Effect of social support interventions on adherence to antiretroviral therapy among people living with HIV: A systematic review and meta-analysis

Shushtari, Zahra Jorjoran; Salimi, Yahya; Sajjadi, Homeira; Paykani, Toktam

AIDS and Behavior

SUBSTANTIVE REVIEW

Effect of Social Support Interventions on Adherence to Antiretroviral Therapy Among People Living with HIV: A Systematic Review and Meta-Analysis

Zahra Jorjoran Shushtari[1] · Yahya Salimi[2] · Homeira Sajjadi[1] · Toktam Paykani[3]

Abstract

This systematic review and meta-analysis examined the effects of social support interventions (SSIs) on adherence to antiretroviral therapy (ART) among people living with HIV. We systematically searched Web of Science, PubMed/MEDLINE, Scopus, and Cochrane Library in September 9, 2020. English-language publications of randomized controlled trials (RCTs) in peer-reviewed journals were considered eligible. To estimate the effects of SSIs on adherence to ART, odds ratios (ORs) with 95% confidence intervals (CIs) were pooled using random effects models. Subgroup analysis was used to investigate the sources of heterogeneity. Of 243 records identified, 17 controlled trials were included. The meta-analysis found significant and moderate effect size in the improvement of adherence to ART from SSIs. Subgroup analysis showed that the study design, follow up duration, source of social support, and year of publication significantly moderated the effect sizes in the meta-analysis. Our findings support the hypothesis that social support interventions can improve adherence to ART. Using various types and sources of social support, further research is needed to assess the effect of SSIs on adherence to ART across different settings.

Keywords Systematic review · HIV · Adherence · Antiretroviral therapy · Social support

Introduction

HIV (human immunodeficiency virus) the virus that can lead to AIDS (acquired immunodeficiency syndrome) continues to be a serious global health and development concern. There is no cure for HIV infection. However, with antiretroviral drugs (ARVs), HIV can be controlled [1]. Therefore, early access to antiretroviral therapy (ART), adherence to ART and support retention in care is vital to improve the health of people living with HIV (PLHIV), as well as to reduce HIV transmission risk [1, 2].

ART adherence rates of 95% or more are required to achieve virologic suppression. However, only 62% of ART patients achieve this optimal ART adherence (≥90%) [3]. Consistent ART adherence is associated with effective viral suppression, improved immune function, quality of life, near-normal life expectancy, and prevention of HIV transmission [4, 5], while poor adherence may lead to the development of resistance to ART and subsequent disease progression and higher rates of mortality [2, 6].

A variety of factors can influence adherence to ART, including complexity of therapeutic regimens [7], stigma [8, 9], treatment side effects [7, 9], knowledge and perception towards ART medications [10], medical privacy [7], relationship with the health care provider [11], and social support [12–17].

Social support is described as the availability of perceived or actual psychological and material resources provided by a social relationship, including instrumental, informational, and emotional support [18]. Social support can improve

✉ Toktam Paykani
   paykani.t@gmu.ac.ir

1 Social Determinants of Health Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

2 Social Development & Health Promotion Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

3 Social Development and Health Promotion Research Center, Gonabad University of Medical Sciences, Gonabad, Iran

coping skills, reduce negative affect, motivate health behavior change, and facilitate treatment adherence [19, 20].

In recent years, there has been an increasing amount of investigation on social support interventions (SSIs) as a facilitator to uptake of HIV testing, promote HIV antiretroviral therapy, and improve retention in care [3, 17].

Prior studies have provided mixed evidence about the association between social support and adherence to ART. Some literature suggests that SSI may increase adherence to ART [10, 12–15], others suggest null or very small effects of SSI on improving adherence [21–25].

Given the lack of clarity about the effects of SSIs on ART adherence, the aim of this study was to use the meta-analytic approach to evaluating the effectiveness of SSIs in improving adherence to ART among PLHIV. Potential moderators such as the study design, year of publication, follow up duration, source of social support, and quality score of the included studies that may affect the effectiveness of SSIs were also tested.

We hypothesized that social support interventions would increase adherence to ART among PLHIV. Examining this hypothesis could help clarify to what extent the SSIs are effective in achieving optimal ART adherence.

Methods

The present study conducted a systematic review and meta-analysis on studies evaluating the effect of SSIs on adherence to ART among PLHIV.

The study selection, assessment of eligibility criteria, data extraction and analyses were performed based on a protocol that has been registered with PROSPERO at http://www.crd.york.ac.uk/Prospero/ (Registration number: CRD42020200085). The protocol was developed in accordance with PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines [26].

Search Strategy

A systematic search was conducted in September 9, 2020, using electronic search in four databases including Web of Science, PubMed/MEDLINE, Scopus, and Cochrane Library. Google Scholar was also searched. The reference lists of relevant primary studies were checked manually to identify other potentially eligible studies.

A sensitive search strategy was used to retrieve relevant studies. Both free text terms and Medical Subject Headings (MeSH) were used to define the keywords.

The search strategy used for PubMed database was ((HIV [Mesh] OR "HIV Infections" OR "HIV Positive" OR "Acquired Immunodeficiency Syndrome" OR "HIV Seropositivity" OR AIDS OR "Human Immunodeficiency virus"[tiab]) AND ("Social Support"[Mesh] OR "Peer Support" OR "Social networking"[Mesh] [tiab]) AND ("Treatment Adherence and Compliance"[Mesh] OR "Treatment Non-adherence" OR "Therapeutic Adherence" OR " Treatment Compliance" OR Adherence OR Compliance[tiab]) AND ("Clinical Trial"[Mesh] OR "Controlled Clinical Trial"[Mesh] OR "Pragmatic Clinical Trial"[Mesh] OR "Randomized Controlled Trial" OR Inversion[tiab])).

We modified our search strategy to suit each database. EndNote (version X8) was used for data management.

Study Selection and Eligibility Criteria

Studies were included if they: (1) were randomized controlled trials (RCTs); (2) were peer-reviewed and published in English up to September 9, 2020; and (3) examined the effects of social support interventions on adherence to ART among PLHIV.

Observational studies and studies that did not provide information on the pre-specified PECOS (Population, Exposure, Comparison, Outcome, Study design) items were excluded.

Following the initial search, a three-stage selection process was used to identify relevant articles: Firstly, titles and abstracts were screened for eligibility by three independent reviewers (Z.J, T.P and H.S). Secondly, discordant results were resolved by third reviewer (Y.S). Finally, full text articles were retrieved and reviewed by the two reviewers (Z.J and T.P), where the abstracts met the inclusion criteria or abstract information was not enough to assess eligibility.

Quality Assessment of Studies

The methodological quality assessment of included studies was conducted independently by the two reviewers (Z.J and T.P) according to the modified Jadad 8-item scale [27]. Each quality item was scored as 1 (=yes), 0 (=no or not described). The overall quality score for each study was calculated by summing the scores across the eight items. Disagreement on ratings was resolved by discussion and a third reviewer (Y.S) was consulted when consensus could not be reached.

