Farmacia Hospitalaria 48 (2024) T252–T258

Farmacia HOSPITALARIA
Órgano oficial de expresión científica de la Sociedad Española de Farmacia Hospitalaria
www.elsevier.es/farmaciahospitalaria

Review

[Translated article] Digital health for promoting adherence to antiretroviral treatment in patients with HIV/AIDS: A meta-review

Griselda Areli Ramírez López[a,b], Diana Lizbeth Gómez Galicia[a], Tania Ximena Zagal Jiménez[b], Cairo David Toledano Jaimes[a] and Christian Díaz de León Castañeda[c,d,*]

[a] Facultad de Farmacia, Universidad Autónoma del Estado de Morelos (UAEM), Morelos, México
[b] Instituto Nacional de Enfermedades Respiratorias (INER) «Ismael Cosío Villegas», Secretaría de Salud, Ciudad de México, México
[c] Investigadoras e Investigadores por México, Consejo Nacional de Humanidades, Ciencias y Tecnologías (CONAHCYT), Ciudad de México, México
[d] Facultad de Enfermería, Universidad Michoacana de San Nicolás de Hidalgo (UMSNH), Michoacán, México

ARTICLE INFO

Article history:
Received 13 October 2023
Accepted 13 February 2024

Keywords:
HIV
e-Health strategies
m-Health
Telehealth
Treatment adherence and compliance
Medication adherence

ABSTRACT

Introduction: Digital health or "e-health" is a set of applications based on information and communication technologies (ICTs) that can be used to promote self-care and medication adherence in patients with chronic diseases. The aim of this study was to carry out a review of systematic reviews (meta-review) on efficacy studies of e-health interventions to promote adherence to antiretroviral therapy (ART) in people living with HIV/AIDS.
Methodology: A review of systematic reviews ("meta-review") was performed using the Medline-PubMed database on efficacy studies of e-health components to promote adherence to ART, in patients with HIV/AIDS, proposing a structured search strategy (PICO question). A selection process for systematic reviews was conducted based on inclusion and exclusion criteria. Subsequently, the corresponding data were extracted, and the analysis was accomplished in descriptive tables.
Results: A total of 29 systematic reviews were identified, from which 11 were selected. These reviews comprised 55 RCTs with different e-health interventions and enrolled a total of 15,311 HIV/AIDS patients. Studies included a total of 66 comparisons (experimental group vs. control group) in indirect adherence measurements based on different measurement techniques (36 statistically significant); 21 comparisons of viral load (VL) measurements (10 statistically significant); and 8 comparisons of $CD4^{+}$ cell count measurements (3 statistically significant). m-Health was the most studied component followed by the telephone call and e-learning.
Conclusion: Evidence was found that supports that some e-health interventions are effective in promoting adherence to ART and improving health outcomes in patients with HIV/AIDS, although it is identified that more studies are needed for more robust evidence.

Salud digital para promover la adherencia al tratamiento antirretroviral en pacientes con VIH/SIDA: meta-revisión

Palabras clave:
VIH
Estrategias de eSalud
m-Salud
Telesalud
Cumplimiento y adherencia terapéutica
Adherencia a la medicación

RESUMEN

La salud digital o «e-Salud» es un conjunto de aplicaciones basadas en Tecnologías de la Información y la Comunicación (TIC) que pueden emplearse para ayudar a promover el autocuidado y la adherencia a los medicamentos en pacientes con enfermedades crónicas.
Objetivo: El objetivo de este trabajo fue realizar una revisión de revisiones sistemáticas («meta-revisión») sobre estudios de eficacia de intervenciones de e-Salud para promover la adherencia al Tratamiento Antirretroviral (TAR) en personas que viven con VIH/SIDA.
Método: Se realizó una revisión de revisiones sistemáticas («meta-revisión») empleando la base datos Medline-PubMed sobre estudios de eficacia de componentes de e-Salud para promover la adherencia al TAR, en pacientes con VIH/SIDA planteando una estrategia de búsqueda estructurada (pregunta PICO). Se realizó un proceso de

DOI of original article: https://doi.org/10.1016/j.farma.2024.02.005.
* Corresponding author.
E-mail address: cddeleon@conahcyt.mx (C. Díaz de León Castañeda).

https://doi.org/10.1016/j.farma.2024.04.015

selección de las revisiones sistemáticas basado en criterios de inclusión y exclusión. Asimismo, se identificaron los estudios basados en el diseño de Ensayo Controlado Aleatorizado (ECA) que incluyeran comparaciones de intervención e-Salud vs grupo control. Se realizó la extracción de los datos de los estudios y se llevó a cabo el análisis en tablas descriptivas.

