence and, specifically, to determine if digital DOT had been used to improve adherence for HIV prevention, care, and treatment

Methods: We searched the electronic databases PubMed, Embase, and the Web of Science in January 2021 for any published studies with terms related to digital technologies and DOT. We included peer-reviewed studies in any population, from any country, for any outcome, and excluded conference abstracts. We included three types of digital DOT interventions: synchronous DOT, asynchronous DOT, and automated DOT. We provide an assessment of the current evidence, gaps in literature, and opportunities for intervention development regarding the use digital DOT to improve antiretroviral therapy (ART) adherence, specifically in the field of HIV.

Results: We identified 28 studies that examined digital DOT. All studies found digital DOT to be acceptable and feasible. Patients using digital DOT had higher rates of treatment completion, observed doses, and adherence compared with in-person DOT, although data were limited on adherence. Only one study examined HIV prevention, and none examined ART adherence for HIV treatment.

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Author's contributions: MCDS and PS conceptualize and designed the review. MCDS and AMB reviewed the literature and abstracted data. MCDS drafted the analysis and manuscript. PS, AMB and ASC provided insight on the analysis of data, reviewed the manuscript and participated in writing.

Declaration of interest statement: The authors report no conflict of interest

Conclusions: Digital DOT is acceptable and feasible but has not been used to remotely monitor and support ART adherence for people living with HIV.

Keywords

Directly observed therapy; Technology; Adherence; Antiretroviral therapy; HIV; Review

Introduction:

Directly observed therapy (DOT), where a patient is observed while taking a medication, has been used across a range of health conditions to increase adherence to medications.[1-5] However, given the patient burden of repeated clinic visits needed for in-person DOT, digital technology such as video-conferencing software and mobile health (mHealth) applications (apps) can facilitate remote monitoring of medication adherence.[1-5] Technology-based DOT strategies have been shown to be more cost-effective and reduce provider and patient burden compared with regular monitoring visits for medication adherence.[6] Although some evidence suggests that these technologies are feasible, accessible, and effective for DOT, there is limited evidence collating information across medical conditions which could inform the development of new interventions to improve medication adherence. Specifically, limited evidence exists describing the use of digital DOT interventions in the context of HIV prevention, care, and treatment.

In the United States, the largest drop-offs in the HIV care continuum are from poor retention in care and viral suppression, whereby 50% of those diagnosed are not retained in care and 43% of those prescribed antiretroviral therapy (ART) do not achieve viral suppression.[7] Poor viral suppression can be largely attributed to suboptimal levels of ART adherence due to factors such as inability to consistently follow daily pill regimens due to housing instability or job insecurity, and/or competing demands in the form of co-morbid health conditions like mental health challenges.[8-12] Nearly two-thirds of new HIV diagnoses are attributed to people living with HIV (PLWH) who are aware of their HIV infection and either not in care or are receiving care but not virally suppressed, making ART adherence a top priority for curbing incidence.[13] ART adherence is strongly correlated with increased survival and improvement in quality of life[14,15] and reductions in adherence have been associated with loss of virologic control, treatment failure, and onward transmission of drug-resistant virus.[16-18] Among PLWH, young adults, Black Americans, and sexual and gender minorities have some of the lowest rates of viral suppression and engagement in care.[7,19] Similarly, oral antiretroviral pre-exposure prophylaxis (PrEP) is over 90% effective at preventing HIV in women and men,[20,21] but low adherence and persistence has undermined the effective use of PrEP to prevent HIV particularly among adolescents and young adults and Black Americans.[22-27] Thus, improved strategies are needed to increase adherence to medications to prevent new HIV infections among those uninfected and improve virologic suppression among PLWH.

We conducted a scoping review to understand the current evidence related to the acceptability, feasibility, and efficacy (i.e., impact on medication adherence) of digital health technologies for DOT to monitor adherence in any population for any outcome,

and to determine if digital DOT had been used to improve medication adherence for HIV prevention, care, and treatment. We conducted a scoping review instead of a systematic review to broadly synthesize evidence on the use of digital DOT to improve medication adherence and, specifically, to assess the scope of evidence in the field of HIV. Here, we provide an assessment of the current evidence, gaps in literature, and opportunities for intervention development regarding the use digital DOT to improve medication adherence in general and specifically among PLWH and those at high risk for HIV acquisition.