Data Extraction and Analysis

The two independent reviewers (Z.J and T.P) screened the full-texts of eligible studies and extracted the information based on a predefined format included primary author, publication year, date and duration of the study, country where the study was conducted, study population, sample size, measurement of ART adherence, quality score,
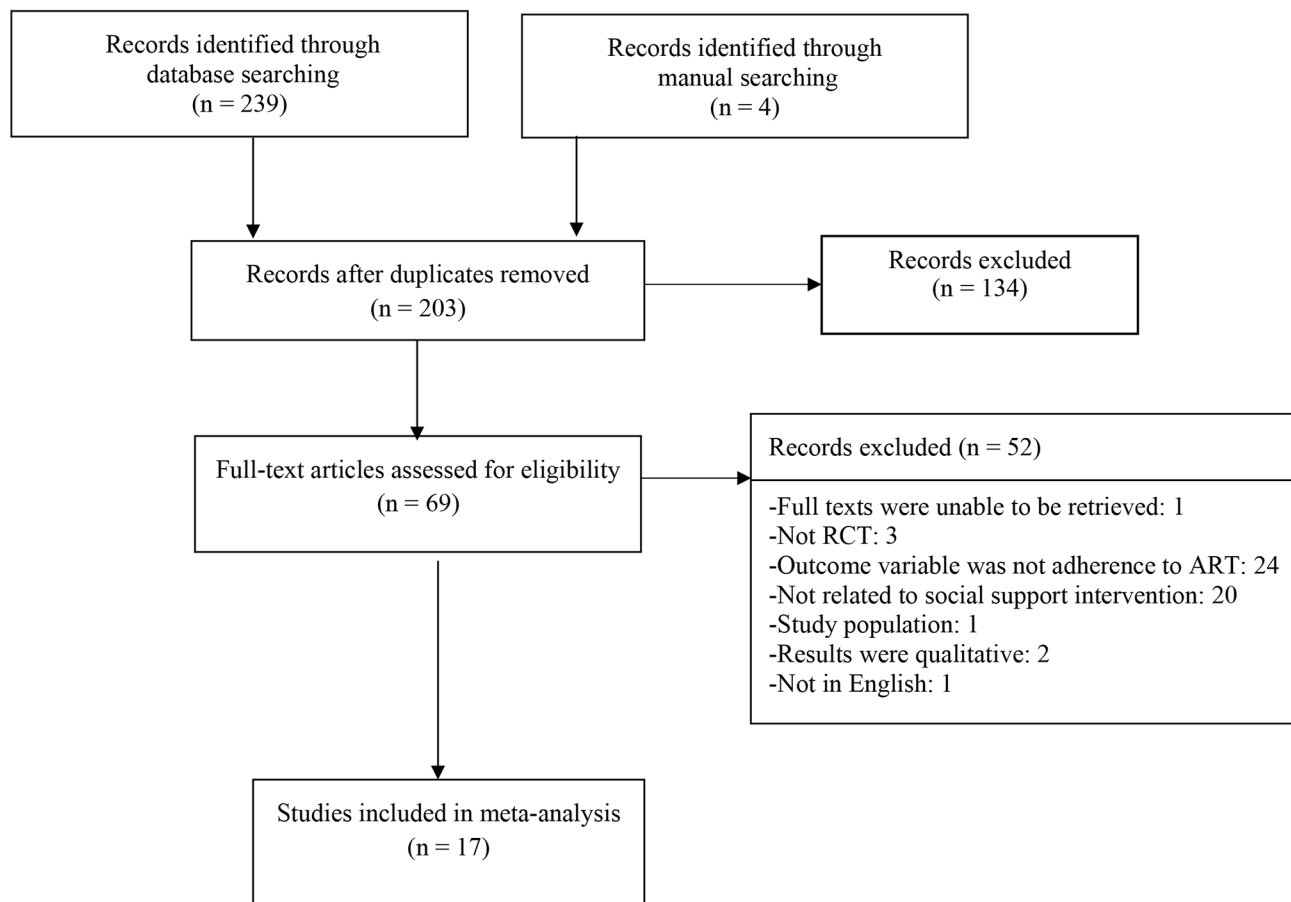
Fig. 1 Selection of studies into the review

characteristics of the social support intervention, and key findings.

When there was a disagreement between the two reviewers, consensus was achieved by judgment of a third person. In some cases, the missing data was acquired by contacting authors.

All eligible studies, regardless of quality scores, were included to the analysis. Publication bias was assessed by funnel plots, Begg's and Egger's tests. We conducted a meta-analysis with a random effects model to assess the effect of social support interventions on adherence to ART.

Statistical heterogeneity between studies was assessed using Cochran's Q test, tau^2, and I^2. Five subgroup analyses were conducted to investigate the source heterogeneity. The meta-analysis was performed using Stata V.12 software.

Results

A total of 239 articles were found from the initial electronic database search. Searching the reference lists identified another four relevant studies. After removing duplicates,

203 articles were screened. Following title and abstract review, 69 articles were identified; and 17 studies were finally included after full-text review. A PRISMA flow diagram illustrates the study selection process in Fig. 1.

Study Characteristics

The 17 included studies were published between 2005 and 2020 in eight countries (Table 1). Nine (53%) studies were done in high income countries that eight of those were conducted in the United States [12–14, 16, 22, 25, 28, 29] and one in Italy [24]. Two (12%) studies were done in Asia [30, 31] and six (35%) studies were done in Sub-Saharan Africa [7, 21, 23, 32–34]. The median sample size was 174 (IQR: 108–246).

The studies defined adherence to ART and its measures in different ways. Ten studies (59%) measured adherence using subjective measures [12, 16, 21–24, 28, 30–32], three studies (18%) used objective measures (pill counts or pharmacy records) [13, 14, 34], with the rest (23%) used both self-reported and objective measures [15, 25, 29, 33].

Table 1 Characteristics of the 17 studies included in the systematic review and meta-analysis on the effectiveness of social support interventions on adherence to antiretroviral therapy (ART) among people living with HIV

First author, year	Country	Study population	Sample size	Date and duration of the study	Measurement of ART adherence	Quality score	Main findings
Remien et al., 2005(14)	USA	Adults aged > 18 years	215	Between August 2000 and January 2004 5 weeks	**Type of measure(s)**: Objective **Adherence measure(s)**: Pill-taking, Medication Event Monitoring System (MEMS caps). **Adherence definition**: The percentage of prescribed doses taken (without regard to timing and within specified time windows). **Follow up**: At baseline, 8 week, 3 and 6-month **Level of optimal adherence:** $\geq$ 95%	8	Intervention participants had a higher mean medication adherence at post-intervention whether adherence was defined as percentage of prescribed doses taken (76% vs. 60%) or doses taken within specified time windows (58% vs. 35%). The intervention arm were significantly more likely to achieve high levels of adherence (>80%, > 90%, or >95%), when compared with controls. However, for many participants, the effect was attenuated over time.
Simoni et al., 2007(29)	USA	Adults aged $\geq$ 18 years	136	Between May 2000 and March 2002 6 months	**Type of measure(s)**: Subjective, Objective **Adherence measure(s)**: (1) Participant self-reported adherence using Adult AIDS Clinical Trials Group Adherence to Antiretroviral Instrument. (2) Electronic drug monitors (EDM)-based medication **Adherence definition**: The percentage of doses taken (according to self-report) over those prescribed (according to medical record) for the past 3 days. **Follow up**: At baseline, 4 week, 3 and 6-month **Level of optimal adherence:** $\geq$ 95%	7	Null findings; No significant differences in adherence between peer support intervention condition and standard of care condition according to self-reported and EDM at 3 and 6 months.
Koenig et al., 2008(13)	USA	Adults aged $\geq$ 18 years	226	Between 1999 and 2002 6 months	**Type of measure(s)**: Objective **Adherence Measure(s)**: Pill-taking, electronically monitored (MEMS caps) **Adherence definition**: The ratio of doses taken to doses prescribed **Follow up**: Monthly, over 6 consecutive months **Level of optimal adherence**: $\geq$ 90%	6	The intervention group were significantly more adherent than the control group (OR = 1.69; 95% CI = 1.08, 2.64), $X^2(1) = 5.35$, p = 0.021. Using a weighted average across the six time points 40.15% and 27.59% of participants were 90% adherent in the intervention and control conditions, respectively.

