Title

Differentiated HIV care in sub-Saharan Africa: a scoping review to inform antiretroviral therapy provision for stable HIV-infected individuals in Kenya.

Authors

Hagey, Jill M
Li, Xuan
Barr-Walker, Jill
et al.

Publication Date

2018-07-23

Peer reviewed

Differentiated HIV Care in sub-Saharan Africa: A Scoping Review to Inform Antiretroviral Therapy Provision for Stable HIV-Infected Individuals in Kenya

Jill M Hagey[a]*, Xuan Li[b], Jill Barr-Walker[c], Jeremy Penner[d,e], Julie Kadima[d], Patrick Oyaro[d], Craig R Cohen[d,f]

[a]Department of Obstetrics and Gynecology, Duke University, Durham, NC, United States; [b]School of Medicine, Rush University, Chicago, IL, United States; [c]ZSFG Library, University of California San Francisco, San Francisco, CA, United States; [d]Family AIDS Care & Education Services, Kisumu, Kenya; [e]Department of Family Practice, University of British Columbia, Vancouver, Canada; [f]Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA, United States

*Corresponding Author: Jill M Hagey

C/o Craig R Cohen

550 16th Street

San Francisco, CA 94158, United States

Phone: 001 650 740 1373

Email: jmhagey@gmail.com

Differentiated HIV Care in sub-Saharan Africa: A Scoping Review to Inform Antiretroviral Therapy Provision for Stable HIV-Infected Individuals in Kenya

Many gaps in care exist for provision of antiretroviral therapy (ART) in sub-Saharan Africa. Differentiated HIV care tailors provision of ART for patients based on their level of acuity, providing alternatives for where, by whom, and how often care occurs. We conducted a scoping review to assess novel differentiated care models for ART provision for stable HIV-infected adults in sub-Saharan Africa, and how these models can be used to guide differentiated care implementation in Kenya. A systematic search was conducted using PubMed, Embase, Web of Science, Popline, Cochrane Library, and African Index Medicus between January 2006 and January 2017. Grey literature searches and handsearching were also used. We included articles that quantitatively assessed the health, acceptability, and cost effectiveness of differentiated HIV care. Two reviewers independently performed article screening, data extraction and determination of inclusion for analysis. We included 40 publications involving over 240,000 participants spanning nine countries in sub-Saharan Africa – 54.4% evaluated clinical outcomes, 23.5% evaluated acceptability outcomes, and 22.1% evaluated cost outcomes. Differentiated care models included: facility fast-track drug refills and appointment spacing, facility or community-based ART groups, community ART distribution points or home-based care, and task-shifting or decentralization of care. Studies suggest that these approaches had similar outcomes in viral load suppression and retention in care and were acceptable alternatives to standard HIV care. No clear results could be inferred for studies investigating task shifting and those reporting cost-effectiveness outcomes. Kenya has started to scale up differentiated care models, but further evaluation, quality improvement and research studies should be performed as different models are rolled out.

Introduction

HIV remains one of the leading causes of morbidity and mortality in Kenya, largely due to challenges testing, recruiting, and maintaining infected individuals in care. In Kenya, an estimated 56,000 adults acquired HIV in 2016, indicating an urgent need to improve HIV services (National AIDS Control Council, 2016; UNAIDS, 2016).

In July 2016, the Ministry of Health in Kenya published new HIV guidelines, including the use of "differentiated care" – adaptations in HIV service delivery including types of care delivery, locations of service delivery, service providers, and frequency of the services (National AIDS and STI Control Programme [NASCOP], 2016a, 2016b; Duncombe et al., 2015). The aim of differentiated care is to offer patient-centered care while reducing costs and burdens on the health system (NASCOP, 2017; World Health Organization [WHO], 2015). Since adoption of these guidelines, toolkits, training packages for healthcare workers, and patient educational materials have been created to help operationalize differentiated care for stable patients living with HIV (NASCOP, 2017; Waldrop, Doherty, Vitoria, & Ford, 2016).

