Community-Based Interventions to Improve and Sustain Antiretroviral Therapy Adherence, Retention in HIV Care and Clinical Outcomes in Low- and Middle-Income Countries for Achieving the UNAIDS 90-90-90 Targets

Authors

Jean B. Nachega[1,2,3], Olatunji Adetokunboh[2], Olalekan A. Uthman[4], Amy W. Knowlton[3], Elvin Geng[5]; Karl Peltzer[6,7,8], Larry W. Chang[3], Gilles Van Cutsem[9], Shabbar S. Jaffar[10], Nathan Ford[11], Claude A. Mellins[12], Robert H. Remien[13], Edward J Mills [14]

Affiliations

1. University of Pittsburgh, Pittsburgh, PA, USA
2. Stellenbosch University, Cape Town, South Africa
3. Johns Hopkins University, Baltimore, MD, USA
4. Warwick Medical School, The University of Warwick, Coventry, UK
5. University of California, San Francisco, CA, USA
6. Mahidol University, Salaya, Thailand
7. University of Limpopo, Polokwane, South Africa
8. Human Sciences Research Council, Pretoria, South Africa
9. Medecins Sans Frontieres, Cape Town, South Africa
10. Liverpool School of Tropical Medicine, Liverpool, UK
11. World Health Organization, Geneva, Switzerland
12. HIV Center for Clinical and Behavioral Studies, Columbia University
13. New York State Psychiatric Institute, New York, NY, USA
14. Precision Global Health, Vancouver, Canada

Corresponding Author:

Jean B. Nachega, MD, PhD, MPH, University of Pittsburgh
Graduate School of Public Health, Department of Epidemiology
130 DeSoto Street, 503 Parran Hall, Pittsburgh, PA 15261; USA
E-mail: JBN16@PITT.EDU

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Abstract

Little is known about the effect of community versus health facility-based interventions to improve and sustain antiretroviral therapy (ART) adherence, virologic suppression, and retention in care among HIV-infected individuals in low- and middle-income countries (LMICs). We systematically searched four electronic databases for all available randomized controlled trials (RCTs) and comparative cohort studies in LMICs comparing community versus health facility-based interventions. Relative risks (RRs) for pre-defined adherence, treatment engagement (linkage and retention in care), and relevant clinical outcomes were pooled using random effect models. Eleven cohort studies and eleven RCTs (N = 97,657) were included. Meta-analysis of the included RCTs comparing community- versus health facility-based interventions found comparable outcomes in terms of ART adherence (*RR* = 1.02, 95 % CI 0.99 to 1.04), virologic suppression (*RR* = 1.00, 95 % CI 0.98 to 1.03), and all-cause mortality (*RR* = 0.93, 95 % CI 0.73 to 1.18). The result of pooled analysis from the RCTs (*RR* = 1.03, 95 % CI 1.01 to 1.06) and cohort studies (*RR* = 1.09, 95 % CI 1.03 to 1.15) found that participants assigned to community-based interventions had statistically significantly higher rates of treatment engagement. Two studies found community-based ART delivery model either cost-saving or cost-effective. Community- versus facility-based models of ART delivery resulted in at least comparable outcomes for clinically stable HIV-infected patients on treatment in LMICs and are likely to be cost-effective.

Introduction

The number of people that have started life-saving antiretroviral therapy (ART) has importantly increased in low- and middle-income countries [1]. However, this positive development has led to health facilities' overcrowding, longer waiting times during visits, and reduced time for counseling and clinical care of newly enrolled patients. In most public sector clinics in resource-limited settings, it has also restricted the workforce's capacity to provide ongoing adherence support and track patients lost to follow-up to ensure optimal ART effects on patient health and community HIV prevention. [2]. Further, in July 2014, UNAIDS called for a global scale-up of Treatment as Prevention (TASP) and efforts to meet the following '90-90-90' targets by 2020: (1) 90% of all people living with HIV should know their HIV status (90% diagnosed); (2) 90% of all people diagnosed with HIV infection should receive ART (90% on treatment); and (3) 90% of all people receiving ART should achieve viral suppression (UNAIDS 2014)[3]. This ambitious target is supported by the latest World Health Organization (WHO) guidelines recommending treating all HIV positive individuals irrespective of immune status. It implies that an additional 21 million people are now eligible for treatment [4]. This underscores the importance of expanding health systems' capacity to meet communities' growing health needs.

Emerging data from both developed and developing countries demonstrate that a substantial reduction in patient retention in medical care occurs between each stage of the HIV treatment continuum, or cascade—from diagnosis and linkage to care, assessment of ART readiness to acceptability, receipt of initial ART, adherence and long-term retention in care, and treatment success as reflected by virologic suppression [5-8]. A systematic review by Fox and Rosen reported that retention of HIV-infected adults on ART at 36 months in middle- and low-income countries averages only 65% to 70%[9]. Success along the HIV treatment cascade is even worse in vulnerable populations, namely, pregnant women, children and adolescents, sex

workers, injecting drug users, and men who have sex with men; and they are at high risk of acquiring as well as transmitting the HIV virus, thus experiencing poor clinical and public health outcomes [10-15]. Against this background, it is critical to determine how effective interventions are at every level of the treatment cascade to prevent new infections and promote health outcomes to achieve the goal of an AIDS- free generation [7].

In Africa, selected approaches to reducing loss at every stage of the HIV treatment cascade include decentralization of services and task-shifting aspects of care to nurses and to non-clinical staff, including lay counselors who may be patients themselves. These approaches have been found to be feasible and to result in good clinical outcomes and are now recommended and being scaled up in resource-limited settings [16-19]. However, such facility-based approaches are reaching their limits as increasing numbers of patients initiate ART. Recently, suggestions have been made to expand accessible and flexible community-based ART services delivery, differentiating the needs of clinically ill patients starting ART or in need of significant adherence counseling from the needs of clinically stable ongoing patients with documented good adherence. Such , have been suggested as important strategies for maintaining and improving ART adherence, retention and quality of care [16].