Resultados: Se identificaron un total de 29 revisiones sistemáticas de las cuales se seleccionaron 11, mismas que incluyeron 55 ECAs con diferentes intervenciones de e-Salud y que enrolaron un total de 15.311 pacientes con VIH/SIDA. Estos estudios incluyeron un total de 66 comparaciones (grupo experimental vs grupo control) en mediciones indirectas de adherencia basadas en diferentes técnicas de medición (36 estadísticamente significativas); 21 comparaciones en mediciones de carga viral (CV) (10 estadísticamente significativas); y 8 comparaciones en mediciones de conteo de células $CD4^+$ (3 estadísticamente significativas). La m-Salud fue el componente más estudiado seguido de la llamada telefónica y el e-Learning.

Conclusiones: Se encontró evidencia que sustenta que algunas intervenciones de e-Salud son eficaces para promover la adherencia al TAR y mejorar los resultados en salud en pacientes con VIH/SIDA, aunque se identifica que son necesarios más estudios para una evidencia más robusta.

Introduction

Appropriate treatment of disease is heavily reliant on patient self-care as well as on their adherence to the therapies prescribed by physicians and other healthcare providers. Therapeutic adherence has been defined as the extent to which a patient's behavior with regard to taking medication (times, doses, and frequency) and to executing lifestyle changes corresponds with the recommendations from a healthcare professional.[1]

In the specific case of patients living with the human immunodeficiency virus (HIV), the role played by adherence to antiretroviral treatment (ART) cannot be overstated, as adherence levels in excess of 95% are required to prevent the disease from progressing to an acquired immunodeficiency syndrome (AIDS). A metanalysis performed in Latin America found mean ART adherence rates of 70% among patients with HIV/AIDS (63–76, 95% CI). In the specific case of Mexico, the following ART adherence rates were obtained for different time periods from initiation of treatment: 87% at 3–4 days ($CI_{95\%}$: 0.85–0.88 %); 95% at 7 days ($CI_{95\%}$: 0.92–0.96 %); 66% ($CI_{95\%}$: 0.53–0.77 %) at 30 days, and 46% ($CI_{95\%}$: 0.36–0.56 %) at 90 days.[2]

In the face of this problem, information and communication technologies (ICTs) could constitute useful tools for the development of strategies aimed at promoting patients' participation in their own care, which would ultimately result in increased therapeutic adherence. Application of these technologies to healthcare is known as “digital health” or “e-health”.[3] These concepts encompass various components that require the development and use of ICTs both on the supply side (the offering of the healthcare services by healthcare providers) and on the demand side (the use of such services by patients and by the population at large).

The building blocks of digital health (or e-health) include electronic medical records (EMRs), personal health records (PHRs), e-learning, m-health, telehealth, and the internet of things (IoT), among others.[4] M-health employs mobile devices to promote health and self-care, while e-learning uses web-based digital or electronic resources to share educational contents. Telehealth for its part, which includes telemedicine, telenursing, and telepharmacy, provides healthcare remotely when traditional in-person services are inaccessible.[5]

Although several countries in Latin America such as Mexico have made significant progress in the development and introduction of ICTs to their public health systems, they still have a long way to go.[6] Moreover, given that these technologies are in continuous evolution, it is essential to keep abreast of the latest evidence on efficacy, effectiveness, and efficiency to promote their implementation. This article presents a meta-review of the literature, intended to analyze the efficacy of digital health (e-health) interventions with a view to promoting adherence to ART among persons living with HIV/AIDS.

Methods

A review was conducted of a collection of systematic reviews of studies on the efficacy of interventions based on one or more digital health (e-health) components aimed at promoting adherence to ART. Such a review of reviews is also known as a “metareview” or an “umbrella review”.[7,8] The different components of the PICO strategy were identified as follows: (1) patients/population: persons living with HIV/AIDS; (2) intervention: digital health (e-health) strategies; (3) comparator: standard treatment; (4) outcome: adherence to ART. The research question was the following: *Is the use of interventions based on one or more of the components of digital health effective for promoting adherence to ART among persons living with HIV/AIDS?* To answer the question, a search was performed in PubMed-Medline using the following terms: (eHealth OR digital health) AND adherence AND (HIV OR AIDS). The filter available on PubMed was used to restrict the search to systematic reviews. No time restrictions were set so that all the existing systematic reviews would be captured.

The systematic reviews obtained were reviewed by 2 members of the team, who applied a series of inclusion and exclusion criteria to the abstract of each study. To be included, systematic reviews were required to: (1) have enrolled participants with an HIV infection; (2) have evaluated the performance of one or several digital health (e-health) components (e.g., telemedicine, m-health, PHRs, etc.); (3) have determined adherence to ART through direct or indirect methods; (4) have used ART without additional digital health interventions as a comparator; and (5) have been designed as randomized controlled studies (RCTs). Narrative reviews, those that failed to include RCTs and those published in languages other than Spanish or English were excluded from the analysis. The selected studies were obtained as full texts and subsequently reviewed for quality based on their compliance with the relevant standards or guidelines.[9,10] This review was carried out using the ARMSTAR-II evaluation tool.[11] A flow diagram was generated to illustrate the identification, screening, selection, and inclusion of the analyzed systematic reviews.