Some strategies for expanding differentiated care are already being initiated in Kenya, including integration of HIV care into other facility-based structures and use of community-based HIV care (Odeny et al., 2013; Turan et al., 2015; Selke et al., 2010). However, implementation and evaluation of these strategies is ongoing, and there remain few reviews that investigate differentiated HIV care across the broad spectrum of care delivery (Callaghan, Ford & Schneider, 2010; Decroo et al., 2013; Harries, Makombe, Schouten, Ben-Smith & Jahn, 2008; Wouters, Van Damme, Van Rensburg, Masquillier & Meulemans, 2012). This scoping review describes the range of HIV care for stable patients within the differentiated care framework, with

the goal of aiding policy makers in Kenya and across sub-Saharan Africa as they expand these services.

Methods

Search Strategy

A systematic search of manuscripts on differentiated HIV care in sub-Saharan Africa published from January 2006 to January 2017 was conducted in PubMed, Embase, Web of Science, Popline, Cochrane Library, and African Index Medicus by a clinical librarian (JBW) using keywords and controlled vocabulary, including MeSH. Search terms included antiretroviral therapy (ART), care delivery, retention or adherence (given our focus on stable patients after initiation of care), and sub-Saharan Africa (Additional File 1). "Differentiated care" is a recent change in terminology to describe these interventions, so this term was not included in our search. Because the original searches yielded irrelevant results about HIV care for pregnant women and mother-to-child transmission, these terms were excluded.

Grey literature was searched to identify unpublished data, with a focus on consortiums involved in HIV care models and delivery. Handsearching of reference lists and key journals was also completed.

Study Selection

Articles were screened for inclusion by one author (JH) based on title and abstract, followed by the full text, with a second author (XL) checking a random sample of five percent to confirm inter-rater reliability. Criteria for inclusion were the following: based in sub-Saharan Africa; examined ART delivery methods for ongoing HIV care and treatment; involved patients who were considered "stable"; quantitatively tracked clinical, acceptability and sustainability, and/or cost effectiveness outcomes; and were analytic or descriptive studies. "Stable" patients

were defined using the Kenya Ministry of Health guidelines including: receiving current ART regimen for > 12 months, no active opportunistic infections, adherence to clinic visits in past six months, most recent viral load <1,000 copies/mL, completed six months of isoniazid prevention therapy, non-pregnant/not breastfeeding, BMI >18.5, and age >20 years (NASCOP, 2016a). As isoniazid prevention therapy is not standard of care across all countries in sub-Saharan Africa, studies were still included if this criteria was not met or explicitly discussed in the paper.

Intervention types are depicted in Figure 1. Appointment spacing increases appointment intervals to three to six months from typical one to two-month intervals. Facility fast-track ART refills also increase appointment intervals, but require patients to come for pharmacist refills between clinical appointments. Pharmacists conduct a brief review of symptoms to detect early signs of clinical instability, side effects or virologic failure. Facility-based ART groups involve groups of 10 to 30 patients who meet on a monthly or bi-monthly basis with a peer health worker. These groups provide adherence support and ART refills, allowing patients to bypass the clinic queues. Patients continue to have one-on-one clinical appointments at increased appointment intervals. Community-based ART groups (CAGs) are similar to their facility-based counterparts, but meetings occur at patients' homes or community meeting places. Community ART distribution allows patients to refill ART closer to their homes through mobile clinics or community meeting points. Home-based care employs healthcare providers or peer health workers to bring patients' ART refills at home. Decentralization is used to shift ART care provision from tertiary care centers to primary and secondary care centers closer to patients. Task shifting allows for stable patients on ART to be cared for by less specialized healthcare workers.

Clinical outcomes studied included retention in care, loss to follow up, improved CD4 count, virologic suppression, or mortality. Acceptability and sustainability outcomes included waiting time for care, willingness to continue in a specific model of care, or a number of qualitative markers regarding patient satisfaction. Cost-effectiveness outcomes included cost per patient-year, full time equivalents of health providers needed for care, and incremental cost-effectiveness ratio. If possible, these outcomes were compared with the standard of care for HIV provision in that country; generally one on one visits with a health provider at a health facility every one to three months.