Indeed, community and home-based programs to promote ART adherence and/or retention in HIV care are now increasingly being recognized as an important and sustainable approach that could contribute significantly toward the UNAIDS 90-90-90 target and ultimately an AIDS-Free generation [20-32]. In addition, they are also seen as an essential mechanism of service delivery, including dispensing of ART, and a means of decongesting formal health services, rather than being purely an adherence adjunct. Furthermore, such interventions are likely to be cost-effective by offering a shift of certain tasks from overburdened healthcare settings directly into communities [33,34].

We aimed to conduct a systematic review and meta-analysis to compare the effect of community-based ART delivery on adherence, virologic outcomes, retention in care and all-cause mortality among HIV-infected individuals in middle- and low-income countries against results obtained through standard health facility care.

Methods

Protocol

The study background, rationale, and methods were specified in advance and documented in a study protocol registered in the PROSPERO database (CRD42016034114).

Study Inclusion Criteria

In order to be eligible for inclusion in the review, studies had to report on adherence, and/or virologic suppression, and/or lost-to-follow up outcomes after initiation of ART. The following selection criteria were used to identify potential studies:

- *Study design*: Observational and experimental studies with primary data using cross-sectional, case – control, and cohort (prospective and retrospective) and randomized controlled trials (RCT s) designs
- *Study population*: HIV-infected individuals initiated on ART.
- *Intervention*: Community-based ART delivery. Models could include: 1) home-based interventions (e.g. friends or family-centred approaches); 2) peer- or HIV patients-led interventions; community ART distribution points (with or without involving primary level formal or informal health facilities); 3) community-based ART adherence clubs (with or without involving primary level formal or informal health facilities); 4) community ART groups (CAGs)
- *Comparator*: health-facility (e.g. hospital or clinics)

- *Outcomes*: Primary: 1) Proportion of HIV-infected patients with optimal ART adherence levels* (>80%); 2) Proportion of HIV-infected patients with virologic suppression (as defined by the studies) at 12 and 24 months' post ART initiation. Secondary: Proportion of patients lost-to-follow up as defined by the studies at 12 and 24 months' post Art initiation; all-cause mortality; and cost to patient and provider.

Data Sources and Searches

We conducted a systematic literature search using the following databases: Medline (PubMed), Scopus, SCI Web of Science and Cochrane Central Register of Controlled Trials (CENTRAL) through January 2016. In addition, abstracts from major HIV/AIDS or infectious diseases conferences such as the Conference on Retrovirus and Opportunistic Infections (CROI), International AIDS Society (IAS), International AIDS Conference and Infectious Diseases Society of America (IDSA) were reviewed for inclusion.

Our search terms included: "community"; 'home-based care"; "health facilities"; "adherence"; "adherence club"; "retention in care"; "retention"; "loss to follow up", "attrition", "antiretroviral therapy"; "HIV"; "community volunteers"; "treatment supporter"; "DAART"; "cost".

Study Selection and Data Extraction

Two of the authors (JBN and OA) screened the search outputs using titles and abstracts and independently went through the full text of all potentially eligible studies to assess whether they meet the inclusion criteria. Discrepancies in the choice of included studies between the two authors were resolved through discussion and consensus. For all eligible studies, the same authors reviewed extracted information regarding publication date, study setting, study design, methods, patient population, study intervention, and outcomes.

Risk of bias (quality) assessment

To appraise the risk of bias for included studies, a tool was adapted from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (Appendix) [35]. Briefly, the risk of bias was assessed as low risk, unclear risk or high-risk for each of the following domains: selection (sample population), selection (participation rate), performance bias (outcome assessment), performance bias (analytical methods to control for bias) and other forms of bias. We used the Cochrane Collaboration's tool for assessing the risk of bias for quality assessment of the included studies[36]. The studies were graded based on: (i) sequence generation, (ii) blinding of outcome assessor, (iii) incomplete outcome data, (iv) selective outcome reporting, and (v) other sources of bias.

Measures of treatment effect and unit of analysis

We used relative risks (RR) for the calculation of dichotomous data (such as adherence and retention in care) and mean differences for continuous data (such as change in CD4 cell count. All the results are presented with 95 % confidence intervals (CI).

Data Synthesis

In the absence of statistical heterogeneity, we used a fixed-effect model, and we used a random-effects model where we detected moderate heterogeneity and it was deemed still reasonable to combine trials. We assessed the presence of statistical heterogeneity in the meta-analyses by visual inspection of the forest plot and applying a chi-squared test for heterogeneity with a threshold P value of 0.10 to determine statistical significance. Inconsistency was quantified across studies using the I^2 value. We used Review Manager 5.3 [37] to conduct analyses and analyzed results for trials and cohort studies separately and also pooled these data. This review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [38].

Results

Study selection and characteristics of included studies

The process of study identification and selection is shown in **Figure 1**. The literature search yielded 7,928 citations after removing duplicates. After review of the title and abstract, 33 full text articles were selected for critical review. A total of eleven trials were included [21,25,26,29,30,36,39-44] and eleven cohort studies [27,36,39,45-54]with a total of 5861 and 89,388 participants, respectively. These studies were conducted in eight different sub-Saharan African countries, including Botswana, Zimbabwe, South Africa, Nigeria, Uganda, Kenya, Tanzania and Zambia. Other studies were conducted in other low and middle income countries such as Brazil, Haiti, Peru and Thailand. See additional details in **Table 1.** We excluded seventeen studies. One study was excluded due to inclusion of a non-African population[44], four studies were excluded due to non-inclusion of community based data [32,55-57] while seven studies were excluded because the studies were non comparative in nature [19,58-62]. A study was also excluded because only baseline data were reported[63] while four did not show data for different arms of the studies[17,64-66].