There was good agreement between the two reviewers concerning the methodological quality.

All included studies were judged to be at low risk of bias for random allocation. Eleven out of the 17 included studies had high methodological quality. Of these, six studies reported adequate concealment of allocation [14, 15, 22, 23, 25, 30]. Only one study was not at risk of loss to follow up [24]. All included studies were judged to have appropriate

statistical method. The overall quality score for each study are presented in Table 1.

A summary of the SSIs are reported in Table 2. Interventions varied by source of support, type of support, and methods used to assess social support. Of the 17 included studies, seven (41%) used a peers/friends SSI [15, 22, 25, 28, 29, 32, 34], two (12%) used family/caregivers [14, 24], one (6%) used HIV-experienced clinicians SSI [12], and

Table 1 (continued)

First author, year	Country	Study population	Sample size	Date and duration of the study	Measurement of ART adherence	Quality score	Main findings
Simoni et al., 2009(25)	USA	Adults aged ≥ 18 years	224	Between March 2003 and May 2005 9 months	**Type of measure(s)**: Subjective, Objective **Adherence measure(s)**: (1) Participant self-reported (Adult AIDS Clinical Trials Group Adherence to Antiretroviral Instrument) (2) EDM-based medication **Adherence definition**: (1) Self-reported measure: the number of doses missed during the previous week. The four-point response scale was dichotomized: "*none of the time*" was recoded as perfectly adherent and "*1–2 times*, *3–5 times*, or *6–10 times*" were recoded as non-adherent. (2) EDM-Based measure: the number of bottle openings recorded by the MEMS cap during the 7 days before each assessment date divided by the number of prescribed doses. **Follow up**: At baseline, 3, 6, and 9-month. **Level of optimal adherence**: Self-reported adherence: 100% EDM: 80, 85, 90, 95, and 100%	8	Results indicated the potential efficacy of peer support (OR = 2.10, 95% CI = 1.10, 4.01) but not pager messaging in increasing short-term ART adherence. Strategies for maintaining optimal adherence over time are needed.
Johnson et al., 2011(12)	USA	Adults aged ≥ 18 years	249	Between February 2005 and March 2007 15 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: Two self-report measures; (1) Adult AIDS Clinical Trials Group Adherence to Antiretroviral Instrument (2) The visual analog scale **Adherence definition**: (1) Mean 3-day adherence was calculated by dividing the number of pills reported as being taken by the number of pills that were prescribed in the regimen. (2) The visual analog scale of 0-100 assessed 30-day adherence separately for each drug. **Follow up**: At baseline, 3, 6, 9, and 15-months **Level of optimal adherence**: Not reported	6	The odds of non-adherence decreased 6% per month in the intervention participants (OR = 0.94, 95% CI = 0.89, 0.99), but the odds of non-adherence remained unchanged over time in the control participants (OR = 1.03, 95% CI = 0.96, 1.10).
Kunutsor et al., 2011(33)	Uganda	Adults aged ≥ 18 years	174	Between December 2008 and June 2009 28 weeks	**Type of measure(s)**: Subjective, Objective **Adherence measure(s)**: (1) A clinic-based pill count (2) A patient self-report questionnaire **Adherence definition**: The percentage of prescribed medication doses taken during each 4-week period **Follow up**: At 4-weekly intervals **Level of optimal adherence: ≥ 95%**	5	Intervention participants had more than four times the odds of achieving optimal adherence (OR = 4.51, 95% CI = 1.22, 16.62) than control participants.

Table 1 (continued)

First author, year	Country	Study population	Sample size	Date and duration of the study	Measurement of ART adherence	Quality score	Main findings
Horvath et al., 2013(22)	USA	Gay/bisexual male aged ≥ 18 years	123	Between February and April 2011 8 weeks	**Type of measure(s)**: Subjective **Adherence measure(s)**: Three self-reported adherence measures. **Adherence definition**: (1) The percentage of time ART was correctly taken as prescribed in the past 30 days (2) The percentage of time ART was taken within two hours of the scheduled dose in the past 30 days (3) The percentage of time ART was taken correctly with food in the past 30 days **Follow up**: At baseline, post-intervention, and 1-month **Level of optimal adherence**: ≥ 90%	7	The intervention had modest effects for the overall sample. However, among current drug-using participants, the intervention group reported significantly higher overall ART adherence compared to control (90.1% vs. 57.5% at follow-up; difference = 31.1, p = 0.02).
Jones et al., 2013(23)	Zambia	Adults aged ≥ 18 years	160	Between September 2006 to June 2008 6 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: Monthly self-reported ARV use and AIDS Clinical Trials Group (ACTG) Questionnaire for Adherence to Anti-HIV Medications **Adherence definition**: Previous 4 days' medication adherence (Monthly self-reported ARV use) and missed doses over 3 months (ACTG Questionnaire for Adherence to Anti-HIV Medications) **Follow up**: At baseline, 3, 4, and 6-months **Level of optimal adherence**: Not reported	8	At 3-month follow-up, the proportion reporting consistent adherence over the past 3 months improved in the group condition (98%, McNemar's test, p = 0.02) but not in the individual condition (88%, McNemar's test, p = 1.0).
Nicastro et al., 2013(24)	Italy	Children aged ≤ 18 years	17	Not reported 8 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: Self-reported adherence measure **Adherence definition**: The number of doses of the total prescribed antiretroviral therapy missed in the previous 4 days **Follow up**: Monthly **Level of optimal adherence**: ≥ 95%	3	Adherence to ART was higher among Intervention participants 6(60%) compared with control participants 5(71%). However, the difference was not significant (p = 0.62).
Williams et al., 2014(31)	China	Adults the mean age of 37 and 38 years for the intervention group and the control group, respectively	110	Between July 2010 and August 2012 12 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: A self-reported adherence to ARV over the 30 days using a visual analog scale (VAS) **Adherence definition**: Participants placed a cross on a 10-cm horizontal line ranging from 0–100% at the point showing their best estimate of medication that had taken in the preceding 30 days. **Follow up**: At baseline, 6 and 1- month **Level of optimal adherence**: > 90%	5	Participants in the intervention group (87%) were significantly more adhered to ARV at 6 months compared with participants in the control group (56%). At 12 months, there was a slight reduction in the percentage of adhering participants in both groups.