Data Extraction

A standardized form was created to extract data on: 1) study setting, 2) study type and methodology, 3) characteristics of the intervention, and 4) results on outcomes of interest. Data extraction was completed by one reviewer (JH) with a second reviewer (XL) checking a random sample of ten percent. Final inclusion for analysis was determined by both reviewers.

Data Compilation and Analysis

Articles were summarized based on the type of intervention and the type of outcome measured. While there were differences in the reliability of the articles included in the final analysis, full appraisal of the quality of the individual articles is beyond the range of a scoping review.

Consultation

A consultation phase was employed in accordance with scoping review methodological standards to identify gaps in findings and contextualize these findings with current strategies of differentiated care in Kenya (Arksey & O'Malley, 2005; Levac, Colquhoun, O'Brien, 2010). Preliminary findings with a short survey were sent to a group of stakeholders, and snowball

sampling was used to reach others with differentiated care expertise. Our consultation yielded information consistent with the preliminary findings with no additional articles identified.

Results

The literature search yielded forty studies to be included in the final analysis, representing forty-eight different interventions spanning nine countries (Figure 2, Table 1, Additional File 2) (Moher, Liberati, Tetzlaff, Altman & The PRISMA Group, 2009).

Clinical Outcomes

Facility fast-track drug refills or appointment spacing

One program in Malawi found that patients enrolled in six-month appointment spacing had half the mortality and lost to follow-up rates compared with patients eligible for longer appointment spacing but who still received standard two-month appointment spacing (Cawley et al., 2016).

A fast-track program in Malawi has shown successful outcomes in 5 years – 97% cumulative retention, 2% loss to follow-up, and less than 1% mortality (MSF, 2013). Another fast-track ART model in Uganda only had 82% retention in the program; however, those not retained in the program were less adherent to ART than those described in other studies (Nakiwogga-Muwanga et al., 2014a). This program did result in similar favorable immune responses (CD4 cell count >500 cells/ul) compared with those receiving standard care (Babigumira et al., 2011).

Facility or community-based ART groups led by health care workers or peers

Patients in facility-based ART groups in Cape Town, South Africa had higher retention in care compared with individuals eligible for groups who did not participate (97% versus 85%), fewer missed appointments (19% versus 37%), and decreased loss to follow-up and viral rebound (MSF, 2013; Bango, Ashmore, Wilkinson, Van Cutsem & Cleary, 2016; Luque-Fernandez et al.,

2013). A similar model of facility-based ART groups in urban Kenya had a 4% lost to follow-up rate and no mortality among group participants after 12 months (Khabala et al., 2015).

CAGs in Tete, Mozambique found 95.1% retention in care, 4% mortality and 0.35% loss to follow-up after 20 months – much lower than the national lost to follow-up rate of 15%; and significantly higher retention in care and lower mortality compared with the standard of care (MSF, 2013; Decroo et al., 2011; Decroo et al., 2014; Decroo et al.; 2016). Similar groups were formed in Maputo, Mozambique with 95.5% retention in care after 2 years (MSF, 2013). These trends continued with national implementation of CAGs (Jobarteh et al., 2016).

Similar programs in Malawi and Lesotho resulted in 92% retention in care after 15 months and 98.7% retention in care after 12 months, respectively (MSF, 2013; Vandendyck et al., 2015). CAGs in South Africa have been implemented with high retention in care, low loss to follow-up, and low mortality rates (Grimsrud, Lesoky, Kalombo, Bekker & Meyer, 2015; Grimsrud, Lesoky, Kalombo, Bekker & Meyer 2015, 2016; Grimsrud, Sharp, Kalombo, Bekker & Meyer, 2015). Increasing the interval between CAG meetings from 2 months to 4 months resulted in similar loss to follow-up and viral load outcomes in a randomized controlled trial of this model in South Africa (Grimsrud et al., 2014).