Risk of bias in included studies

The risk of bias of included cohort studies is summarised in **Table 2.** All the included studies had low risk of bias with respect to the selection of sample population and explaining the rationale for case and control selection while the included cohort studies were at risk of bias for sample selection ambiguity and having samples that were unlikely to be representative. All the studies had a high participation rate (>70-85%). In terms of outcome assessment, seven of the included studies had objective measures of adherence such as 'pill count', while two had high risk of bias by measuring the outcome using self-reporting format. All the trials and cohort studies used one or more analytical methods to control for bias in individual studies.

The risk of bias in the included studies was highest from other form of bias, followed by selection of sample population, and lowest from participation rates and analytical methods to control for bias.

The risk of bias of included trials is shown in **Table 3**. Allocation sequence generation was adequate in all the eleven trials. Allocation concealment was adequate in nine trials and unclear in the remaining two trials. Masking of outcome assessors was not clear in all the nine trials. Potential risk of bias due selective reporting and other bias was low in all eleven trials.

Optimal ART adherence

Seven RCTs and three cohort studies reported optimal adherence as an outcome. Individual and pooled RRs for optimal adherence are shown in **Figure 2**. The result of pooled analysis from the RCTs showed no statistically significance difference in optimal adherence rates between the two treatment groups (pooled RR = 1.02, 95% CI 0.99 to 1.04, I^2 = 68%), such that among 6358 participants randomised to community-based ART 5827 (91.7%) achieved optimal ART adherence compared with 4083 of 4619 in the facility-based ART group (88.4%). However, three cohort studies provided evidence that participants in community-based ART had statistically significant higher optimal adherence rate compared to those in facility-based ART group (RR = 1.80, 95% CI 1.04 to 3.13), such that among 274 participants randomised to community-based ART 295 (92.9%) achieved optimal ART adherence compared with 196 of 288 in the facility-based ART group (68.1%).

Virologic suppression

Eight RCTs and Eight cohort studies reported virologic suppression as an outcome. Individual and pooled RRs for virologic suppression are shown in **Figure 3**. The result of pooled analysis from the RCTs showed no statistically significance difference in virologic suppression rates between the two treatment groups (pooled RR = 1.00, 95% CI 0.97 to 1.03), with evidence of

no statistically significant heterogeneity between studies (I^2 = 0%, p=0.49). Similarly, the result of pooled analysis from the cohort studies showed no statistically significant difference in virologic suppression rates between the two treatment groups (pooled RR = 1.06, 95% CI 0.77 to 1.46), with evidence of statistically significance substantial heterogeneity between studies (I^2 = 100%, p<0.00001).

Retention in care

Seven RCTs and four cohort studies reported retention in care as an outcome. Individual and pooled RRs for retention in care are shown in **Figure 4**. The result of pooled analysis from the RCTs showed that participants assigned to community-based ART (80.3% [3157 of 3931]) had statistically significant higher rates of retention in care than those in facility-based ART (75.9% [2334 of 3074]) at the end of the follow-up period (RR = 1.03, 95% CI 1.01 to 1.06, I^2 = 0%). Similarly, the result of pooled analysis from the cohort studies showed that participants assigned to community-based ART (89.4% [1074 of 1203]) had statistically significant higher rates of retention in care than those in facility-based ART (84.9% [2578 of 3038]) at the end of the follow-up period (RR = 1.09, 95% CI 1.03 to 1.15, I^2 = 69%)

Change in CD4+ T-cell count

Three RCTs reported CD4+ T-cell count as an outcome. The results of pooled analysis from the three RCTs show no significance difference in change in CD4+ T-cell count between the two treatment groups (mean difference = 0.93, 95% CI -11.36 to 13.21, I^2 = 0%) (**Figure 5)**.

All-cause mortality

Ten RCTs and eight cohort studies reported all-cause mortality as an outcome. Individual and pooled RRs for all-cause mortality are shown in **Figure 6**. The result of pooled analysis from the RCTs showed there was no statistically significant difference in rates of all-cause mortality in assigned to community-based ART (9.3% [388 of 4160]) than those assigned to facility-based ART (10.3% [338 of 3272]) at the end of the follow-up period (RR = 0.93, 95% CI 0.73 to 1.18, I^2 = 38%). Similarly, the result of pooled analysis from the cohort studies showed there was no statistically significant difference in rates of all-cause mortality in assigned to community-based ART (4.2% [1,075 of 25,506]) than those assigned to facility-based ART (6.0% [3,299 of 54,708]) at the end of the follow-up period (RR = 0.44, 95% CI 0.19 to 1.02, I^2 = 96%).

Loss to follow-up

Six RCTs and seven cohort studies reported loss to follow-up as an outcome. Individual and pooled RRs for loss to follow-up are shown in **Figure 7**. The result of pooled analysis from the RCTs showed there was no statistically significant difference in rates of loss to follow-up in assigned to community-based and those assigned to facility-based ART at the end of the follow-up period (RR = 0.88, 95% CI 0.77 to 1.11, I^2 = 0%). However, the result of pooled analysis from the cohort studies showed that the rate of loss to follow-up was statistically significantly lower in those participants in community-based ART (5.1% [1,289 of 25065]) than those in facility-based ART (9.7% [5268 of 54,545]) at the end of the follow-up period (RR = 0.34, 95% CI 0.14 to 0.81, I^2 = 97%).

Cost to the patient and provider

Jaffar et al.[25] reported costs to access care per patient including transport, lunch, child care costs and lost work time. The average total cost per patient in the first year was US $29 among the community-based participants compared to the US $60 facility-based patients. In terms of health-service costs, the same study reported average cost per patient per year to be US$793 among the community-based participants compared to US$838 among facility-based patients in Jinja, Uganda. Also, Bango and colleagues reported from South Africa, that ART adherence clubs (AAC) were most cost-effective than standard of care (SOC), with a cost per patient year of $296 for AAC vs. $374 for SOC. Retention in care at one year was 95% (95% CI: 94.88-95.86) for SOC, and 98% for ACC (95% CI: 97.6-98.3)[67].