Table 1 (continued)

First author, year	Country	Study population	Sample size	Date and duration of the study	Measurement of ART adherence	Quality score	Main findings
Chang et al., 2015(32)	Uganda	Adults, aged ≥ 18 years	442	Between June 2011 to July 2013 24 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: Engagement in care (Survey-based) **Adherence definition**: HIV clinic attendance, either self-reported or based on clinical records **Follow up**: At baseline and 12-month **Level of optimal adherence**: Not reported	6	The peer support intervention did not affect ART use. After one year, intervention participants were more likely to report engagement in care (92% vs. 84%; PRR 1.09, p = 0.039). The effect was observed only among participants who were not in care and were not taking Cotrimoxazole At baseline.
Robbins et al., 2015(15)	South Africa	Adults aged ≥ 18 years	55	Between August 2008 and April 2010 5–6 weeks	**Type of measure(s)**: Subjective, Objective **Adherence measure(s)**: (1) The standard clinic-based pill count (2) Self-reported ART adherence **Adherence definition**: (1) The standard clinic-based pill count as established by the clinic pharmacy and City Department of Health and conducted at each pharmacy ARV refill (2) A self-reported single-item on a 5-point Likert scale asking participants to rate their adherence over the past 4 weeks **Follow up**: At baseline and approximately 5–6 weeks after baseline **Level of optimal adherence**: ≥ 90%	7	In this pilot study, adherence to ART was higher among intervention participants (10%) compared to control (8%) (p = 0.17). Based on the clinic-based pill counts, the proportion of participants who achieved ≥ 80% adherence at post-intervention, was 67% among intervention participants (vs. 16% control) (p < 0.05). Self-reported adherence improved slightly in both groups, but the difference in the changes between groups was not significant.
Bouris et al., 2017(16)	USA	Black/ African American male aged 16–29 years old	106	Between 2012 and 2015 12 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: A self-reported measure of ARV adherence using a visual analog scale **Adherence definition**: Adherence for medications taken in the previous 30 days from 0–100%. **Follow up**: At baseline, 3 and 12-months post-intervention **Level of optimal adherence**: ≥ 90%	5	Intervention participants were 2.91 times more likely to report ≥ 90% ARV adherence (95% CI = 1.10, 7.71) than control participants.

Table 1 (continued)

First author, year	Country	Study population	Sample size	Date and duration of the study	Measurement of ART adherence	Quality score	Main findings
Phiri et al., 2017(34)	Malawi	Pregnant or breastfeeding women aged ≥18 years	1269	Between November 2013 and November 2014 24 months	**Type of measure(s)**: Objective **Adherence measure(s)**: Documented receipt of antiretroviral drugs **Adherence definition**: (1) Uptake: Documented receipt of antiretroviral drugs at the initial and second scheduled ART clinic visit (2) Defaulted: Failed to return within 60 days after a scheduled appointment date (adverse outcome in time-to-event analysis) (3) Stopped treatment: Documented stop of ART for more than 60 days (adverse outcome in time-to-event analysis) **Follow up**: Monthly for the first 6 months and 3 monthly thereafter **Level of optimal adherence**: ≥ 90%	6	Facility-based intervention participants (86%), (RD = 6%, 95% CI= -3%, 15%) and community-based intervention participants (90%); (RD = 9%, 95% CI = 1%, 18%) were more likely to uptake ART than control participants (81%). However, only the difference between community-based intervention and control was statistically significant.
Attonito et al., 2020(28)	USA	Alcohol use disorders aged 18–60 years	243	Between February 2009 and December 2012 About 4 years	**Type of measure(s)**: Subjective **Adherence measure(s)**: The self-reported scale of Community Programs for Clinical Research on AIDS (CPCRA). **Adherence definition**: The percentage of time ART medications were taken as prescribed over a week. Participants rated their adherence for each medication used according to the scale: "all" (100%), "most" (75%), "about half" (50%), "few" (25%), or "none" (0%) **Follow up**: At baseline, 3 and 6-month **Level of optimal adherence**: ≥ 95%	4	The intervention participants significantly reported more adherence (93%) than control participants (80.6%) at 6 months (RR = 1.55, 95% CI = 1.09, 2.18).
Nestadt et al., 2019(30)	Thailand	Children aged 9–14 years old	88	Between May 2015 to March 2016 9 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: Self-reported ART adherence **Adherence definition**: A self-reported scale asking youth and caregiver the number of day's youth missed medication in the past 30 days, when they last missed medication, and how well they took medication in the past 30 days. **Follow up**: At baseline, 6 and 9-month **Level of optimal adherence**: Not reported	8	The intervention participants were significantly more adherent (91%) than control participants (70%) at 9 months*.
Denison et al., 2020(21)	Zambia	Youth aged 15–24 years	273	Between October 2018 to February 2019 6 months	**Type of measure(s)**: Subjective **Adherence measure(s)**: Self-reported ART adherence treatment gap **Adherence definition**: Participants were asking about ART adherence treatment gap at the two time points: "In the past three months, did you have a day when you did not take any ART drugs?" and "What were the most days in a row that you missed swallowing your drugs in the past three months?" **Follow up**: At baseline and the 6-month midline **Level of optimal adherence**: Not reported	5	Intervention participants had significantly higher odds of non-adherence or treatment gap (OR = 1.74, 95% CI = 1.06, 2.86) than control participants At baseline. Having a treatment gap did not change for the control group between baseline and midline (OR = 1.05, 95% CI = 0.68, 1.61], but there was a significant relative change for the intervention participants (OR = 0.63, 95% CI = 0.35, 1.13].

* Information was obtained by direct contact with the author

seven studied (41%) used multiple sources of support [13, 16, 21, 23, 30, 31, 33].

We found less than half of the studies (35%) reported how social support was measured [15, 23, 28–31].

All interventions except one provided informational support. The type of social support was not reported in one study [31]. Seven studies (41%) used emotional support [12, 16, 24, 25, 28, 29, 33], seven studies (41%) used some sort of tangible support [12, 13, 15, 16, 28, 32, 33], and six studies (35%) used a combination of at least three types of social support [12, 16, 25, 28, 29, 33].

Five of the 17 reviewed studies (29%) referred to information motivation behavioral skills (IMB) theories and models [16, 22, 23, 28, 32], three studies (18%) used social action theory [14, 15, 30], two studies (12%) used problem-solving models [12, 13], one (6%) referred to social cognitive theory [21], one (6%) used pedagogical theory of Paolo Freire [31], and one study used social support theory [13]. Five studies (29%) did not report any theory or pathway to explain how social support may influence adherence to ART [24, 25, 29, 33, 34].

Overall Estimate and Heterogeneity of Studies

The included studies reported odds ratios (ORs) ranged from 0.14 to 9.33. The results of meta-analysis showed that social support interventions can increase adherence to ART (Overall OR = 1.66, 95% CI: 1.24, 2.22). The heterogeneity across all 17 studies was moderate (chi^2 16 = 38.34, p = 0.001; I^2 = 58.3%). The between-study variances tau^2 was 0.18.

Figure 2 shows a forest plot of individual estimates from included studies along with pooled estimate and heterogeneity measures.

Publication Bias and Tests for Funnel Plot Asymmetry

There was no evidence of publication bias using both of the Egger's and Begg's tests. However, Fig. 3 presents the funnel plot with two missing studies imputed by the trim-and-fill method.

Subgroup Analysis

To check potential sources of the observed heterogeneity, we conducted five subgroup analyses to assess the effect of study design, year of publication, follow up duration, source of social support, and quality score of the included studies. The heterogeneity in all subgroups was similar to overall estimate ranged from 35 to 70%.

The results of subgroup analyses showed a higher overall OR for studies with follow up duration of ≥ 7 months (Overall OR = 1.98, 95% CI: 1.23, 3.19) compared to ≤ 6 months (Overall OR = 1.43, 95% CI: 0.98, 2.07), a higher overall OR was also reported in the categories of parallel design, studies with multiple sources of social support, and both studies with high and low quality scores (Table 3).