Comparisons of facility-based ART groups and CAGs found lower retention in care and higher rates of referral back to standard care among CAGs, but similar viral load and CD4 cell count results between both models (Hanrahan et al., 2016; Pasipamire et al., 2016).

Community ART distribution points or home-based care

A comparison of community ART distribution points to standard care in rural Uganda found similar retention in care and ART adherence. Among patients using community ART distribution points, there was lower loss to follow-up and mortality, and higher mean CD4 count compared

with those in standard care (TASO, 2015). Similarly, another community distribution model in the Democratic Republic of Congo had 89% retention in care (MSF, 2013). Mobile clinics in Uganda had lower retention in care (79.0% at 24 months), but still low loss to follow-up (6.2%) and transfer of care (7.4%) (Kalibala et al., 2016).

Decentralization or task-shifting

Decentralization from hospitals to primary healthcare centers in Uganda and South Africa resulted in higher retention in care, lower loss to follow-up, similar mortality rates, and higher percentage of patients with undetectable viral loads (O'Connor, Osih & Jaffer, 2011; Long et al., 2011; Kipp et al., 2011; Grimsrud, Kaplan, Bekker & Meyer, 2014). Many countries such as Nigeria have incorporated decentralized care into their national ART programs, and similar retention in care was found among the sites before and after decentralization (Johns & Baruwa, 2016).

Patients receiving nurse-based care versus doctor-based care in South Africa reported similar rates of undetectable viral loads, retention in care and mortality (Barton et al., 2013; Fairall et al., 2012; Brennan et al., 2011). There was a significant increase in CD4 cell count for those receiving nurse-based care compared with doctor-based care (Fairall et al., 2012). A similar model elsewhere in South Africa found an increase in CD4 count for those receiving nurse-based care, but viral failure rates also decreased over the same time span. Nurses were less likely to identify virologic failure, and only slightly more than half of patients with virologic failure were referred for more specialized care (Uzodike, Ross & Harbor, 2015).

A review of different task-shifting models of care in Uganda found similar percentages of patients were retained in care, lost to follow-up, or died after 24 months in care;

but more patients reported good adherence at the minimally task shifted sites compared with maximally task shifted sites (70.7% versus 54.5%) (Kalibala et al., 2016).

Acceptability Outcomes

Facility fast-track drug refills or appointment spacing

Increasing appointment spacing from one to two-month appointments in Uganda significantly decreased waiting times and overall clinic time (Alamo et al., 2013). Pharmacist fast-track ART refills in Uganda also reduced waiting time, resulted in high patient satisfaction, and allowed patients to send a friend or relative on their behalf to pick up refills (Nakiwogga-Muwanga et al., 2014b; Castelnuovo et al., 2009).

Facility or community-based ART groups

Facility-based ART groups in Cape Town, South Africa reported shorter waiting times (67 minutes versus 176 minutes) and improved perception of adequate staffing (49% versus 34%) compared with standard of care (MSF, 2013; Bango, Ashmore, Wilkinson, van Cutsem & Cleary, 2013). CAGs in Mozambique were acceptable for providers as well, with an approximate 4-fold reduction in consultations among patients who were in CAGs (Decroo et al., 2011). The Malawi CAG program reduced ART refill visits by 62% and clinic visits by 49.6% after implementation of the CAG model, illustrating clinic decongestion with this model of care (MSF, 2013). Roll-out of similar groups in Lesotho led to shorter travel times and decongestion of the health facilities. Further, participants in the CAGs reported receiving support from others in their groups and decreased stigma (Vandendyck et al., 2015).

Community ART distribution points or home-based care

There is some conflicting data regarding waiting time and acceptability of community-based ART distribution points, particularly mobile clinics. Community-based ART distribution in the

Democratic Republic of Congo decreased mean waiting time from 85 to 12 minutes in comparison with hospital-based care (MSF, 2013). Mobile clinic ART refills in rural Uganda also resulted in decreased patient waiting time and increased patient and provider satisfaction (Sethi et al., 2010). However, a similar mobile clinic in Uganda resulted in a slightly lower satisfaction than in facility-based care, and there was still a considerable waiting time of 205 minutes before seeing a provider (Kalibala et al., 2016).