Materials and Methods:

The scoping review was conducted according to the standard protocol for Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews checklist (PRISMA-ScR).[28] We included quantitative or qualitative studies of digital DOT technologies on adherence from any prior date until January 8, 2021. Digital DOT interventions were defined as interventions that allow a human or technology (e.g., a smartphone app) to digitally observe or view a participant consume a medication at the time of dosing. We included three types of digital DOT interventions: synchronous DOT, asynchronous DOT, and automated DOT. Synchronous DOT is where a patient and provider both simultaneously log onto a video-conferencing software and the provider observes medication ingestion by the patient in real time.[2-4] Asynchronous DOT involves a smartphone app or platform where a patient records a video of themselves taking the medication which is then uploaded for later review by a provider or researcher.[2-4] Automated DOT interventions use smartphone apps with artificial intelligence and facial recognition to confirm medication ingestion without the use of a provider. [29,30] We did not include studies with ingestible sensors or reminders via text message as these constitute a different type of intervention that do not include observation by a provider or researcher. Therefore, the studies that met inclusion criteria were those that 1) included the use of a digital DOT technology, 2) focused on improving medication adherence for any medical condition, 3) were peer-reviewed publications, and 4) were published in English. We included interventions in any population and did not restrict by comparator group or study design. The outcomes of interest were medication adherence and the acceptability and feasibility of the intervention. Cost-effectiveness outcomes were not included. We did not restrict studies by type of reported statistics (e.g., odds ratio).

We reviewed published, peer-reviewed literature across a range of studies, from pilot and descriptive studies to randomized trials. The first search was conducted on November 23, 2020, with a second search on January 8, 2021, to confirm that we were able to identify key publications of interest. We searched the electonic databases PubMed, Embase, and the Web of Science, including published peer-reviewed literature and excluded conference abstracts. We used the following keywords: (digital* OR technolog* OR application* OR "app" OR "apps" OR smartphone* OR smart phone* OR mobile OR mhealth* OR telehealth OR tele-health OR telemedicine OR tele-medicine OR video* OR videoconferenc* OR telerehabilitation OR tele-rehabilitation OR remot*) AND ("directly observed therap*" OR "directly observed treatment*" OR "directly observed intervention*" OR "directly observed" OR "direct observation"). We also conducted a manual search of references of citations identified through the electronic searches, to identify any additional relevant citations.

Abstracts were imported from each electronic database and combined within Covidence online software, which automatically removes duplicates.[31] One co-author screened the abstracts and examined the full text of articles in relation to inclusion criteria. A second co-author then reviewed a random sample of 10% of the articles and flagged discrepancies which were reviewed again by the first co-author. If there were any discrepancies, an additional 10% of articles were reviewed and so on. A third co-author was consulted for any unresolved discrepancies. Additional studies that were abstracts, scoping reviews, or commentaries on the topic were only included in the introduction and discussion to provide information on newly conducted research or opinions in the field. Data charting was performed using a standard form that was created by the team through Covidence software and included variables of interest to extract. One reviewer extracted information from all studies including the citation, year, population, inclusion criteria, sample size, study design, medical condition (e.g., HIV, tuberculosis [TB]), outcome, intervention description, if incentives were provided, follow-up period, and findings. The same process for review of extracted data was used as was done for the inclusion process whereby a second co-author reviewed a random sample of 10% of the articles and flagged discrepancies. Extracted information was based on agreement between the two co-authors. We conducted a critical appraisal of study quality and potential biases for each study by examining the strength of the study design (e.g., pilot, programmatic data, randomized trial) and sample size. Given that most of the studies were not randomized trials and used different research designs and outcomes, we opted not to use a standardized critical appraisal tool. Study data were summarized overall and by medical condition (e.g., HIV) being examined to assess the overall evidence for medication adherence according to the type of medical condition and type of intervention (e.g., automated versus asynchronous DOT). Data are presented in table format by medical condition and type of intervention. A protocol was developed and distributed internally prior to conducting the review .

Results:

After exclusion of duplicate citations, a total of 93 studies were identified from the three databases (Figure 1). The titles and abstracts were screened for relevance by one reviewer, and 64 were retained for full text review. Reasons for exclusion are reported in Figure 1. A total of N = 28 studies were eligible for inclusion. These studies are summarized in Table 1, grouped by medical condition and type of intervention.