The selected systematic reviews examined the design of the studies used to analyze the population living with HIV/AIDS. The RCTs included in these reviews were analyzed by extracting data such as the number of subjects enrolled, the e-health interventions performed, the techniques and instruments used to measure adherence to ART,[12,13] and the comparisons between the levels of adherence obtained (e-health intervention vs. control group) as well as their statistical significance. Finally, a fairly comprehensive quantitative synthesis was drawn up of the various adherence comparisons conducted, specifying which e-health interventions resulted in higher levels of adherence and in which cases the differences were statistically significant.

Determinations of adherence to ART were classified as direct (direct measurement of the plasma levels of the drug or its metabolites) or indirect. Indirect determinations were subclassified into: (1) comparisons between adherence determinations obtained using various techniques: patient self-reports, use of electronic devices, pill counting, discontinuation of treatment, dispensing records, and pharmacy refills; and (2) measurements based on specific clinical biomarkers in persons living with HIV/AIDS: viral load (VL) and CD4+ T-cell count.

Results

Flow diagram

Fig. 1 shows a flow diagram for the search and systematic review selection process. A total of 29 systematic reviews were identified of which 18 were excluded and 11 included.

Evaluation of the quality of the selected systematic reviews

Table 1 presents an evaluation of the quality of the selected systematic reviews. Only 2 reviews contained a quantitative synthesis or a meta-analysis of the impact of e-health interventions on the adherence to ART among persons living with HIV/AIDS. Of particular interest is the low compliance observed with some of the domain items of the ARMSTAR-2 tool, such as recording the protocol for the review (item 2: 3/11); providing a list of excluded studies (item 7: 2/11); reporting the sources of funding of the selected studies (item 10: 1/11); and discussing the heterogeneity observed in the outcomes (item 14: 1/11).

Characteristics of the selected systematic reviews

Some of the reviews included studies on chronic conditions other than HIV/AIDS, mainly non-transmissible chronic diseases. The details of the selected studies including persons living with HIV in the selected systematic reviews are described more fully in Table 2. The studies included in the reviews looked into various e-health interventions such as m-health, e-learning, phone calls, telehealth, and PHRs, as well as some combinations of interventions including m-health + e-learning and m-health + phone calls.

Analysis of the randomized controlled trials included in the selected reviews

Table 3 shows the RCTs included in the selected systematic reviews of persons living with HIV as well as the number of patients enrolled, per type of e-health intervention. A total of 55 RCTs were examined, which enrolled 15, 311 patients.

As also shown in Table 3, the RCTs included in the selected systematic reviews compared 2 different kinds of indirect determinations of adherence to ART: (1) comparisons between different techniques used