Discussion

This systematic review and meta-analysis aimed to evaluate the effectiveness of social support interventions in improving adherence to ART among PLHIV.

We identified 17 RCTs, representing 4110 participants in eight countries: China, Italy, Malawi, South Africa, Thailand, Uganda, United States, and Zambia.

The results of this meta-analysis showed a significant positive effect in increasing adherence to ART with acceptable heterogeneity among included studies. These findings support our hypothesis, which posits that social support interventions can improve adherence to ART among PLHIV.

Subgroup analyses indicated some significant moderators on SSIs effectiveness, namely study design, follow up duration, source of social support, and year of publication. The results showed larger effect sizes for interventions of longer duration. Previous studies have also revealed that adherence levels decline with time and the positive effect of receiving information, emotional, and affirmation support may reduce when the support is discontinued [14, 25] .

We also found that different sources of social support may modify the effect of SSIs on ART adherence. Support from all sources, except family support alone, had a positive effect on adherence to ART. However, the positive effect was statistically significant only for interventions with multiple sources of support. This can be explained in part by the synergistic effects of different types of support served by various members of PLHIV's network [42, 43]. More research is needed to examine the effect of social support from various sources on adherence to ART.

The literature suggests a consistency in the positive effect of social support on adherence to treatment for various disease conditions [44].This consistency is also obvious in the forest plot of our meta-analysis.

These findings may be explained by two broad conceptual models linking social support to health outcome: (1) stress-related and (2) direct effect models [18, 42, 45].

The stress–related model suggests that social support can operate as a stress buffer and influence health by providing psychological and material resources required to manage stress and help individuals to engage in more adaptive

Table 2 Characteristics of the social support interventions to improve adherence to antiretroviral therapy (ART) among people living with HIV

First author, year	Social support intervention	Source of social support	Type of social support	Measurement of Social support	General or HIV specific support	Measurement of satisfaction of social support intervention	Use of theory
Remien et al., 2005(14)	**SMART couples intervention** A four-session couple-based ART adherence intervention administered to individual couples. Key components included education about ART and adherence, identifying adherence barriers, developing communication and problem-solving strategies, optimizing partner support, and building confidence in the couple for optimal adherence.	Sexual partner	Informational support (According to the details of the intervention)	Not specified	HIV specific support	No	Ewart's social action theory
Simoni et al., 2007(29)	**HAART intervention** A 3-month peer support intervention consisted of two parts: (1) "peer meetings": six twice-monthly 1-hour group meetings at the clinic (2) weekly phone calls from peers to participants	Peers	Appraisal, spiritual, emotional, and informational adherence-related social support	The modified version of the UCLA Social Support Inventory [35]	HIV specific support	Yes	Not specified
Koenig et al., 2008(13)	**Project HEART** A clinic-based intervention delivered one-on-one and through group sessions to HIV + patients and their support partners; five phone contacts were made between the intervention sessions.	Support partner(family, peers) and nurse-interventionist	Tangible and informational support	Not specified	HIV specific support	No	• Problem-Solving Model • Self-Determination Theory • Social Support Theory
Simoni et al., 2009(25)	**HAART intervention** A 3-month peer support intervention consisted of two parts: (1) "peer meetings": six twice-monthly 1-hour group meetings at the clinic (2) weekly phone calls from peers to participants.	Peers	Emotional, informational, and affirmation social support	Not specified	HIV specific support	No	Not specified
Johnson et al., 2011(12)	Five 60-min individual counseling sessions, clinicians delivered ART side effects coping skills.	HIV-experienced clinicians	Tangible, emotional and informational support	Not specified	HIV specific support	No	Social problem solving training and coping effectiveness training rooted in Stress and Coping Theory

Table 2 (continued)

First author, year	Social support intervention	Source of social support	Type of social support	Measurement of Social support	General or HIV specific support	Measurement of satisfaction of social support intervention	Use of theory
Kunutsor et al., 2011(33)	**Treatment Supporter (TS) intervention** TSs were chosen by the patient with the assistance of the health workers and were educated with WHO-IMAI educational materials. Treatment supporter meetings at the clinic every 2 or more weeks to deal with barriers to treatment and adherence.	Family members (a partner, mother, daughter, sister, brother, a relative), friend, or neighbor/friend and health workers	Emotional, informational, and financial support	Not specified	both	No	Not specified
Horvath et al., 2013(22)	**Thrive With Me (TWM)** An online peer-to-peer social support intervention. Intervention content includes: (a) video; (b) articles about HIV and medication adherence; and (c) links to other HIV-related websites and webpages.	Peers	Informational support (According to the details of the intervention)	Not specified	HIV specific support	Yes	Information, Motivation, and Behavioral Skills (IMB) model
Jones et al., 2013(23)	A series of group and individual sessions with peers and health care providers focused on HIV and medication knowledge, barriers and solutions in the use of ARVs.	Peers and facilitators	Informational support	Social Support Questionnaire (SSQ) that is an 8-item Likert scale [36]	HIV specific support	No	Information Motivation Behavioral Skills (IMB) Mode
Nicastro et al., 2013(24)	Eight monthly sessions of family group psychotherapy with parents or caregiver, a psychologist, and a social worker in a friendly context.	Parents (mother, father), or other caregiver, the medical staff and the team of psychologist	Informational and empathetic support	Not specified	HIV specific support	No	Not specified
Williams et al., 2014(31)	**Ai Sheng Nuo (Love, Life, Hope)** Home-based intervention including in person or telephone visits.	Nurses and peer educators	Not specified	The Social Support Rating Scale (SSRS) that is a questionnaire with 10-item comprising three subscales: objective social support, subjective social support, and utility of social support (31).	HIV specific support	No	Pedagogical theory of Paolo Freire

Table 2 (continued)

First author, year	Social support intervention	Source of social support	Type of social support	Measurement of Social support	General or HIV specific support	Measurement of satisfaction of social support intervention	Use of theory
Chang et al., 2015(32)	**PeerCARE intervention** Monthly peer visits at home or other places to (1) assessing participants health status and behavior; (2) providing psycho-social support; and (3) facilitating access to care	Peers	Peers provided psychosocial support, encouragement, information on and reminders of clinic appointments and the basic care package (BCP)	Not specified	HIV specific support	No	situated Information, Motivation, and Behavioral Skills (sIMB)
Robbins et al., 2015(15)	**Masivukeni intervention** A multimedia computer based ART adherence intervention performed by lay counselors who had received counseling training from the local NGO.	Peers	Informational and practical support	Medication-specific social support was measured using 8 item, 5-point Likert scale [37]. Perceived availability of social support was assessed using an 8-item, 5-point Likert scale [38, 39]	both	No	Social Action Theory
Bouris et al., 2017(16)	**Project nGage** A social-network support intervention among young black men who have sex with men (YBMSM). This client-centered, 1.5-h session consists of individual and dyadic components between an index young man and a support confidant who is identified by the index participant (IP). The social work interventionist delivers four telephone boosters to the IPs.	Mother, sister, sexual partner, female relatives, friend	Informational, emotional, and instrumental support	Not specified	HIV specific support	Yes	Information-Motivation-Behavioral Skills (IMB) theory
Phiri et al., 2017(34)	Facility-based and community-based models of peer support intervention consisted of one-on-one patient education, support groups, visit reminders, and missed visit follow-up.	Peers	Informational support (According to the details of the intervention)	Not specified	HIV specific support	No	Not specified