Most studies examined medication adherence related to TB (n = 22, 79%; Table 1). Of the remaining six studies each examined adherence to medications for different medical conditions or needs: schizophrenia, stroke, HIV prevention, asthma (inhaler use), dietary supplement use, and opioid use. Most publications were cohort studies (n = 19; 68%), five were single arm pilot studies (18%), three were randomized trials (11%), one was a non-randomized experimental study (4%), and one was a pilot study where patients were randomized to either immediate or delayed DOT with an mHealth app intervention (4%). Samples sizes ranged from 6 to 405. Nearly all studies (n = 24; 86%) recruited clinic patients. Studies were conducted in North America (n = 17, 61%; in the contiguous United States [n = 15; 54%], Puerto Rico, and Mexico), Asia (n = 5, 18%; in China [n = 2], Singapore, Taiwan, Vietnam), Europe (n = 3, 11%; in England, Norway, Belarus), Africa

(n = 2, 7%; in Kenya, Uganda), and one study in Australia. Intervention types included synchronous DOT (n = 11; 39%), asynchronous DOT (n = 14; 50%), and automated DOT (n = 3; 11%).

Asynchronous DOT

Of the 14 asynchronous DOT studies, all found the tool to be acceptable and feasible to use (Table 2).[3,32-43] Participants were satisfied with the intervention, would recommend it to a friend, would use it in the future and thought it was convenient, private, and easy to use. Both patients and providers found the app acceptable and thought it saved time and money compared to in-person DOT.[39,40,44] A study of inhaler use in children found that all but one child mentioned that daily recoding of their use of the inhaler was fun and enjoyable.[32] In five studies, patients stated that they preferred or would choose asynchronous DOT over in-person DOT.[33,36,39,41,42] Concerns with asynchronous DOT included technical difficulties, privacy concerns, and discomfort taking a video of oneself.

Treatment completion and adherence were high across studies (82-93%). All studies that compared treatment completion between asynchronous DOT and in-person DOT found increased treatment completion with asynchronous DOT.[3,38-40] A randomized trial of 226 patients reported that 70% of asynchronous DOT patients achieved 80% or more scheduled observations compared with 31% of in-person DOT patients.[38] Only one study explicitly compared adherence between asynchronous DOT and a control group that measured adherence through in-person DOT visits. The study found that medication adherence on DOT was comparable to that of in-person DOT (94% vs 98%, P = 0.17).[40]

Synchronous DOT

Of the 11 studies that assessed synchronous DOT, all studies found synchronous DOT to be acceptable and feasible.[45-55] Patients and providers thought the tool was convenient, comfortable, easy to use, and ensured privacy. In all studies that compared synchronous DOT to in-person DOT, participants and providers preferred digital DOT due to increased convenience and ease of use.[47,49,54,55] Synchronous DOT reduced time and costs for clinic visits and lead to fewer missed visits and higher treatment completion than in-person DOT.[45-53,55] One cohort study found treatment completion (i.e., completing a course of TB treatment regardless of daily adherence) among patients using synchronous DOT was 88% (44/50) compared with 65% (196/302) among patients using in-person DOT (P < 0.001).[45] None of the studies compared adherence between synchronous DOT and a control arm.

Automated DOT

Of the two studies that assessed acceptability of automated DOT (aDOT), all found the intervention acceptable and feasible.[1,56] Patients reported that the artificial intelligence (AI) platform improved the doctor-patient relationship,[56] high satisfaction, that they would recommend the app to a friend, that they would use it in the future, and that it helped with medication adherence.[30] Patients with little experience using a smartphone were able to successfully use aDOT.[56] Two studies assessed adherence measured using the AI platform versus adherence through mobile DOT or plasma drug concentration levels and found increases in adherence with aDOT. One study in patients who had experienced a stroke

found that adherence based on plasma drug concentration levels was 100% (15 of 15) in patients using aDOT compared with 50% (6 of 12) in the control group. The second study found that mean adherence over 24 weeks was 90% (standard deviation [SD] = 24.9) for participants who were monitored using aDOT, compared with 72% (SD = 39.8) in those who were monitored in person by study staff (or a third party) for a difference of 18% (95% confidence interval [CI] = −2.0 to 37.7; P = 0.08).

Among all 28 studies, only one used digital DOT with an HIV prevention outcome.[30] Among young men who have sex with men in San Francisco, California, automated DOT was highly acceptable, 84% reported the app helped with taking pre-exposure prophylaxis (PrEP), and median PrEP adherence was 91%.[30]

Discussion:

We identified 28 studies that examined digital DOT interventions to improve adherence to medication for any health indication. All studies found digital DOT to be acceptable and feasible and noted that digital DOT provided more autonomy, convenience, and ease of use for patients and providers compared with in-person DOT.[1,3,29,32-37,39-43,45,47,48,50,51,55,57] Patients using digital DOT had higher rates of treatment completion, observed doses, and adherence compared with in-person DOT. [29,58] More research is needed from large randomized trials examining the impacts of digital DOT on adherence compared with other interventions and comparing different types of digital DOT. Evidence largely shows that digital DOT is acceptable, feasible, and has the potential to improve medication adherence.