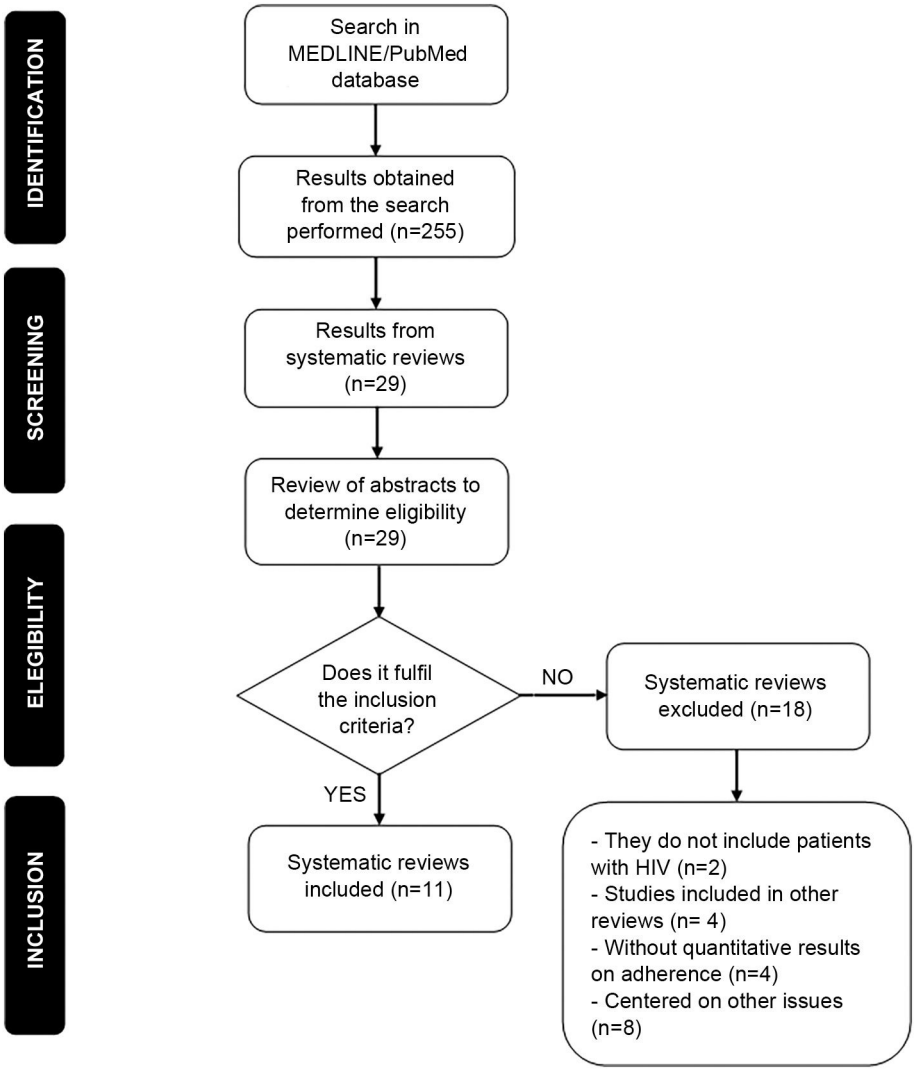

Fig. 1. Flow diagram of the search and systematic review selection process.

Table 1
Evaluation of the quality of the selected systematic reviews.

Systematic review	AMSTAR II items[a,b]																
	1	2[d]	3	4[d]	5	6	7[d]	8	9i[d]	9ii	10	11i[d]	11ii*	12	13[d]	14	15[d]	16
Claborn et al., 2015[14]	1	0	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Van Velthoven et al., 2012[15]	1	0	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Van Velthoven et al., 2013[16]	1	0	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Daher et al., 2017[17]	1	0	1	1	1	1	0	1	1	NA	0	1	NA	0	1	0	0	1
Quintana et al., 2018[18]	1	1	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Purnomo et al., 2018[19]	1	0	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Wang et al., 2019[20]	1	0	1	1	1	1	1	1	1	NA	0	1	NA	0	1	0	1	1
Andrikopoulou et al., 2019[21]	1	1	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Diedrich et al., 2020[22]	1	0	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Demena et al., 2020[23]	1	0	1	1	1	1	0	1	1	NA	0	NM	NA	NM	1	0	NM	1
Gonçalves-Bradley et al., 2020[24]	1	1	1	1	1	1	1	1	1	NA	1	NM	NA	NM	1	1	NM	1
Total[c]	11/11	3/11	11/11	11/11	11/11	11/11	2/11	11/11	11/11	–	1/11	2/2	–	0/2	11/11	1/11	1/2	11/11

[a] Items of the AMSTAR II instrument: 1 = Did the research question and inclusion criteria include the components of PICO (participants, intervention, comparator, outcomes)?; 2 = Did the review follow a pre-established protocol?; 3 = Was there an explanation of the method used to select certain study designs rather than others?; 4 = Was a comprehensive literature review strategy employed?; 5 = Was the study selection performed in duplicate?; 6 = Was the extraction of data performed in duplicate?; 7 = Was a list of excluded studies provided and were exclusions justified?; 8 = Was a detailed description of the studies included provided?; 9i = Was a satisfactory technique used to evaluate the risk of bias of the RCTs?; 9ii = Was a satisfactory technique used to evaluate the risk of bias of non-randomized interventional studies (NRISs)?; 10 = Were the sources of funding of the studies included specified?; 11i = If metanalyses were reported, was an appropriate method used for the statistical combination of RCT results?; 11ii = If metanalyses were reported, was an appropriate method used for the statistical combination of NRIS results?; 12 = Was an evaluation carried out of the impact of a potential risk of bias on the metanalysis; 13 = Did the discussion section consider the impact of the risk of bias on the results obtained; 14 = Was there justification or a discussion of any observed heterogeneity?; 15 = Was an evaluation performed of the potential for a publication bias?; 16 = Were there any conflicts of interest stated?

[b] Item scores: no = 0; yes partially = 0.5; yes = 1; NA = not applicable; NM = no metanalysis.

[c] The total value was calculated for each item.

[d] Domains considered critical.

to determine adherence: patient self-reports, electronic devices, pill counting, treatment discontinuation, dispensing records, and pharmacy refills; and (2) comparisons based on specific clinical biomarkers in persons living with HIV/AIDS: VL and CD4 + T-cell counts. A total of 66 comparisons of indirect determinations of adherence were included (36 of them statistically significant); 21 comparisons of VL measurements (10 of them statistically significant); and 8 comparisons of CD4 + T-cell counts (3 of them statistically significant).

Fig. 2 shows a graphical representation of the various comparisons (made with indirect techniques and with clinical biomarkers) between the different kinds of e-health interventions in terms of the degree of adherence to ART obtained by each of them, as reported by the selected RCTs. The figure shows the number of comparisons reported as statistically significant. M-health was found to be the intervention with the highest number of comparisons between outcome measurements, followed by phone calls and e-learning.

Table 4 contains a description of the different adherence determination techniques used in the comparisons between the different groups. Of a total of 95 comparisons, 29 (30.5%) used techniques based on clinical biomarkers and 66 (69.5%) used other indirect techniques, among them 40 (42.1%) employed self-reporting techniques, 5 (5.3%) used manual pill counting, 13 (13.7%) electronic pill counting, 4 (4.2%) pharmacy refills and dispensing records, and 4 (4.2%) resorted to other techniques.