Another model using persons living with HIV as community care coordinators to provide ART dispensing at home or in the community was found to be acceptable in western Kenya. After two years, 64% of those receiving care from community care coordinators versus 52% of patients receiving standard care were willing to continue their method of care (Wools-Kaloustian et al., 2009).

Decentralization or task-shifting

No data on the acceptability of decentralization met criteria for inclusion in the review; however, task-shifting had some discrepant results in waiting time and patient satisfaction. A nurse-based care model in Uganda had higher waiting times than doctor-based care models; due in large part to nurse-clinicians spending twice as long with patients (Wanyenze et al., 2010). This is contrasted with task-shifting models in Nigeria and Uganda that showed a significant decrease in waiting time (Castelnuovo et al., 2009; Umar, Hajara & Khalifa, 2011).

Task-shifting of ART distribution from pharmacists to pharmacist assistants or nurses was not associated with a significant difference in waiting time (Foster & McIntyre, 2012).

Cost-Effectiveness Outcomes

Facility fast-track drug refills or appointment spacing

Minimal data is available on cost effectiveness of fast-track ART refills or appointment spacing. One study on pharmacist-only refills found a decreased cost per patient per year compared to standard care, with an incremental cost effectiveness ratio of US$13,500 per patient to achieve a CD4 count of greater than 500 cells/ul (Babigumira et al., 2011).

Facility-based or community-based ART groups

Analysis of facility-based ART groups in Cape Town, South Africa found that the absolute cost for facility-based ART groups was US$60 per stable patient per year compared with US$128 per stable patient per year for the standard of care (MSF, 2013; Bango et al., 2013). CAGs in Lesotho were found to have decreased patient transport cost, but no information was published on health facility costs (Vandendyck et al., 2015).

Community ART distribution points or home-based care

Cost analysis of a community-based ART distribution model in the Democratic Republic of Congo indicated decreased human resource expenditures and transportation costs compared with nearby hospitals (MSF, 2013). Additionally, a Ugandan mobile clinic found patients paid on average US$0.88 per month for ART refills, an average monthly net savings of US$10.70 per patient (Sethi et al., 2010). However, other cost analyses of mobile clinics in Uganda found a higher annual cost of providing services of US$404 per patient than facility-based models (US$257-332) (Kalibala et al., 2016).

Decentralization or task-shifting

Decentralization and task-shifting have largely been found to be cost-effective, but can also be associated with large start-up costs. Referral to a lower level of care in urban South Africa

resulted in the cost per retained patient in care responding to treatment after 12 months of US$509 compared with US$602 among those who stayed in hospital care (Long et al., 2011). Another study in rural Uganda found that the cost per patient in both a centralized model and a decentralized model were similar at approximately US$100 per patient per year (Kipp et al., 2011). The cost per patient-year at decentralized care was higher than standard care in one region of Nigeria while lower in another region, indicating local factors may contribute to cost discrepancies (Johns & Baruwa, 2016).

Task-shifting models in Uganda decreased costs per patient and national costs for HIV care with nurse-based care or pharmacist-based care, largely due to the decrease in full time equivalents (FTEs) of physician time (Kalibala et al., 2016; Babigumira et al., 2009). The opposite trend was true in South Africa – nurse-based care was more expensive than doctor-based care with an incremental cost effectiveness ratio of US$12,539 per patient with an undetectable viral load annually. However, the authors noted that long-term costs of nurse-based care could be cheaper after initial start-up costs (Barton et al., 2013).

One final study found that the total cost per patient was slightly higher with full-time pharmacist care in comparison with pharmacist assistant or nurse care, but this task-shifting was not helpful in increasing the ratio of FTEs to patients enrolled in care (Foster & McIntyre, 2012).