Given the challenges with adherence to PrEP and ART, digital DOT has a high potential to improve HIV prevention, care, and treatment. However, we identified only one study that had an HIV prevention outcome.[30] The automated DOT approach used AI in a smartphone app and was found to be highly acceptable with high PrEP adherence.[30] This study highlights the potential benefit of using digital DOT technologies to increase adherence in the context of HIV prevention, care, and treatment. We did not identify any studies examining ART adherence for HIV; however, two excluded studies used mobile phone-based reminders to increase ART adherence.[59,60] Our findings highlight the potential benefit of using digital DOT technologies to increase adherence in the context of HIV prevention and the gap in research focused on digital DOT to improve adherence to HIV treatment.

Technology-based interventions may be particularly appropriate to increase ART adherence among youth living with HIV (YLWH) given that youth are the largest group of consumers of technology and internet.[61-63] In addition, research has shown that younger age is associated with lower ART adherence and higher risk of virologic failure among PLWH.[65-69] A systematic review examining the HIV care continuum in YLWH found that only 54% of youth who initiate ART achieve viral suppression and an additional 43% are retained in care.[7] Suboptimal ART adherence and retention in care can increase risk of treatment failure, HIV transmission, and poor health outcomes. Thus, YLWH are a key population with whom to examine digital DOT interventions aimed at improving HIV clinical outcomes.

There are some limitations to our review. We reviewed only three databases and included studies in English. Therefore, there may have been studies that were not captured in our review that would have been using a more systematic review approach. While there were 28 studies that used digital DOT, there were few studies that were randomized trials and most had a small number of participants. Most studies focused on TB outcomes and were in the United States. More data are needed from regions outside of the United States and from large trials and those that examine adherence outcomes using digital DOT compared to other methods as well as studies that compare different types of digital DOT to each other. Additionally, while over 96% of individuals age 18–29 in the United States have a smartphone,[64] we acknowledge that there will be more marginalized groups who may not have smartphone access and this intervention may not be accessible to them. Further studies are also needed to review implementation outcomes with the scale up of digital DOT in healthcare settings and should also investigate digital DOT and other tools to assess adherence for non-clinic-based provision of long-acting injectables for HIV treatment and prevention.

Given the recent COVID-19 pandemic, remote-based research and the use of digital tools to support medication adherence are becoming increasingly important.[70] Digital DOT may offer a solution by which to remotely monitor and support medication adherence. However, there is a critical gap in literature on the use of these strategies to increase ART adherence among PLWH. It may be a particularly useful tool to promote ART adherence among groups experiencing inequities in HIV care such as youth, and people of color. Digital DOT may increase convenience and reduce patient and provider burden compared to in-person DOT. Compared to in-person DOT, several studies found improved treatment completion and adherence with digital DOT. However, randomized studies assessing adherence outcomes are limited. More data are needed from larger, experimental randomized trials, in settings with limited access to healthcare such as rural settings and comparing the different methods of digital DOT that now exist.

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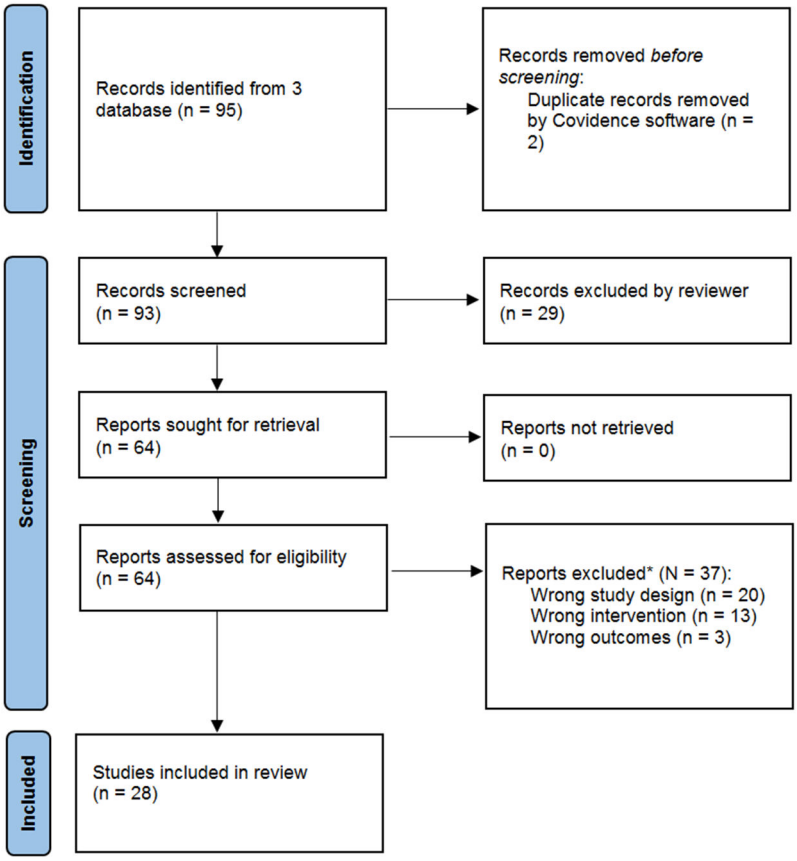