Table 2 (continued)

First author, year	Social support intervention	Source of social support	Type of social support	Measurement of Social support	General or HIV specific support	Measurement of satisfaction of social support intervention	Use of theory
Attonito et al., 2020(28)	**HHRP-A intervention** A group-level risk-reduction intervention for PLHIV who have a history of alcohol abuse, eight 2-hour group sessions scheduled 1 to 2 times per week over consecutive weeks, involved both didactic presentation of materials and experiential exercises.	Peers	Four functional support: Emotional/ informational, tangible, affectionate, and positive social interaction	Social support was measured using all 19 items from the Medical Outcomes Study (MOS) [40].	HIV specific support	No	Information-Motivation-Behavioral Skills (IMB) model
Nestadt et al., 2019(30)	**CHAMP+ intervention** Eleven cartoon-based sessions delivered to child-caregiver dyads by a social worker/counselor over 6 months.	Caregivers, social worker/counselor	Informational support (According to the details of the intervention)	Social support was assessed based on caregivers' responses to some questions asked about the frequency of help, advice, comfort, or other support received in the past month from people in their lives [41].	HIV specific support	No	Modified Social Action Theory (SAT)
Denison et al., 2020(21)	**Project YES! Youth Engaging for Success** HIV clinic-based peer mentoring program consisted of multiple components. Participants attended an orientation meeting with a healthcare provider, an assigned youth peer mentor, and an adult caregiver (if invited). After the orientation meeting, participants met with their assigned youth peer mentor monthly for one-on-one meetings over 6 months, as well as monthly youth group meetings.	Peer mentor, and an adult caregiver	Informational support (According to the details of the intervention)	Not specified	HIV specific support	No	Social Cognitive Theory

SMART: Sharing Medical Adherence Responsibilities Together

IMAI: Integrated Management of Adolescent and Adult Illness

PeerCARE: Peer Community Assistant in Retention and Engagement

CHAMP+: Collaborative HIV Prevention and Adolescent Mental Health Program adapted for Thailand
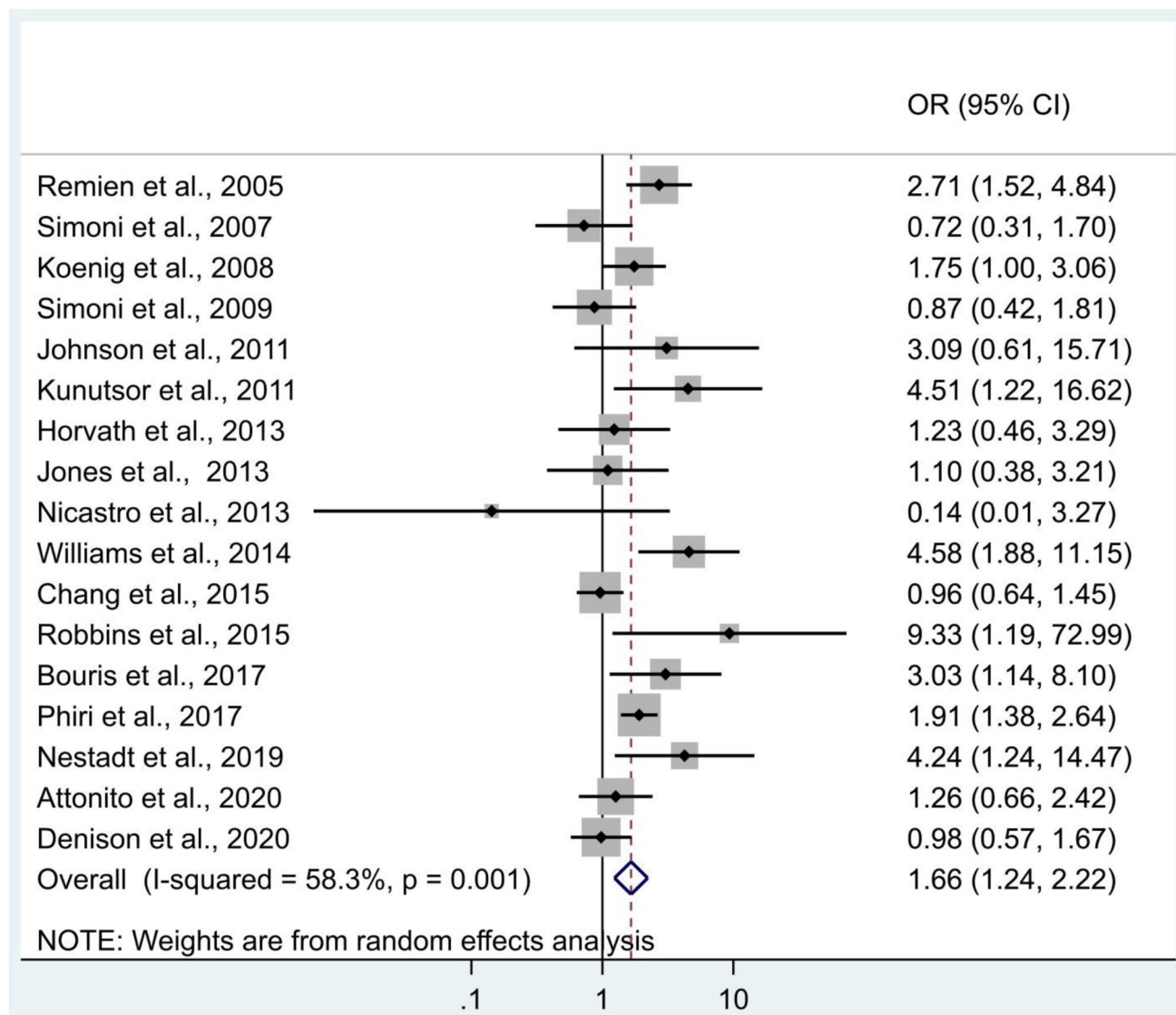
Fig. 2 Forest plot showing the effect of social support interventions on adherence to antiretroviral therapy (ART) among people living with HIV.

sick-role behaviors, as well as to achieve greater adherence to medication [44, 45].

The direct-effect model highlights the overall benefits of integration into a social network and states that individuals with high social support may have better health, regardless of whether or not they are in dealing with life stressors [45].

It should be noted that the relationship between social support and treatment adherence is complex and may be explained by variety of sub-models of these two broad perspectives (e.g., social control or matching hypotheses) [45].

The social control hypothesis, which is a major variant of the direct effect model, suggests that social networks are health promoting because they can facilitate and support healthier behaviors [45]. The presence of close others may lead to the direct or indirect social control of behavior,

facilitating adherence through norm internalization and the provision of punishment for unhealthy behaviors [42, 44].

According to the matching hypothesis, which is a major variant of the stress-buffering model, the effectiveness of any type of social support depends on the extent to which it meets the particular demands of the stressful event [42, 45, 46]. For example, informational support could be most effective for stressors that are more controllable, whereas emotional support may be most effective for uncontrollable stressful events [45].

As shown in Table 2, different theories and models of behavior change were used in the reviewed studies. However, researchers rarely referred to social support theory to establish a clear pathway between social support and medication adherence in PLHIV.