Discussion

This meta-analysis of nine cohort studies and seven RCTs found no statistical difference in optimal ART adherence, virologic suppression, change in CD4+ T-cell count, all-cause mortality and loss to follow-up between those participants assigned to community-based ART and facility-based ART, when analysis was restricted to RCTs. However, in the pooled analysis from both RCTs and cohort studies, we documented that participants assigned to community-based ART had significantly higher rates of retention in care than those in facility-based ART at the end of the follow-up period.

The above results corroborate the fact that providing patient support and education programs at community level are not inferior compared to facility-based ones and may in fact be superior when it comes to selected outcomes such as lost-to-follow up. Of note, our analysis may be underpowered to show superiority on selected outcomes such as virological outcomes and all-cause mortality. Furthermore, it appears that mortality in the observational studies might be

slightly higher in the community-based studies whereas retention and loss to follow-up seems to suggest that these outcomes in community-based are better than facility-based. It is possible that they are both likely artefacts, particularly in the non-randomized studies, of the fact that outcome ascertainment is better in the community than in the facility based studies since mortality in facility-based studies may be under-ascertained, this will make mortality in the community look higher[68]. At the same time, silent and even official community patient transfers in facility based also tend to be under-captured, thus making retention look worse[68]. For these reasons, studies, retention outcome is usually retention in facility and therefore interpretation of such outcome must with caution.

In building decentralized ART delivery, adherence and retention in care support, community-based ART programs encourage patient autonomy, build social networks and minimize the structural barriers, such as cost of transport to the clinic, which in turn appear to result in better outcomes. Such community-based interventions are likely to be impactful since they tend to involve trained community health workers, peers, volunteers, or patient's own social network members (e.g., family and friends) who assist with ART adherence counselling and support. In addition, there is evidence that they may provide material, instrumental and emotional support, as well as promote other healthy behaviours, such as decreased alcohol and drug use, leading to better health outcomes--- including survival [14,24,29,32]. Furthermore, enhancing certain aspects of the patient–supporter relationships—such as trust, supporter availability, communication, reciprocity of support, and medication assistance—in a manner consistent with patients' expectations may help to optimize the relationship, and its positive impact on patient health [14,24,29].

Our study complements the findings of a previous review that assessed the effect of home-based interventions on viral outcomes in sub-Saharan Africa; this review found that there was

insufficient data to be conclusive [69]. Another recent review summarized the evidence supporting different models of community participation for ART care, or community-based ART in sub-Saharan Africa; these community ART programs made treatment readily accessible and affordable[70]. In Uganda and Kenya community health workers or volunteers delivered ART at home [41,62] while in Tete, Mozambique a demonstration project of people living with HIV/AIDS used self-formed community-based ART groups to deliver ART in the community [19]. Also, in South Africa, Medicines Sans Frontiers, piloted ART adherence clubs with promising results[27]. These clubs may provide some adherence counseling and peer support, as well as enable a "fast track" refill mechanisms. Patients are placed in groups of approximately six patients and one member of the group (rotating each month) is permitted to obtain refills for all of the patients in his or her group. These approaches decrease the patient burden on health facilities, reduce transportation costs and waiting times for patients, and help overcome structural barriers. They also reduce treatment fatigue and loss to follow up, increase disclosure and treatment education, and may help patients develop necessary social ties. While supportive of community-based interventions, these evaluations used observational study designs with possibility of selection and observational bias as well as confounding and most of them did not have a valid comparator and could not be included in our meta-analysis.

We also investigated as secondary outcomes two potential concerns related to community-based ART adherence and retention programs, including reported stigma and low quality of care which could result in an increased all-cause mortality. In terms of stigma, an RCT reported that only 3% of patients refused to participate in the home-based ART program due to stigma [25] Furthermore, it has even been suggested that involvement of community-health care workers in HIV care reduced stigma[71] and being part of peer groups has been found to decrease the perception of social stigma [72].

Our results have important clinical and public health implications in the context of reaching UNAIDS 90-90-90 target for an AIDS-free generation: first, community-based interventions aim to deliver a package of essential ART care functions beyond the clinic into the community such as ART refills, monitoring of treatment adherence and outcomes, and detection of sick patients and rapid referral to care. This, in turn, frees up capacity within the clinic-based medical workforce to be able to focus on complicated tasks such as clinical care for sick patients, training and supervision of lower cadres, and management of health care services. Second, community-based ART delivery and adherence monitoring and support models for clinically stable patients with documented virological suppression holds the potential of enabling countries to build sustainable, cost effective and equitable HIV care for populations in countries with a scarce health care workforce. Indeed, a cost-effectiveness study by Marseille and colleagues concluded that a home-based ART programme in rural Africa may be more cost effective than most previous estimates for facility-based HAART programs [73].

Only three cohort studies, Fatti et al. [46], Grimwood et al. [49] and Massavon et al. [52] involved children. The outcomes reported by these studies were virological suppression, mortality and loss to follow up and all of these were not different from what was obtainable in the adult population. These studies were conducted in South Africa and Uganda

Our study has several strengths. We performed a comprehensive search of several databases and sources to identify eligible cohorts and RCTs with the latter providing the highest quality of evidence. Two authors independently evaluated each study for inclusion and data extraction. Regarding limitations, inclusion of cohort study designs may bias the overall estimate of effects due to unmeasured confounding not adjusted for in multivariate analyses. Indeed, the fact that we are observing a difference between RCTs and observational studies for the ART adherence outcome may reflect that in many if not all of these community based interventions, the patients who end up in the intervention, if it is not randomized, are likely to be quite a bit different – selected somehow – for stability even if not measured. However, in the context of implementation science, observational studies often provide strong signals of

important direction of effect. We could not do subgroup analysis for the primary outcomes based on the location of studies ie sub-Saharan African population versus other low and middle income countries. Finally, with only eleven RCTs, we may be underpowered to show superiority of either type interventions.