Figure 1:
Flow diagram for Study Inclusion

Table 1:

Characteristics of 28 studies included in the scoping review

Study ID	Disease state	Study design	Total number of participants	Location	Population description	Type of intervention
Bain 2017	schizophrenia	Non-randomized experimental study	53	US	Patients with schizophrenia	Automated DOT
Labovitz 2017	stroke	Randomized controlled trial	28	US	Stroke patients on anticoagulation therapy	Automated DOT
Liu 2020	HIV prevention	Other: Mixed-methods optimization pilot study	35 focus group; 20 pilot	US	Young men who have sex with men at high risk of HIV infection and HIV negative	Automated DOT
Shields 2018	Inhaler use for Asthma	Other: Pilot Randomized to either immediate or delayed MDOT intervention	24	US	Children with difficult to manage asthma	Asynchronous DOT
Molton 2016	dietary supplement	A single arm pilot study	42	Singapore	Online healthy volunteer in Singapore	Asynchronous DOT
Godersky 2020	opioid use	Cohort study	14	US	Adult clinic patients	Asynchronous DOT
Lam 2018	TB	Cohort study	50	US	Patients treated for latent TB infection (LTBI) with 3-month, once-weekly isoniazid and rifapentine (3HP)	Synchronous DOT
Story 2019	TB	Randomized controlled trial	226	England	Patients diagnosed with active TB	Asynchronous DOT
Guo 2020	TB	Randomized controlled trial	405	China	Hospital patients	Synchronous DOT
Guo 2020	TB	Cohort study	393	China	Patients in the TB control program	Asynchronous DOT
Holzman 2018	TB	Cohort study	28	US	TB patients	Asynchronous DOT
Chen 2020	TB	Non-randomized experimental study	240	Taiwan	Patients with latent tuberculosis infection who received a 9 month isoniazid treatment regimen	Synchronous DOT
DeMaio 2001	TB	Cohort study	6	US	TB cases	Synchronous DOT
Chuck 2016	TB	Cohort study	390	US	TB patients	Synchronous DOT
Garfein 2015	TB	A single arm pilot study	52	US and Mexico	TB patients	Asynchronous DOT
Wade 2012	TB	Cohort study	132	Australia	Patients in a community nursing service	Synchronous DOT
Hoffman 2010	TB	Cohort study	13	Kenya	Hospital patients	Asynchronous DOT
Buchman 2017	TB	Cohort study	118	US	Patients at Nassau County Department of Health Tuberculosis Control	Synchronous DOT
Donahue 2019	TB	Cohort study	16	US	Patients at military pediatric infectious diseases clinic.	Synchronous DOT
Garfein 2018	TB	Cohort study	274	US	Patients receiving DOT for active or suspected pulmonary TB	Asynchronous DOT

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Study ID	Disease state	Study design	Total number of participants	Location	Population description	Type of intervention
Olano-Soler 2017	TB	Cohort study	17	Puerto Rico	TB patients in a long-term care facility for cognitively impaired adults located in Puerto Rico	Asynchronous DOT.
Holzman 2019	TB	A single arm pilot study	25	US	Patients diagnosed with or treated for TB	Asynchronous DOT
Holzschuh 2017	TB	Cohort study	27	US	TB patients	Synchronous DOT
Bendiksen 2020	TB	Cohort study	17	Norway	Patients receiving treatment for tuberculosis	Synchronous DOT
Sekandi 2020	TB	Cohort study	50	Uganda	Patients aged 18 to 65 years with 3 months remaining of their TB treatment	Asynchronous DOT
Mirsaeidi 2015	TB	Cohort study	11	US	Patients at TB clinic	Synchronous DOT
Nguyen 2017	TB	Cohort study	40	Vietnam	TB patients at three outpatient tuberculosis clinics	Asynchronous DOT
Sinkou 2017	TB	Cohort study	10	Belarus	Patients in a TB program	Asynchronous DOT

Table 2:

Acceptability, feasibility, and adherence outcomes among 28 studies included in the scoping review.