Discussion

This scoping review seeks to fill the gaps in knowledge around differentiated HIV care for stable patients in sub-Saharan Africa. Across all models of differentiated care, similar outcomes were found in retention in care, loss to follow up, and virologic suppression in comparison to the standard of care. Acceptability outcomes were generally improved with the differentiated care models; however, certain community-based ART distribution points and task shifted models that

actually increased waiting time, likely due to inefficiencies in non-routine healthcare providers implementing clinical care. Additionally, given that acceptability is a subjective outcome, there were few models that provided a standardized rubric for measuring acceptability. Finally, cost-effectiveness outcomes were varied as well, with mostly decreased costs overall, but with some increased start-up costs for both community-based ART distribution points and task shifted models. All studies that evaluated cost to the patient showed decreased patient costs with decentralized models.

While the initial search attempted to identify differentiated care models across all of sub-Saharan Africa, interventions from only nine countries met our inclusion criteria, an indication that this is an area where more research is sorely needed. Additionally, assessing differentiated care for other key groups such as pregnant women and children were beyond the scope of this review. Lastly, assessing the quality of these studies was outside the range of this review; however, the number of descriptive studies as opposed to empirical investigations is indicative of the need for use of more rigorous study designs.

Conclusions

Our findings show that in key countries in sub-Saharan Africa, differentiated care models have similar outcomes in viral load suppression and retention in care and were acceptable alternatives to standard HIV care. Focus on program quality and efficiency must be highlighted, and Kenya must learn from evaluations of pilot programs within the country. Kenya has the opportunity to be a leader in differentiated care, but evaluation, quality improvement, and robust research studies must follow to ensure improved care for those living with HIV in Kenya.

Acknowledgements: The authors would like to thank the stakeholders who participated in the consultative phase of this scoping review: Maureen Inimah, Edwin Mulwa, and Rena Patel for providing commentary and insights regarding differentiated care in Kenya.

The authors would like to acknowledge the Family AIDS Care & Education Services (FACES) Differentiated Care Team: Dr. Lisa Abuogi, Dr. Maurice Aluda, Cinthia Blat, Dr. Elvin Geng, Mary Guze, Dr. Charles Kibaara, Jayne Lewis-Kulzer, Edwin Mulwa, Dr. Thomas Odeny, and Dr. Rena Patel for their support of this work. The authors would also like to thank the Kenya Ministry of Health and the National AIDS and STI Control Programme for their leadership in differentiated care.

References:

Alamo, S.T., Wagner, G.J., Ouma, J., Sunday, P., Marie, L., Colebunders, R., & Wabwire-Mangen, F. (2013). Strategies for Optimizing Clinic Efficiency in a Community-Based Antiretroviral Treatment Programme in Uganda. *AIDS Behav*, 17(1), 274-83.

Arksey, H. & O'Malley, L. (2005). Scoping studies: towards a methodological framework. *International J Soc Res Meth*. 8(1), 19-32.

Babigumira, J.B., Castelnuovo, B., Lamorde, M., Kambugu, A., Stergachis, A., Easterbrook, P., & Garrison, L.P. (2009). Potential impact of task-shifting on costs of antiretroviral therapy and physician supply in Uganda. *BMC Health Serv Res*, 9:192.

Babigumira, J.B., Castelnuovo, B., Stergachis, A., Kiragga, A., Shaefer, P., Lamorde, M., … Garrison, L.P. (2011). Cost Effectiveness of a Pharmacy-Only Refill Program in a Large Urban HIV/AIDS Clinic in Uganda. *PLoS ONE*, 6(3), e18193.

Bango, F., Ashmore, J., Wilkinson, L., Van Cutsem, G., Cleary, S. (2013, December). *Cost effectiveness of ART adherence clubs for long term management of clinically stable ART patients* [Poster]. Presented at 17th International Conference on AIDS and STIs in Africa (ICASA), Cape Town, South Africa.