In summary, we found that community as compared to facility-based ART interventions were effective in achieving optimal ART adherence and virologic suppression. Retention in HIV care was not different in the two groups, but, overall, we found lower all-cause mortality and loss to follow up in favour of community-based interventions, mostly within cohort studies rather than RCTs. As ART rollout expands in Africa and the need of health systems to adjust for such expansion in Africa, community-based ART delivery adherence monitoring and support models for stable patients hold the promise of enabling countries to build sustainable, cost effective and equitable HIV care for populations in countries with a scarce health workforce. Further research with well powered studies may be needed to further explore effectiveness of such community-based ART programs and their cost-effectiveness and the resources needs of families and communities to sustain optimal outcomes.

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The present study did not receive any specific funding. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Authors' contributions: JBN and EJM conceived the review. JBN, KP and OA drafted the protocol. OA and JBN conducted eligibility of the searches and researched the data. JBN, OA, OAU and AWK drafted the manuscript. The paper was revised critically for intellectual content by all the co-authors and gave final approval for publication.

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Tables

Table 1 Table of included studies

Study	Type	Age –median (years)		Countries included	Duration of study	Sample size (n)	Participants / healthcare service description	
		Intervention	Comparator				Intervention	Comparator
Chang et al. [21]	Cluster-randomized trial	35.5	34.0	South Africa	27 months; May 2006 - July 2008	1,336	Patients with Community-based peer health workers	Control group-accessing standard of care
Fatti et al. [45]	Cohort	35.1	34.6	South Africa	69 months ; January 2004 - September 2010	66,953	Patients who received community-based adherence support	Patients without community-based adherence support
Fatti et al. [46]	Cohort	6.3	6.6	South Africa	69 months; January 2004 - September 2010	4,853	Patients who received community-based adherence support	Patients without community-based adherence support
Franke et al. [47]	Prospective cohort	37.0	37.0	Rwanda	15 months; June 2007 to August 2008	610	Community-Based Accompaniment	Clinic-Based Care
Grimsrud et al. [48]	Cohort	33.9	33.2	South Africa	20 months; May 2012 - December 2013	8,150	Community based adherence club	Community Health Centre
Grimwood et al. [49]	Cohort	6.8	6.2	South Africa	57 months; January 2004 - September 2009	3563	Children with patient advocates	Children without patient advocates
Jaffar et al. [25]	Cluster-randomized equivalence trial	37.0	38.0	Uganda	48 months; February 2005 - January 2009	1,453	Home-based care	Facility based care
Johnston et al [50]	Retrospective cohort	36.0	43.0	South Africa	75 months; January 2003 - March 2010	417	Community cohort	Workplace cohort

Kipp et al. [51]	Cohort	36.8	34.8	Uganda	15 months; March 2006 - May 2007	385	Centre/Community-based cohort	Hospital-based cohort
Kiweewa et al. [39]	Randomized controlled trial	27.0	27.8	Uganda	29 months; May 2007 - September 2009	92	Nurse–Peer model	Doctor–Counsellor model
Luque-Fernandez et al. [27]	Cohort	Not reporter	Not reported	South Africa	40 months; November 2007 - February 2011	2,834	Adherence clubs	Traditional clinic-based care
Massavon et al. [52]	Retrospective cohort	91.0 months	45.9 months	Uganda	2003-2010	1,623	Community home-based care approach	Facility-based family-centred approach
Mfinanga et al. [40]	Open-label, randomized controlled trial	38.0 35.0	37.0 35.0	Tanzania Zambia	19 months; February, 2012 - September, 2013	1,999	Clinic plus community support	Standard care
Nachega et al. [29]	Open-label, randomized controlled trial	35.7	36.7	South Africa	42 months; February 2005 – July 2008	274	Directly observed therapy (DOT-ART) arm	Self-administered ART (Self-ART arm)
Selke et al. [41]	Cluster randomized controlled clinical trial	38.7	37.5	Kenya	26 months; March 2006 - April 2008.	208	Community Care Coordinators arm patients	Standard of Care arm patients
Taiwo et al [42]	Randomized controlled trial	Not reported	Not reported	Nigeria	19 months; June 2006 - December 2007	499	Treatment partner–assisted ART	Patient-administered standard of care ART
Gross et al. [44]	Randomized controlled trial	38	37	Botswana, Brazil, Haiti, Peru, South Africa, Uganda, Zambia, Zimbabwe	30 months; April 2009-September 2011	259	Partner-based modified directly observed therapy	Standard of care
Nakigozi et al [30]	Randomized controlled trial	37.6	37	Uganda	15 months; October 2010 - January 2012	1209	Patient-selected care buddy	Standard of care

Kaihin et al [53]	Cohort	18.2	19.4	Thailand	4 months; April–July 2011	46	Experimental Group (Empowerment Intervention)	Control
Kunutsor et al [26]	Randomized controlled trial	39.1	39.2	Uganda	8 months; March-September 2010	174	Standard adherence intervention package plus treatment supporter intervention	Standard intervention package
Munoz et al [54]	Cohort	31.7	31.9	Peru	17 months; December 2005 - April 2007	120	Community-based accompaniment with supervised antiretrovirals	Control
Coker et al [43]a	Randomized controlled trial	Not reported	Not reported	Nigeria	18 months; August 2006-January 2008	400	Peer educators arm	Standard of care
Coker et al [43]b	Randomized controlled trial	Not reported	Not reported	Nigeria	18 months; August 2006-January 2008	400	Home visits and peer educators arm	Standard of care