The patient self-report-based instruments used in the selected studies included generic surveys such as SMAQ (*Simplified Medication Adherence Questionnaire*),[25] which is derived from the Morisky Green-Levine test and comprises 6 dichotomous questions aimed at evaluating whether respondents have the right attitudes with regard to their treatment. Other generic instruments such as the visual analog scale, and more specific ones such as the AACTG questionnaire (*Adult AIDS Clinical Trials Group*)[26] were also used. The latter asks questions about the number of tablets/capsules missed in the previous 4 days and includes 3 consecutive items about patients' compliance with dosing intervals and special instructions, and about the time elapsed since the last dose of the antiretroviral. Another specific instrument cited is the CEAT-VIH (questionnaire to evaluate adherence to HIV therapy),[27] validated to evaluate adherence to ART through 6 different outcomes: compliance, lack of adherence history, doctor–patient communication, beliefs and expectations about the treatment, satisfaction with the treatment, and an "overall adherence index." Finally, use of the CPCRA (*Programs for Clinical Research instrument*),[28] which evaluates 7-day adherence and includes a list with the reasons for potential drug-related problems, was also reported.

Discussion

The present analysis was aimed at providing an overall picture of the available evidence on the efficacy of e-health interventions for promoting adherence to ART in persons living with HIV/AIDS. The methodology used consisted in performing a review of the published systematic reviews on the subject. The same approach had been used previously in this field of inquiry by Soriano et al.,[29] who evaluated the effectiveness of m-health interventions for addressing chronic conditions, including HIV infection. These authors found that the said interventions had a positive impact on the improvement of adherence to ART, with reductions even in VL levels. Similarly, Hall et al.[30] found m-health interventions (text messaging) to be effective in the context of conditions such as HIV as they tend to result in improved adherence to drug therapy. Against that background, this study may be considered an update to the current wisdom in the field not only of m-health but also of other e-health interventions. We herein propose a quantitative analytical strategy, which looks into the results reported by the studies examined in the various systematic reviews, aimed at determining whether they were statistically significant. Special emphasis is laid on the evidence resulting from RCTs as they constitute the gold-standard for generating therapeutic evidence.

Most of the RCTs included in the selected systematic reviews reported a wide range of e-health interventions, representing various applications of the ICTs geared toward promoting adherence to ART. All the systematic reviews included indirect adherence determination techniques (patient self-reported questionnaires and questionnaires based on clinical interviews) as well as determinations based on clinical biomarkers (VL and CD4 + T-cell counts). As regards direct adherence determination techniques, which include determination of the plasma concentration of a drug or its metabolites,[12] their use was not reported in the studies included in the selected reviews, possibly because of the objective, often very costly, nature of these techniques. Five of the systematic reviews analyzed interventions where one single e-health component was applied, whereas 6 included interventions where more than

Table 2
Characteristics of the randomized controlled studies included in the selected reviews.