Bango, F., Ashmore, J., Wilkinson, L., Van Cutsem, G., & Cleary, S. (2016). Adherence clubs for long-term provision of antiretroviral therapy: cost-effectiveness and access analysis from Khayelitsha, South Africa. *Trop Med Int Health*, 21(9), 1115-23.

Barton, G.R., Fairall, L., Bachmann, M.O., Uebel, K., Timmerman, V., Lombard, C., & Zwarenstein, M. (2013). Cost-effectiveness of nurse-led versus doctor-led antiretroviral treatment in South Africa: pragmatic cluster randomised trial. *Trop Med Int Health*, 18(6), 769-77.

Brennan, A.T., Long, L., Maskew, M., Sanne, I., Jaffray, I., MacPhail, P., & Fox, M.P. (1022). Outcomes of stable HIV-positive patients down-referred from a doctor-managed antiretroviral therapy clinic to a nurse-managed primary health clinic for monitoring and treatment. *AIDS*, 25(16), 2027-36.

Callaghan, M., Ford, N., & Schneider, H. (2010). A systematic review of task-shifting for HIV treatment and care in Africa. *Hum Resour Health*, 8(1), 8.

Castelnuovo, B., Babigumira, J., Lamorde, M., Muwanga, A., Kambugu, A., & Colebunders, R. (2009). Improvement of the patient flow in a large urban clinic with high HIV seroprevalence in Kampala, Uganda. *Int J STD AIDS*, 20, 123-4.

Cawley, C., Nicholas, S., Szumilin, E., Perry, S., Amoros Quiles, I., Masiku, C., & Wringe, A. (2016). Six-monthly appointments as a strategy for stable antiretroviral therapy patients: evidence of its effectiveness from seven years of experience in a Medecins Sans Frontieres supported programme in Chiradzulu district, Malawi [Abstract]. *J Int AIDS Soc*, 19(6 Suppl 5), 21264.

Decroo, T., Koole, O., Remartinez, D., Dos Santos, N., Dezembro, S., Jofrisse, M., … Laga, M. Four-year retention and risk factors for attrition among members of community ART groups in Tete, Mozambique. *Trop Med Int Health*, 19(5), 514-21.

Decroo, T., Rasschaert, F., Telfer, B., Remartinez, D., Laga, M., & Ford, N. (2013). Community-based antiretroviral therapy programs can overcome barriers to retention of patients and decongest health services in sub-Saharan Africa: a systematic review. *Int Health*, 5(3), 169-79.

Decroo, T., Telfer, B., Biot, M., Maikere, J., Dezembro, S., Cumba, L.I., … Ford, N. (2011). Distribution of Antiretroviral Treatment Through Self-Forming Groups of Patients in Tete Province, Mozambique. *J Acquir Immune Defic Syndr*, 56(2), e39-44.

Decroo, T., Telfer, B., Das Dores, C., Candrinho, B., Dos Santos, N., Mkwamba, A., … Metcalf, C. (2016). The effect of community ART groups on retention-in-care among patients on ART in Tete province, Mozambique [Abstract]. *J Int AIDS Soc*, 19(6 Suppl 5), 21264.

Duncombe, C., Rosenblum, S., Hellmann, N., Holmes, C., Wilkinson, L., Biot, M., … Garnett, G. (2015). Reframing HIV care: putting people at the centre of antiretroviral delivery. *Trop Med Int Health*, 20(4), 430-447.

Fairall, L., Bachmann, M.O., Lombard, C., Timmerman, V., Uebel, K., Zwarenstein, M., … Bateman, E. (2012). Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial. *Lancet*, 380, 889-98.

Foster, N., McIntyre, D. (2012). Economic evaluation of task-shifting approaches to the dispensing of anti-retroviral therapy. *Hum Resour Health*, 10, 32.

Grimsrud, A., Kaplan, R., Bekker, L.G., & Myer, L. (2014). Outcomes of a nurse-managed service for stable HIV-positive patients in a large South African public sector antiretroviral therapy programme. *Trop Med Int Health*, 19(9), 1029-39.