Table 2 Risk of bias in included studies of cohort studies

Study	Selection (sample population)	Selection (participation rate)	Performance bias (outcome assessment)	Performance bias (analytical methods to control for bias)	Other form of bias
Fatti et al. [45]	High	Low	Unclear	Low	High
Fatti et al. [46]	High	Low	Unclear	Low	High
Franke et al. [47]	High	Low	Unclear	Low	High
Grimsrud et al. [48]	High	Low	Low	Low	High
Grimwood et al. [49]	High	Low	Unclear	Low	High
Johnston et al [50]	High	Low	Unclear	Low	High
Kipp et al. [51]	High	Low	Low	Low	High
Luque-Fernandez et al. [27]	High	Low	Unclear	Low	High
Massavon et al. [52]	High	Low	Low	Low	High
Kaihin et al [53]	High	Low	Low	Low	High
Munoz et al. [54]	High	Low	Low	Low	High

Table 3 Risk of bias in included studies of randomized controlled trials

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessors (performance bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chang et al. [21]	Low	Unclear	Unclear	Low	Low	Low
Jaffar et al. [25]	Low	Low	Unclear	Low	Low	Low
Kiweewa et al. [39]	Low	Low	Unclear	Low	Low	Low
Mfinanga et al. [40]	Low	Low	Unclear	Low	Low	Low
Nachega et al. [29]	Low	Low	Unclear	Low	Low	Low
Selke et al. [41]	Low	Low	Unclear	Low	Low	Low
Taiwo et al. [42]	Low	Unclear	Unclear	Low	Low	Low
Gross et al. [44]	Low	Low	Low	Low	Low	Low
Nakigozi at el. [30,44]	Low	Low	High	Low	Low	Low
Kunutsor et al. [26]	Low	Low	Unclear	Low	Low	Low
Coker et al. [43]	Low	Low	Unclear	High	Low	Low

Figure legends

Figure 1: PRISMA flow for study selection

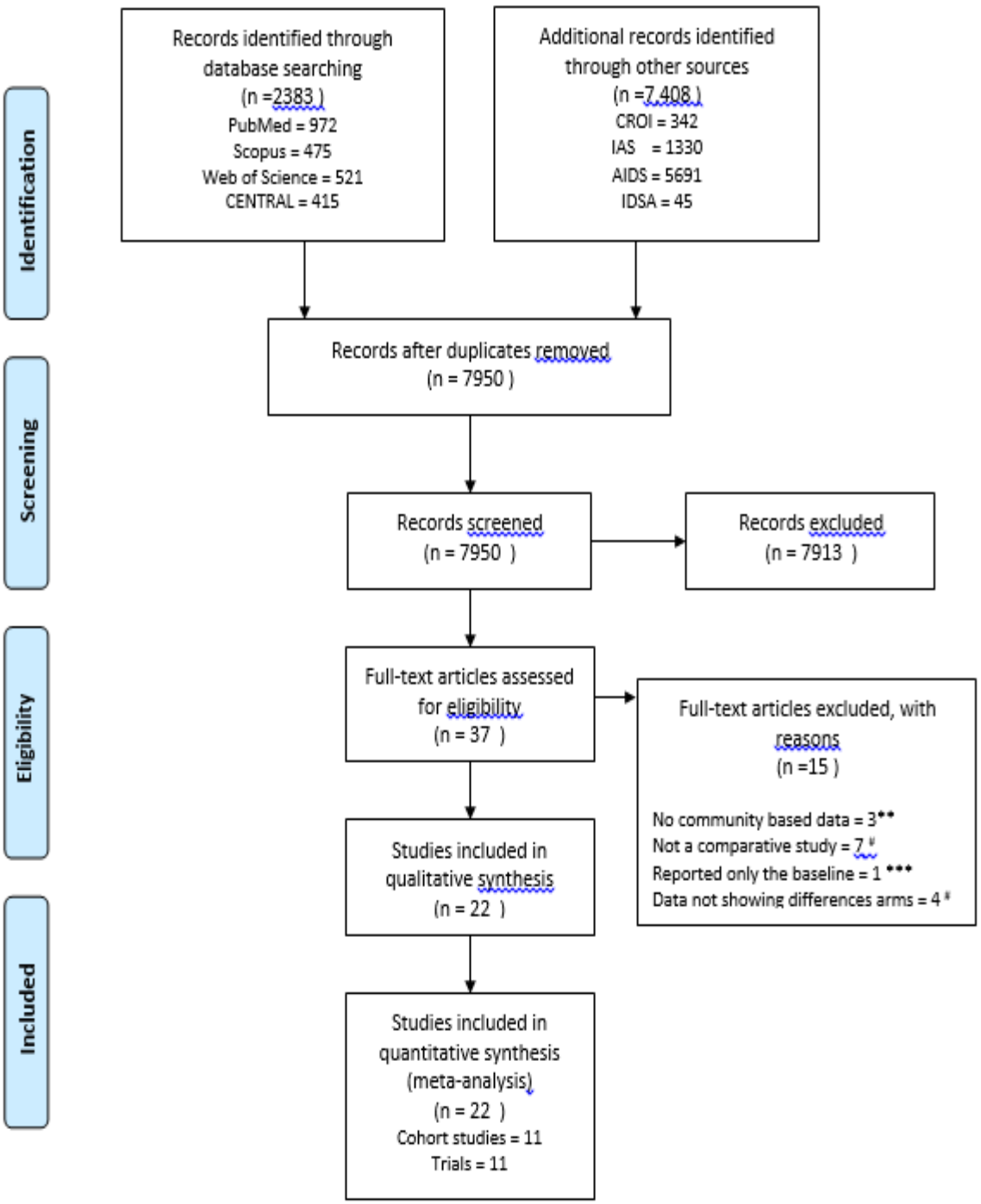

Figure 2: Forest plot of optimal ART adherence comparing community-based ART versus facility-based ART