Study ID	Disease state	Type of intervention	Acceptability	Feasibility	Adherence
Bain 2017	Schizophrenia	Automated DOT		Subjects were able to use the technology successfully for up to 6 months in an ambulatory setting.	Mean adherence over 24 weeks was 90% (standard deviation [SD] 24.9) for subjects receiving ABT-126 who were monitored using the AI platform, compared with 72% (SD 39.8) for subjects receiving ABT-126 who were monitored by mDOT. The difference was 18% (95% CI: 2 to 38; P=.08).
Labovitz 2017	Stroke	Automated DOT	In the pre- and post-study questionnaire, 73% and 83% of patients, respectively, answered ‘extremely good’ when asked to rate the AI Platform as a medication management tool and to improve the doctor/patient relationship	Patients, some with little experience using a smartphone, successfully used the technology	Mean (SD) cumulative adherence based on the AI Platform was 90.5%. Plasma drug concentration levels indicated that adherence was 100% (15 of 15) and 50% (6 of 12) in the intervention and control groups, respectively
Liu 2020	HIV prevention	Automated DOT	Median System Usability Scale scores were in the excellent range (80/100). At week 8, nearly two-thirds (63%) were very satisfied with the app, and the remainder (37%) were mostly satisfied. Over two-thirds (68%) would definitely recommend the app to a friend. Overall, 84% reported they were likely to use the app to take PrEP in the future. Most (84%) participants reported the app helped with taking PrEP, while one participant (5%)	App use was high, with median PrEP adherence of 91% based on aDOT-confirmed dosing.	

Study ID	Disease state	Type of intervention	Acceptability	Feasibility	Adherence
			reported the app didn't help and 2 (11%) reported the app made things worse.		
Shields 2018	Inhaler use for Asthma	Asynchronous DOT	Most children were satisfied with the MDOT system. Parents reported that their children were enthusiastic and interested in the use of the MDOT approach Older children themselves mentioned that twice daily recoding of their use of the inhaler was fun and enjoyable. The parents of one child said he was bored by the end of the study.	By week 5, all children still engaging in MDOT (n=18) were judged to have effective inhaler technique. Spirometry values did not vary to significantly between baseline and 12 weeks (P>0.05), however, mean fraction of exhaled nitric oxide (FeNO) values normalized (mean 38.7 to 19.3ppm) and mean Asthma Control Test values improved (13.1 to mean 17.8).	
Molton 2016	dietary supplement	Asynchronous DOT	The system was perceived to be beneficial by the participants (a median score of 6 (range 4–7), when asked whether the system helped them to adhere to the course of medication	Videos were classified as confirmed pill intake (3475, 83% of the 4200 videos expected), certain pill intake(16, <1%), fake pill intake (31, <1%), not received technical issues (223, 5%) or not received assumed non-adherence (455, 11%). Overall median estimated participant adherence by MIST was 90%, like that obtained by pill count (94%). There was a good relationship between participant adherence as measured by MIST and by pill count (Spearman's r=0.66, p<0.001	
Godersky 2020	opioid use	Asynchronous DOT	Most participants (10/14; 71%) reported being very satisfied with the application; of the remaining 4 participants, 2 were satisfied and 2 were neutral.	All participants except 1 (93%) used the application successfully to upload videos. The percentage of daily videos uploaded per participant ranged from 18% to 96%; on average, daily videos were submitted by participants 72% of the time.	
Story 2019	TB	Asynchronous DOT		Intent-to-treat analyses show 70% of VOT patients achieved 80%+ scheduled observations compared to 31% of DOT patients.	
Guo 2020	TB	Asynchronous DOT	Significantly more patients (191/235,81%) in the VOT group preferred their treatment method compared to those on in person DOT (37/131, 28%) (P<.001), and 92% (61/66) of the health care workers thought that the VOT method was more convenient than DOT.	79% (186/235) of the VOT patients had >85% of their doses observed, while only 16% (26/158) of the DOT patients had >85% of their doses observed. The VOT group showed a significantly higher fraction of doses observed (P<.001), less missed observed doses (P<.001), and fewer treatment discontinuations (P<.05) than the DOT group.	
Holzman 2018	TB	Asynchronous DOT	Video DOT was well received by staff and patients alike, who cited increased treatment flexibility, convenience, and patient privacy.	A higher percentage of total treatment doses observed during the vDOT period (72% vs 66%, P = .03)	Medication adherence on vDOT was comparable to that of in-person DOT (94% vs 98%, P = 0.17)
Garfein 2015	TB	Asynchronous DOT	Most participants preferred VDOT over in-person DOT. Compared to time on in-person DOT, 92% preferred VDOT, 81% thought VDOT was more confidential, 89% never/rarely had problems recording videos, and 100% would recommend VDOT to others.	Documented observation of nearly all expected doses (mean 93% in San Diego and 96% in Tijuana) was achieved using VDOT. Adherence was similar in San Diego (93%) and Tijuana (96%).	
Hoffman 2010	TB	Asynchronous DOT	8 patients preferred MDOT to clinic DOT or DOT through visiting Community Health Workers.	All agreed that MDOT was a viable option to increase adherence	