Selected systematic review	Design of the studies performed on persons living with HIV	E-health interventions in persons living with HIV evaluated in RCTs	Persons living with HIV enrolled in the selected RCTs	Authors' conclusions
Claborn et al., 2015[14]	- RCTs: 2[a] - pilot RCTs: 3[a] - Feasibility studies: 3 - Single-arm studies: 1 - Protocols: 1	e-learning (3 RCTs)	935	The review shows limited evidence given the small number of studies included. Further research is required to show the impact of e-health interventions
Van Velthoven et al., 2012[15]	RCTs: 3[a]	Telephone calls (3 RCTs)	505	Evidence on the effectiveness of phone calls as an e-health intervention was limited
Van Velthoven et al., 2013[16]	- RCTs: 2[a] - pilot RCTs: 3[a] - Feasibility studies: 3 - Single-arm studies: 1 - Protocols: 1	m-health (4 RCTs)	550	Although m-health interventions (relying mainly on landline and mobile phones) showed benefits in terms of adherence to ART and other health outcomes, the evidence was considered limited given the small number of studies.
Daher et al., 2017[17]	- RTCs: 26[a] - Non-controlled trials: 9 - Quasi-experimental studies: 5 - Retrospective quasi-experimental studies: 2 - Feasibility studies: 5 - Cross-sectional studies: 1	m-health (14 RCTs) Phone call (3 RCTs) m-health + phone call (5 RCTs) e-learning (2 RCTs) m-health + e-learning (1 RCT)	2.060	Interventions showed a trend toward the use of a combination of strategies, as well as a positive impact and feasible results. However, the need to carry out large-scale studies with impact and profitability measures is mentioned.
Quintana et al., 2018[18]	- RCTs: 18[a] - CRTs: 1[a] - Prospective cohort studies: 3 - Retrospective cohort studies: 1 - Ambidirectional cohort studies: 2 - Quasi-experimental cohort studies: 1	m-health (19 RCTs)	1.781	The review revealed the need for larger-scale studies capable of demonstrating m-health's impact on the improvement of adherence in persons living with HIV.
Purnomo et al., 2018[19]	- RCTs: 6[a] - Quasi randomized RCT: 1 - Cohort studies: 1 - Cross-sectional studies: 1	m-health (4 RCTs) Phone call (2 RCTs) m-health + phone call (1 RCT) e-learning (1 RCT)	508	Evidence is provided on the use of e-health interventions in promoting adherence in persons living with HIV, particularly in vulnerable populations.
Wang et al., 2019[20]	RCTs: 19[a]	m-health (12 RCTs) Phone call (4 RCTs) m-health + phone call (1 RCT) e-learning (2 RCTs)	2.305	E-health interventions are effective in increasing adherence to ART in persons living with HIV, as well as in improving their biochemical outcomes.
Andrikopoulou et al., 2019[21]	- RCTs: 2[a] - Qualitative studies: 1	PHR (2 RCTs)	57	PHRs may improve adherence to ART. However, evidence is still scarce.
Diedrich et al., 2020[22]	RCTs: 1[a]	Telehealth (1 RCT)	83	Telehealth can improve health outcomes. However, further research is required.
Demena et al., 2020[23]	- RCTs: 17[a] - Pilot RCTs: 2[a] - CRTs: 2[a] - Cohort studies: 2 - Cross-sectional studies: 1 - Quasi-experimental studies: 2 - Quasi-experimental cohort studies: 1	m-health (17 RCTs) Phone call (2 RCTs) m-health + phone call (2 RCTs)	5.557	The evidence shows variable results with regard to the effectiveness of m-health in the context of adherence to and persistence with ART. The authors therefore recommend following up interventions over longer periods and on larger cohorts of patients.
Gonçalves-Bradley et al., 2020[24]	CRT: 1	m-health (1 CRT)	970	Only one study was included that evaluated adherence to ART. M-health interventions showed no statistically significant improvement in terms of adherence or viral load reductions.

CRT: cluster randomized trial; RCT: randomized controlled trial; PHR: personal health record; ART: antiretroviral therapy; HIV: human immunodeficiency virus.
[a] The data from interventions, studies, and enrolled patients reported is exclusively the one addressing the PICO questions of interest (HIV population, digital health interventions [e-health], and direct or indirect adherence determination techniques as outcome measures).

Table 3
Randomized controlled trials included, persons living with HIV/AIDS enrolled, and comparisons between different types of e-health intervention with regard to adherence to antiretroviral treatment.

E-health intervention	Selected RCTs	Number of subjects with HIV enrolled in the RCTs	Comparisons based on indirect determinations of adherence to ART[a]	Comparisons based on VL measurements[a]	Comparisons based on CD4 + T-cell counts +[a]
m-health	28	10.891	38 (19)	9 (4)	5 (2)
e-learning	7	1,437	7 (6)	4 (1)	0 (0)
Phone call	12	2,121	12 (6)	4 (3)	1 (0)
m-health + e-learning	1	124	3 (1)	0 (0)	0 (0)
m-health + phone call	4	598	2 (2)	2 (1)	1 (1)
Telehealth	1	83	1 (0)	1 (0)	1 (0)
PHRs	2	57	3 (2)	1 (1)	0 (0)
N	55	15,311	66 (36)	21 (10)	8 (3)

VL: viral load; RCT: randomized controlled trial; PHR: personal health record; ART: antiretroviral therapy.
[a] The results shown between brackets correspond to the statistically significant comparisons between adherence determination techniques.

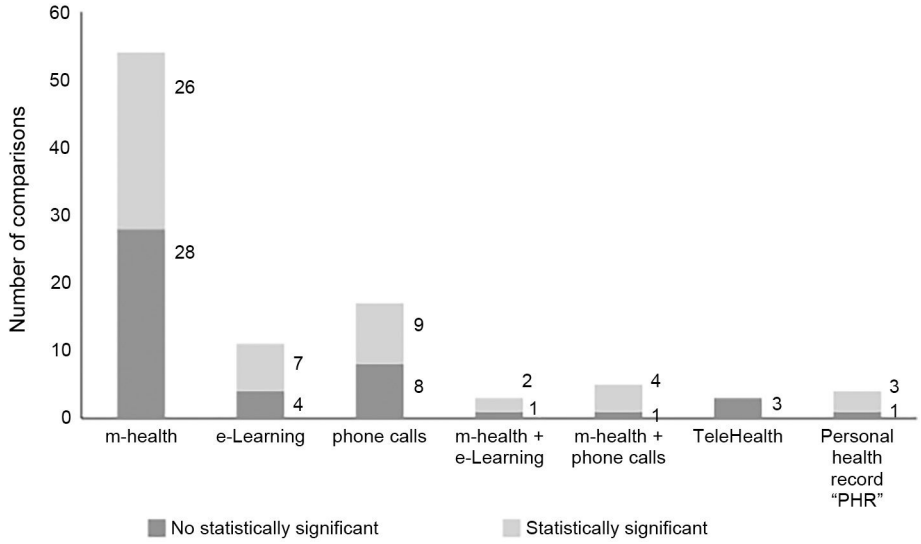

Fig. 2. Total number of comparisons between the various types of e-health intervention in terms of the degrees of adherence to antiretroviral treatment achieved by each of them.

one component was applied, or where several components were combined.