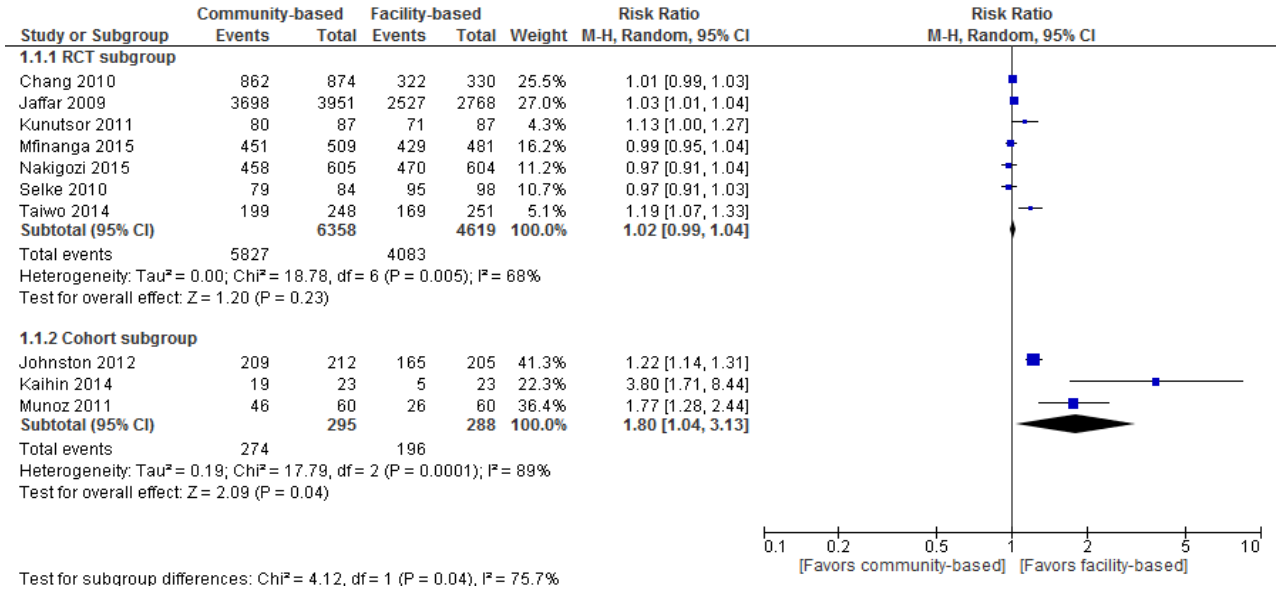

Figure 3: Forest plot of virologic suppression comparing community-based ART versus facility-based ART

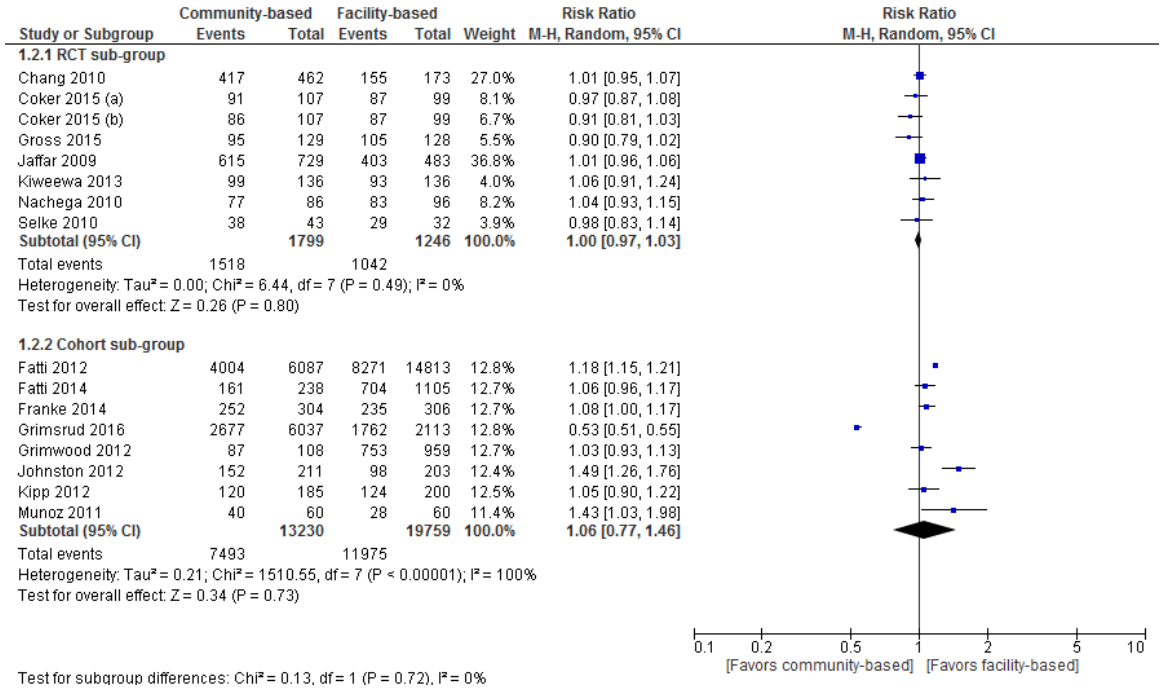

Figure 4: Forest plot of retention in care comparing community-based ART versus facility-based ART