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Study ID	Disease state	Type of intervention	Acceptability	Feasibility	Adherence
Garfein 2018	TB	Asynchronous DOT	Most participants (96%) would recommend VDOT to others; 90% preferred VDOT over DOT.	Median fraction of expected doses observed (FEDO) among VDOT participants was higher (93% [interquartile range (IQR) 83- 97%]) than among patients receiving DOT (66% [IQR 55%- 89%]).	
Olano-Soler 2017	TB	Asynchronous DOT.		All 11 patients with active TB disease and all 6 with LTBI had completed treatment with recommended 80% of scheduled doses taken. All patients with active TB disease showed clinical signs of improvement	
Holzman 2019	TB	Asynchronous DOT	A total of 91% (20/22) of surveyed patients described app as easy to use. All were able to communicate concerns and medication side effects effectively through the platform. The majority felt vDOT was more convenient (20/22, 91%) and preferred (20/22, 91%) over in-person DOT. While 82% (18/22) felt vDOT preserved patient privacy over in-person, 18% (4/22) disagreed and felt in-person DOT was more private.	The median number of weeks on vDOT was 13 (interquartile range [IQR] 11-16). Median adherence was 74% (IQR 62%-84%), and median verifiable fraction was 86% (IQR 74%-98%). More than 90% of patients reported recording and uploading videos without difficulty.	
Nguyen 2017	TB	Asynchronous DOT	Participants rated the VDOT interface highly, despite facing initial technical difficulties. Participants rated the system highly, with 35 (87%) finding the system easy to use, and 35 (87%) patients stating they would recommend the method to others.	Among participating patients, 27(71%) of patients took all required doses. A median of 88% (interquartile range 76%-94%) of doses were correctly recorded and uploaded.	
Sinkou 2017	TB	Asynchronous DOT	Qualitative feedback from patients was supportive, with most welcoming the time and cost-saving attributes of VOT. Eight out of 10 patients felt that VOT was easier than daily commuting to take treatment at the tuberculosis dispensary and that the cost of internet connection was cheaper than public transport. All patients were prepared to recommend VOT to other patients	There were 595 VOT episodes registered (100% of the planned video sessions), of which 577 (97%) were classified of good quality and 18 (3%) of insufficient quality to confirm intake of medication (16 of which were from male patients).	
Sekandi 2020	TB	Asynchronous DOT	92% of patients reported being very satisfied with using VDOT	Of the 5150 videos expected, 4231 (82%) were received. The median fraction of expected doses observed was 85% (interquartile range 66%-94%) and this significantly differed by follow-up duration. Phone malfunction, uncharged battery and VDOT app malfunctions were common reasons for missed videos.	
Lam 2018	TB	Synchronous DOT		A total of 360 video sessions were conducted with a median of 8 (range: 1-11) sessions per patient and a median time of 4 (range: 1-59) minutes per session. Issues (e.g., >15 minutes late) during video sessions occurred 104 times. Treatment completion among patients was 88% (44/50) compared with 64.9% (196/302) among patients on clinic DOT (P<.001).	
Buchman 2017	TB	Synchronous DOT		20% of the caseload used SDOT and 100% of patients who were eligible opted in. Average SDOT success was 79%.	
Donahue 2019	TB	Synchronous DOT		94% (15/16) completed treatment in 12 weeks. For 81% (13/16) of the patients, encounters were able to be completed within 10 minutes. Average one-way travel time to our facility for patients was	