M-health interventions were the ones most commonly reported (7 out of the 11 systematic reviews), both individually and in combination with other strategies such as phone calls and e-learning. Phone calls were the strategy with the highest number of studies published. Although they could be considered an m-health strategy (they can be implemented from a mobile phone), they were considered a separate strategy for this analysis.

E-learning strategies, which were addressed mainly to patients in an attempt to promote self-care and therapeutic adherence, were discussed in 4 reviews. Studies typically employed web-based digital resources to create virtual educational programs. The e-learning tools reported were either synchronous, where participants could ask questions or make comments in real time, or asynchronous, where participants could access educational contents at their own pace.

Other interventions, such as PHRs and telehealth strategies, were also examined in some of the studies, although they were mentioned in only one of the 11 reviews. Telehealth strategies included video consultations where patients were cared for remotely in situations where in-person consultations were unfeasible, as well as health outcomes related to quality of life (patient-reported outcomes). As far as PHRs are concerned, they were used as a platform allowing patients to access their health data as well as as educational resources. Given that these interventions were reported only in a small number of studies, it will be necessary to perform further analyses to generate evidence on their efficacy and effectiveness in promoting adherence to ART and better health outcomes in persons living with HIV/AIDS.

It should also be noted that some of the systematic reviews selected included a quantitative synthesis (metanalysis) of the evidence available on the effectiveness of e-health for promoting adherence to ART. For example, Daher et al.,[17] reported a 69% increase in adherence to ART following m-health interventions conducted both in isolation of in combination with other e-health strategies. Wang et al.,[20] for their part, also identified statistically significant improvements in terms of VL and CD4 + T-cell count.

The present meta-review found that some e-heath interventions, such as m-health, are supported by a significant amount of evidence as they have been the subject of a large number of studies and/or systematic reviews. There is, however, a need to perform more systematic reviews, or update existing ones, for certain e-health strategies such as e-learning, where the last review was carried out in 2015,[14] or telehealth, where our analysis identified only one systematic review.[22] It is, however, true that phone calls could also be included under the telehealth category. Another interesting area is that of PHRs, which allows patients to access their own health records.

One of the main strengths of this analysis is the comprehensiveness of the meta-review carried out, which included interventions based on different areas of e-health. Another positive aspect is the fact that data were extracted from each and every one of the studies in the selected systematic reviews. This allowed performance of a fairly comprehensive quantitative analysis. On the other hand, the main weakness of the study lies in the fact that the search was made in one single database (Medline/PubMed).

In short, evidence was found showing that certain e-health interventions may prove effective in promoting adherence to ART and achieving better health outcomes in persons living with HIV/AIDS. More research is nevertheless needed to generate more robust evidence.

Table 4
Adherence determination techniques used in the randomized controlled trials analyzed.

Comparisons of various adherence determination methods n (%) 95 (100)	
Indirect techniques 66 (69.5)	Techniques based on clinical biomarkers 29 (30.5)
Patient self-reports 40 (42.1)	Decrease of VL 21 (22.1)
Manual pill counting 5 (5.3)	Increased CD4 + T-cell counts 8 (8.4)
Electronic pill counting 13 (13.7)	
Pharmacy refills and dispensing records 4 (4.2)	
Other 4 (4.2)	

VL: Viral load.

Funding

No funding.

Presentation at congresses and conferences

54th National and 9th International Congress of Pharmaceutical Science, organized (virtually) by the Asociacion Farmaceutica Mexicana (Mexican Pharmaceutical Association), from 18 to 22 October 2021.

CRediT authorship contribution statement

Griselda Areli Ramírez López: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Diana Lizbeth Gómez Galicia:** Supervision. **Tania Ximena Zagal Jiménez:** Supervision. **Cairo David Toledano Jaimes:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Christian Díaz de León Castañeda:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors have declared no conflict of interest.