Fig. 3 The funnel plot with two missing studies imputed by the trim-and-fill method showing there is no publication bias among studies evaluating adherence to antiretroviral therapy (ART) after social support intervention for people living with HIV.
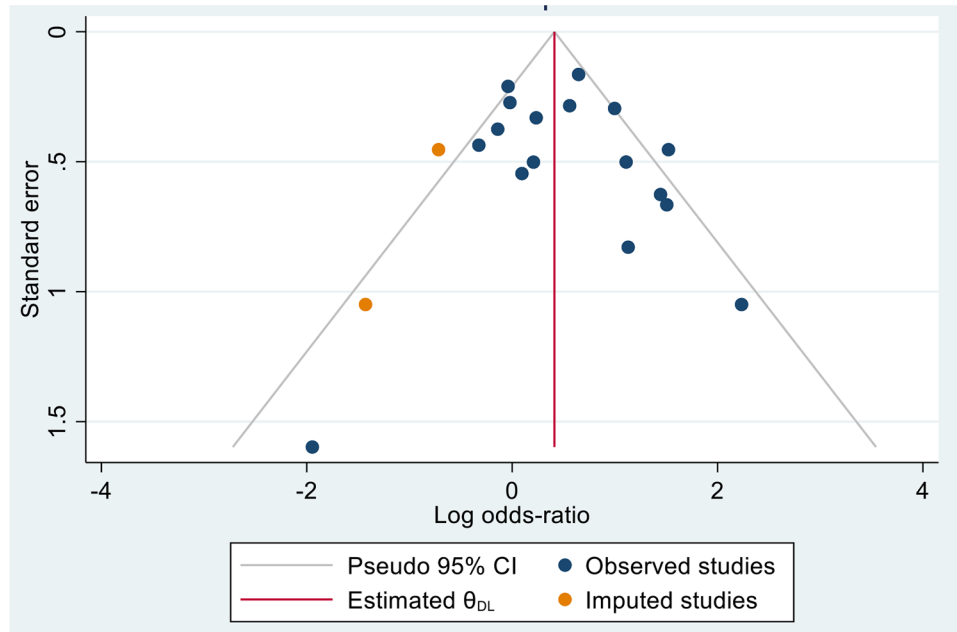

Table 3 Subgroup analysis of social support interventions to improve adherence to antiretroviral therapy (ART) among people living with HIV

Subgroups		Overall OR	95% CI	P-value*
Study design				
	Parallel design	1.80	1.25, 2.60	0.002
	Others (Factorial, Cross-over design)	1.36	0.78, 2.38	0.279
Year of publication				
	Before 2010	1.39	0.78, 2.50	0.269
	After 2010	1.79	1.25, 2.56	0.002
Follow up duration				
	≤ 6 months	1.43	0.98, 2.07	0.061
	≥ 7 months	1.98	1.23, 3.19	0.005
Source of social support				
	Family/Caregiver	0.94	0.06, 15.37	0.965
	Peer/Friend	1.24	0.85, 1.81	0.267
	Health/Social worker	3.09	0.61, 15.71	0.173
	Multiple sources	2.19	1.31, 3.66	0.003
Methodological Quality Score				
	Low quality (Score ≤ 5)	1.93	0.98, 3.77	0.056
	High quality (Score ≥ 6)	1.56	1.12, 2.17	0.009
	* P-value for Chi^2 statistic for heterogeneity			

It was also surprising that most studies did not measure social support, while ideally social support should be measured at several different points in time to evaluate the association between SSI and adherence [45].

The literature suggests that social support has been conceptualized and measured in various ways [47]. Researchers have often measured it through the structural and functional components of support. The structural measures examine the availability and frequency of contact with different types of relations, for example, the number of close friends or contact frequency with family members. The functional measures of support can assess either received or available emotional support, informational support, tangible support, and belonging support that served by social network members [42, 45]. We found that functional approach was usually used to measure social support among included studies. Measuring both social network structure and function by multi-item scales is recommended for future studies.

This study had some strengths and limitations. We followed PRISMA guidelines and registered the protocol of this systematic review in PROSPERO. However, some limitations are worth highlighting.

First, unpublished studies were not included in the current review. Second, six of the included studies [16, 21, 24, 28, 31, 33] categorized in low quality studies, which may overestimate the overall effect size. Third, social support interventions differ in many ways. It remains unclear that SSIs in which setting (e.g., group, individual or family) result in better behavior change and adherence to ART.

Finally, we were not able to reduce the observed heterogeneity by using subgroup analysis. It should be noted that the differences in estimated ORs by source of support may be results of the small numbers of studies in some categories (e.g., family/caregivers and HIV-experienced clinicians).

Conclusion

The current systematic review and meta-analysis provides empirical quantitative evidence on impact of SSIs on adherence to ART. The findings suggest that providing social support can increase medication adherence among PLHIV. However, more ART adherence interventions with various types and sources of social support should be designed and evaluated. Developing SSIs based on social support theory and using appropriate measures of social support can help future researchers to more accurately assess the effectiveness of SSIs, as well as examine theoretical models linking social support to health outcomes.

Declarations

References

1. WHO. HIV/AIDS Key facts. 2021.
2. Duwell MM, Knowlton AR, Nachega JB, Efron A, Goliath R, Morroni C, et al. Patient-nominated, community-based HIV treatment supporters: patient perspectives, feasibility, challenges, and factors for success in HIV-infected South African adults. AIDS Patient Care STDs. 2013;27(2):96–102.
3. Ortego C, Huedo-Medina TB, Llorca J, Sevilla L, Santos P, Rodríguez E, et al. Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. AIDS Behav. 2011;15(7):1381–96.
4. Gallant JE, Adimora AA, Carmichael JK, Horberg M, Kitahata M, Quinlivan EB, et al. Essential components of effective HIV care: a policy paper of the HIV Medicine Association of the Infectious Diseases Society of America and the Ryan White Medical Providers Coalition. Clin Infect Dis. 2011;53(11):1043–50.
5. Katz IT, Maughan-Brown B. Improved life expectancy of people living with HIV: who is left behind? The lancet HIV. 2017;4(8):e324-e6.
6. Wang H, Zhou J, He G, Luo Y, Li X, Yang A, et al. Consistent ART adherence is associated with improved quality of Life, CD4 counts, and reduced hospital costs in central China. AIDS Res Hum Retroviruses. 2009;25(8):757–63.
7. Roberson DW, White BL, Fogel CI. Factors influencing adherence to antiretroviral therapy for HIV-infected female inmates. J Assoc Nurses AIDS Care. 2009;20(1):50–61.
8. Nyblade L, Mingkwan P, Stockton MA. Stigma reduction: an essential ingredient to ending AIDS by 2030. The Lancet HIV. 2021;8(2):e106-e13.
9. Wasti SP, Van Teijlingen E, Simkhada P, Randall J, Baxter S, Kirkpatrick P, et al. Factors influencing adherence to antiretroviral treatment in Asian developing countries: a systematic review. Tropical Med Int Health. 2012;17(1):71–81.
10. Simoni JM, Nelson KM, Franks JC, Yard SS, Lehavot K. Are peer interventions for HIV efficacious? A systematic review. AIDS Behav. 2011;15(8):1589–95.
11. Beach MC, Keruly J, Moore RD. Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? J Gen Intern Med. 2006;21(6):661–5.
12. Johnson MO, Dilworth SE, Taylor JM, Neilands TB. Improving coping skills for self-management of treatment side effects can reduce antiretroviral medication nonadherence among people living with HIV. Ann Behav Med. 2011;41(1):83–91.
13. Koenig LJ, Pals SL, Bush T, Pratt Palmore M, Stratford D, Ellerbrock TV. Randomized controlled trial of an intervention to prevent adherence failure among HIV-infected patients initiating antiretroviral therapy. Health Psychol. 2008;27(2):159.
14. Remien RH, Stirratt MJ, Dolezal C, Dognin JS, Wagner GJ, Carballo-Dieguez A, et al. Couple-focused support to improve HIV medication adherence: a randomized controlled trial. Aids. 2005;19(8):807–14.
15. Robbins RN, Mellins CA, Leu C-S, Rowe J, Warne P, Abrams EJ, et al. Enhancing lay counselor capacity to improve patient outcomes with multimedia technology. AIDS Behav. 2015;19(2):163–76.
16. Bouris A, Jaffe K, Eavou R, Liao C, Kuhns L, Voisin D, et al. Project nGage: results of a randomized controlled trial of a dyadic network support intervention to retain young black men who have sex with men in HIV care. AIDS Behav. 2017;21(12):3618–29.
17. Rouhani SA, O'Laughlin KN, Faustin ZM, Tsai AC, Kasozi J, Ware NC. The role of social support on HIV testing and treatment adherence: A qualitative study of HIV-infected refugees in southwestern Uganda. Glob Public Health. 2017;12(8):1051–64.