Study ID	Disease state	Type of intervention	Acceptability	Feasibility	Adherence
				51 minutes. Actual time spent in most vDOT encounters was less than 10 minutes. 100% treatment compliance and completion	
Guo 2020	TB	Synchronous DOT	Most patients in both groups believed that observed treatment (VDOT/DOT) helped them not to miss doses (185[93%] vs. 171 [87%], p=0.057). More patients in the VDOT group thought their intervention was convenient and comfortable (191 [96%] vs. 111 [57%], p<0.001), would choose the intervention if necessary (191 [96%] vs. 113 [58%],p<0.001), and would recommend the method to other patients(191 [96%] vs. 113 [58%],p<0.001)	High rates of treatment completion (96% with VDOT vs. 95% with DOT). The two observed treatment methods had no statistical differences, and all could accomplish their tasks well. Average time per dose observed was 16 min (standard deviation [SD] 12.1) for VDOT, while 44 min (SD 3.7) for DOT (including travel time),p<0.01.	
Chen 2020	TB	Synchronous DOT	Satisfactions with location arrangement (p<0.001), ensuring treatment adherence (p=0.027), and privacy issues (p=0.005) were superior int the SVOT group	The rate of treatment completion was 91%. One (1%) and 20 (12%) of the participants in the SVOT and CDOT groups, respectively, quit treatment (p=0.008). Development of adverse events [aHR 8.0(3.4 -18.8)], and the concern of privacy infringement [aHR 5.9(2.7-12.8)] by the DOT program independently increased the risk of withdrawal. SVOT program [aHR 0.2(0.1 - 0.7)] and a belief in the importance of adherence on treatment efficacy [aHR 0.3(0.1- 1.0)] were independent predictors preventing patients from withdrawing from treatment.	
DeMaio 2001	TB	Synchronous DOT	Patients found videophone technology easy to master (average satisfaction score 8.4). Overall satisfaction with V-DOT was very high (average satisfaction score, 9.2), compared with S-DOT.	The average time required for a S-DOT visit was 1 hour, compared with 3 min for a V-DOT visit. Patient adherence to therapy was 97% on S-DOT and 95% on V-DOT.	
Chuck 2016	TB	Synchronous DOT		VDOT enabled a DOT worker to observe a maximum of 25 patients per day, like DOT workers who observed patients in clinic (n=25), but twice that of DOT workers who observed patients in the community (n=12). Treatment completion with VDOT was like that with in-person DOT (96% vs. 97%, P=0.63). Problems during VDOT sessions were interruption of video and audio connectivity. Adherence to scheduled VDOT sessions was 95% (3292/3455) compared to 91% (32 204/35 442) with in-person DOT (P,0.01).	
Wade 2012	TB	Synchronous DOT	Qualitative analysis found positive factors of flexible timing, high patient acceptance, staff efficiency, and clinic support.	Missed observations for the telehealth service was 12% (n = 58), compared to 31% for the in-person service (n = 70). Most of the difference of 19% (95% CI: 12 - 25) was due to fewer pre-arranged absences. The video service used less staff time and became dominant if implemented on a larger scale and/or with decreased technology costs. Substantial technical problems were manageable, and improved liaison between the nursing service and the clinic was an unexpected side-benefit	
Mirsaeidi 2015	TB	Synchronous DOT	Patient experience included that seven (88%) out 11 patients were well satisfied with VDOT, and all respondents (100%) considered VDOT an improvement over to the traditional DOT and strongly recommended it to other TB patients	11 successfully completed treatment with cure outcomes; 1083 -DOT observations were performed with a 97% compliance rate.	
Holzschuh 2017	TB	Synchronous DOT	Fifteen of the 27 persons opted for VDOT over conventional DOT.	One of the persons being monitored via VDOT discontinued treatment because of an adverse medication reaction. The remaining	

Study ID	Disease state	Type of intervention	Acceptability	Feasibility	Adherence
				14 persons completed treatment with 100% compliance. Use of VDOT saved an estimated $2,066 in mileage and staff time and allowed patients to continue treatment during international travel and family relocation.	
Bendiksen 2020	TB	Synchronous DOT	14 /17 patients and 14/ 17 home nurses preferred video conferencing over home visits. 15 patients and all home care nurses would recommend video conferencing to others.	The median daily time spent by the home care service was 17 minutes for home visits and 3 minutes for video conferences.	