References

1. Aremu TO, Oluwole OE, Adeyinka KO, Schommer JC. Medication adherence and compliance: recipe for improving patient outcomes. Pharmacy. 2022;10(5):106.
2. Mattos Costa J, Silva Torres T, Esteves Coelho L, Mendes Luz P. Adherence to antiretroviral therapy for HIV/AIDS in Latin America and the Caribbean: systematic review and meta-analysis. J Int AIDS Soc. 2018;21(1), e25066. doi: 10.1002/jia2.25066.
3. Renzi E, Baccolini V, Migliara G, De Vito C, Gasperini G, Cianciulli A, et al. The impact of eHealth interventions on the improvement of self-care in chronic patients: an overview of systematic reviews. Life. 2022;12(8):1253.
4. Díaz de León-Castañeda C. Salud electrónica (e-Salud): Un marco conceptual de implementación en servicios de salud. Gac Med Mex. 2019;155(2):176–83.
5. Viegas R, Dineen-Griffin S, Åke Söderlund L, Acosta-Gómez J, Guiu JM. Telefarmacia y atención farmacéutica: Una revisión narrativa de la Federación Internacional Farmacéutica. Farm Hosp. 2022;46(Supl 1):86–91.
6. Díaz de León-Castañeda C. Las TIC en el sector público del Sistema de Salud de México: Avances y oportunidades. Acta Univ. 2020;30.
7. Aromataris EFR, Godfrey C, Holly C, Khalil H, Tungpunkom P. Umbrella reviews. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. JBI; 2020;Chapter 10.
8. Cant R, Ryan C, Kelly MA. A nine-step pathway to conduct an umbrella review of literature. Nurse Author Editor. 2022;32(2):31–4.
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
10. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane Handbook for Systematic Reviews of Interventions. 2nd ed. John Wiley & Sons; 2019.
11. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.
12. Pagès-Puigdemont N, Valverde-Merino MI. Métodos para medir la adherencia terapéutica. Ars Pharm. 2018;59(3):163–72.
13. Shah KK, Touchette DR, Marrs JC. Research and scholarly methods: measuring medication adherence. J Am Coll Clin Pharm. 2023;6(4):416–26.
14. Knobel H, Alonso J, Casado JL, Collazos J, González J, Ruiz I, et al. Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study. AIDS. 2002;16(4):605–13.
15. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). AIDS Care. 2000;12(3):255–66.
16. Remor E. Valoración de la adhesión al tratamiento antirretroviral en pacientes VIH+. Psicothema. 2002;14(2):262–7.
17. Mannheimer S, Friedland G, Matts J, Child C, Chesney M. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. Clin Infect Dis. 2002;34(8):1115–21.
18. Soriano M, Queiroz JA, D'Agostino M, Ribeiro AL, Moreira MB, Novillo D, et al. The impact of mHealth interventions: systematic review of systematic reviews. JMIR mHealth uHealth. 2018;6(1)#,44]:,e23.
19. Hall AK, Cole-Lewis H, Bernhardt JM. Mobile text messaging for health: a systematic review of reviews. Annu Rev Public Health. 2015;36:393–415.
20. Daher J, Vijh R, Linthwaite B, Dave S, Kim J, Dheda K, et al. Do digital innovations for HIV and sexually transmitted infections work? Results from a systematic review (1996–2017). BMJ Open. 2017;7(11):1–11.
21. Wang Z, Zhu Y, Cui L, Qu B. Electronic health interventions to improve adherence to antiretroviral therapy in people living with HIV: systematic review and meta-analysis. JMIR Mhealth Uhealth. 2019;7(10):e14404.
22. Claborn KR, Fernandez A, Wray T, Ramsey S. Computer-based HIV adherence promotion interventions: a systematic review. Transl Behav Med. 2015;5(3):294–306.
23. Diedrich L, Dockweiler C. Video-based teleconsultations in pharmaceutical care – a systematic review. Res Social Adm Pharm. 2021;17(9):1523–31.
24. van Velthoven MHMMT, Tudor Car L, Car J, Atun R. Telephone consultation for improving health of people living with or at risk of HIV: a systematic review. PLoS One. 2012;7(5):1–11.
25. van Velthoven MHMMT, Brusamento S, Majeed A, Car J. Scope and effectiveness of mobile phone messaging for HIV/AIDS care: a systematic review. Psychol Health Med. 2013;18(2):182–202.
26. Quintana Y, Gonzalez Martorell EA, Fahy D, Safran C. A systematic review on promoting adherence to antiretroviral therapy in HIV-infected patients using mobile phone technology. Appl Clin Inform. 2018;9(2):450–66.
27. Purnomo J, Coote K, Mao L, Fan L, Gold J, Ahmad R, et al. Using eHealth to engage and retain priority populations in the HIV treatment and care cascade in the Asia-Pacific region: a systematic review of literature. BMC Infect Dis. 2018;18:82.
28. Andrikopoulou E, Scott P, Herrera H, Good A. What are the important design features of personal health records to improve medication adherence for patients with long-term conditions? A systematic literature review. BMJ Open. 2019;9(9):e028628.
29. Demena BA, Artavia-Mora L, Ouedraogo D, Thiombiano BA, Wagner N. A systematic review of mobile phone interventions (SMS/IVR/Calls) to improve adherence and retention to antiretroviral treatment in low-and middle-income countries. AIDS Patient Care STDS. 2020;34(2):59–71.
30. Gonçalves-Bradley DC, Maria ARJ, Ricci-Cabello I, Villanueva G, Fønhus MS, Glenton C, et al. Mobile technologies to support healthcare provider to healthcare provider communication and management of care. Cochrane Database Syst Rev. 2020;2020(8), CD012927.