18. Cohen S. Social relationships and health. Am Psychol. 2004;59(8):676.

19. Forouzan AS, Jorjoran Shushtari Z, Sajjadi H, Salimi Y, Dejman M. Social support network among people living with HIV/AIDS in Iran. AIDS research and treatment. 2013;2013.

20. Hogan BE, Linden W, Najarian B. Social support interventions: Do they work? Clin Psychol Rev. 2002;22(3):381–440.

21. Denison JA, Burke VM, Miti S, Nonyane BA, Frimpong C, Merrill KG, et al. Project YES! Youth Engaging for Success: A randomized controlled trial assessing the impact of a clinic-based peer mentoring program on viral suppression, adherence and internalized stigma among HIV-positive youth (15–24 years) in Ndola, Zambia. PLoS ONE. 2020;15(4):e0230703.

22. Horvath KJ, Oakes JM, Rosser BS, Danilenko G, Vezina H, Amico KR, et al. Feasibility, acceptability and preliminary efficacy of an online peer-to-peer social support ART adherence intervention. AIDS Behav. 2013;17(6):2031–44.

23. Jones DL, Zulu I, Vamos S, Cook R, Chitalu N, Weiss SM. Determinants of engagement in HIV treatment and care among Zambians new to antiretroviral therapy. J Assoc Nurses AIDS Care. 2013;24(5):e1–12.

24. Nicastro E, Continisio GI, Storace C, Bruzzese E, Mango C, Liguoro I, et al. Family group psychotherapy to support the disclosure of HIV status to children and adolescents. AIDS Patient Care STDs. 2013;27(6):363–9.

25. Simoni JM, Huh D, Frick PA, Pearson CR, Andrasik MP, Dunbar PJ, et al An RCT of peer support and pager messaging to promote antiretroviral therapy adherence and clinical outcomes among adults initiating or modifying therapy in Seattle, WA, USA. Journal of acquired immune deficiency syndromes (1999). 2009;52(4):465.

26. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336–41.

27. Oremus M, Wolfson C, Perrault A, Demers L, Momoli F, Moride Y. Interrater reliability of the modified Jadad quality scale for systematic reviews of Alzheimer's disease drug trials. Dement Geriatr Cogn Disord. 2001;12(3):232–6.

28. Attonito J, Villalba K, Dévieux JG. Effectiveness of an intervention for improving treatment adherence, service utilization and viral load among HIV-positive adult alcohol users. AIDS Behav. 2020;24(5):1495–504.

29. Simoni JM, Pantalone DW, Plummer MD, Huang B. A randomized controlled trial of a peer support intervention targeting antiretroviral medication adherence and depressive symptomatology in HIV-positive men and women. Health Psychol. 2007;26(4):488.

30. Nestadt DF, Saisaengjan C, McKay MM, Bunupuradah T, Pardo G, Lakhonpon S, et al. CHAMP + Thailand: pilot randomized control trial of a family-based psychosocial intervention for perinatally HIV-infected early adolescents. AIDS Patient Care STDs. 2019;33(5):227–36.

31. Williams AB, Wang H, Li X, Chen J, Li L, Fennie K. Efficacy of an evidence-based ARV adherence intervention in China. AIDS Patient Care STDs. 2014;28(8):411–7.

32. Chang LW, Nakigozi G, Billioux VG, Gray RH, Serwadda D, Quinn TC, et al. Effectiveness of peer support on care engagement and preventive care intervention utilization among pre-antiretroviral therapy, HIV-infected adults in Rakai, Uganda: a randomized trial. AIDS Behav. 2015;19(10):1742–51.

33. Kunutsor S, Walley J, Katabira E, Muchuro S, Balidawa H, Namagala E, et al. Improving clinic attendance and adherence to antiretroviral therapy through a treatment supporter intervention in Uganda: a randomized controlled trial. AIDS Behav. 2011;15(8):1795–802.

34. Phiri S, Tweya H, van Lettow M, Rosenberg NE, Trapence C, Kapito-Tembo A, et al. Impact of facility-and community-based peer support models on maternal uptake and retention in Malawi's option B + HIV prevention of mother-to-child transmission program: a 3-arm cluster randomized controlled trial (PURE Malawi). JAIDS J Acquir Immune Defic Syndr. 2017;75:140-S8.

35. Schwarzer R, Dunkel-Schetter C, Kemeny M. The multidimensional nature of received social support in gay men at risk of HIV infection and AIDS. Am J Community Psychol. 1994;22(3):319–39.

36. Zich J, Temoshok L. Perceptions of social support in men with AIDS and ARC: relationships with distress and hardiness 1. J Appl Soc Psychol. 1987;17(3):193–215.

37. Pearson CZ, Fredriksen-Goldsen F. K. Barriers associated with self-reported adherence to antiretroviral therapy in Beijing, China. Poster presented at: 3rd Annual International. Conference on HIV Treatment Adherence; March, 2008; Jersey City, NJ.

38. Barrera M. A method for assessing social support networks in community survey research. Connections. 1980;3:8–13.

39. Arnsten JH, Li X, Mizuno Y, Knowlton AR, Gourevitch MN, Handley K, et al. Factors associated with antiretroviral therapy adherence and medication errors among HIV-infected injection drug users. JAIDS J Acquir Immune Defic Syndr. 2007;46:64–71.

40. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med. 1991;32(6):705–14.

41. Westbrook L, Bauman L. Perceived stigma of HIV/AIDS scale. Bronx: Albert Einstein College of Medicine; 1996.

42. Cohen S, Wills TA. Stress, social support, and the buffering hypothesis. Psychol Bull. 1985;98(2):310.

43. Latkin CA, Knowlton AR. Social network assessments and interventions for health behavior change: a critical review. Behav Med. 2015;41(3):90–7.

44. DiMatteo MR. Social support and patient adherence to medical treatment: a meta-analysis. Health Psychol. 2004;23(2):207.

45. Uchino BN. Social support and physical health. Yale university press; 2008.

46. Cutrona CE, Russell DW. Type of social support and specific stress: Toward a theory of optimal matching. 1990.

47. Gottlieb BH, Bergen AE. Social support concepts and measures. J Psychosom Res. 2010;69(5):511–20.