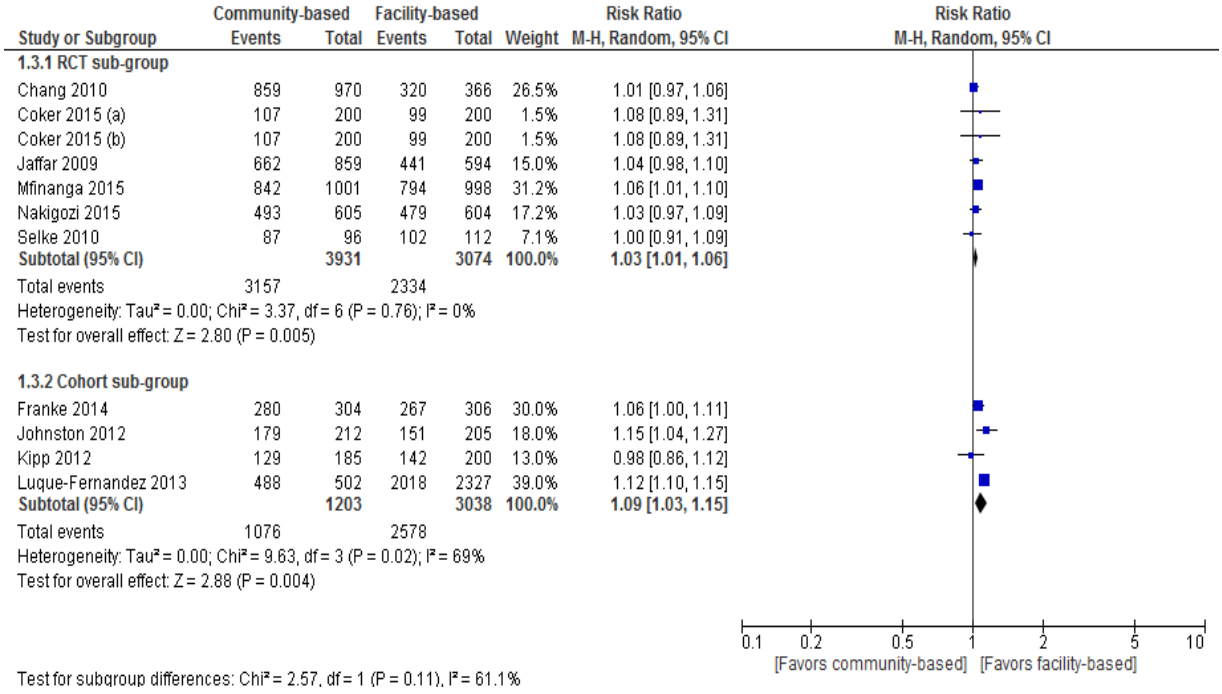

Figure 5: Forest plot of change in CD4 count comparing community-based ART versus facility-based ART

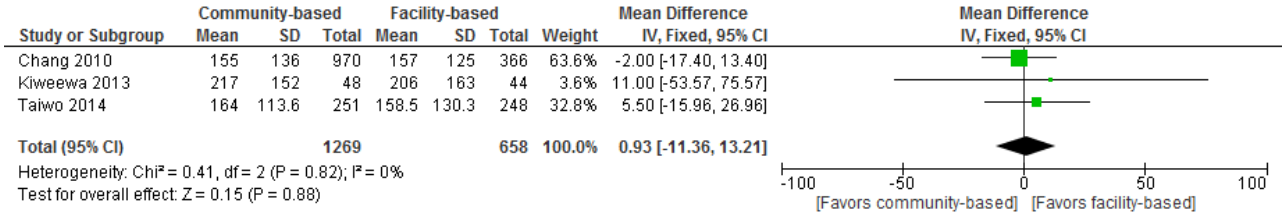

Figure 6: Forest plot of all-cause mortality comparing community-based ART versus facility-based ART

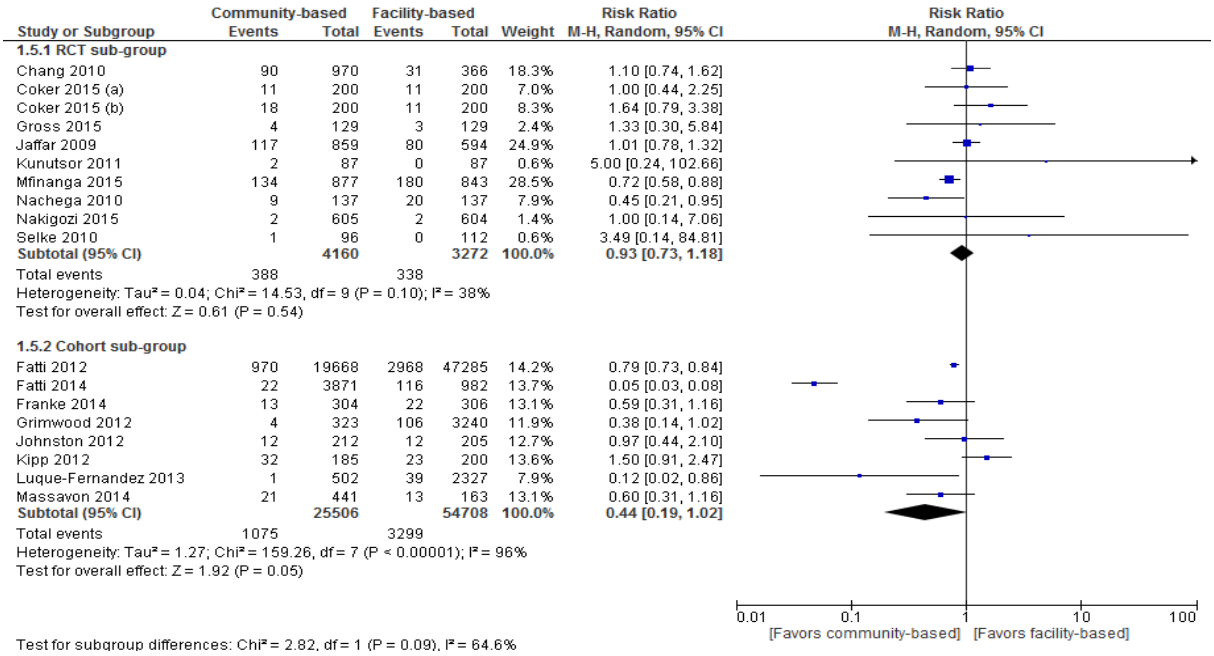

Figure 7: Forest plot of loss to follow-up comparing community-based ART versus facility-based ART