Grimsrud, A., Lesosky, M., Kalombo, C., Bekker, L.G., & Myer, L. (2015). Community-based adherence clubs improve outcomes for stable antiretroviral therapy patients: findings from Gugulethu, South Africa [Abstract]. *J Int AIDS Soc*, 18, 77.

Grimsrud, A., Lesosky, M., Kalombo, C., Bekker, L.G., & Myer, L. (2016). Community-Based Adherence Clubs for the Management of Stable Antiretroviral Therapy Patients in Cape Town, South Africa: A Cohort Study. *J Acquir Immune Defic Syndr*, 71, e16-25.

Grimsrud, A., Patten, G., Sharp, J., Myer, L., Wilkinson, L., & Bekker, L.G. (2014). Extending Dispensing Intervals for Stable Patients on ART [Letter]. *J Acquir Immune Defic Syndr*, 66(2), e58-60.

Grimsrud, A., Sharp, J., Kalombo, C., Bekker, L.G., & Myer, L. (2015). Implementation of community-based adherence clubs for stable antiretroviral therapy patients in Cape Town, South Africa. *J Int AIDS Soc*, 18, 19984.

Hanrahan, C., Keyser, V., Schwartz, S., Soyizwaphi, P., West, N., Mutunga, L., … Van Rie, A. (2016). One year retention in community versus clinic-based adherence clubs for stable ART patients in South Africa: findings from a randomized controlled trial [Abstract]. *J Int AIDS Soc*, 19(6 Suppl 5), 21264.

Harries, A.D., Makombe, S.D., Schouten, E.J., Ben-Smith, A., & Jahn, A. (2008). Different delivery models for antiretroviral therapy in sub-Saharan Africa in the context of "Universal Access." *Trans R Soc Trop Med Hyg*, 102(4), 310-1.

Igumbor, J., Pascoe, S., Rajap, S., Townsend, W., Sargent, J., Darkoh, E. (2014). A South African Public-Private Partnership HIV Treatment Model: Viability and Success Factors. *PLoS ONE*, 9(10), e110635.

Jobarteh, K., Shiraishi, R.W., Malimane, I., Samo Gudo, P., Decroo, T., Auld, A.F., … Couto, A. (2016). Community ART Support Groups in Mozambique: The Potential of Patients as Partners in Care. *PLoS One*, 11(12), e0166444.

Johns, B., & Baruwa, E. (2016). The effects of decentralizing anti-retroviral services in Nigeria on costs and service utilization: two case studies. *Health Policy Plan*, 31, 182-91.

Kalibala, S., Okal, J., Zieman, B., Jani, N., Vu, L., Ssali, L., … Yiga, R. (2016). *Retrospective review of task-shifting community-based programs supporting ARV treatment and retention in Uganda*. Washington, DC: United States Agency for International Development (USAID).

Khabala, K.B., Edwards, J.K., Baruani, B., Sirengo, M., Musembi, P., Kosgei, R.J., … Reid, T. (2015). Medication Adherence Clubs: a potential solution to managing large numbers of stable patients with multiple chronic diseases in informal settlements. *Trop Med Int Health*, 20(10), 1265-70.

Kipp, W., Konde-Lule, J., Rubaale, T., Okech-Ojony, J., Alibhai, A., & Saunders, D.L. (2011). Comparing antiretroviral treatment outcomes between a prospective community-based and hospital-based cohort of HIV patients in rural Uganda. *BMC Int Health Hum Rights*, 11(S2), S12.

Levac, D., Colquhoun, H., & O'Brien, K.K. (2010). Scoping studies: advancing the methodology. *Implement Sci*, 5, 69.

Long, L., Brennan, A., Fox, M.P., Ndibongo, B., Jaffray, I., Sanne, I., & Rosen, S. (2011). Treatment Outcomes and Cost-Effectiveness of Shifting Management of Stable ART Patients to Nurses in South Africa: An Observational Cohort. *PLoS Med*, 8(7), e1001055.

Luque-Fernandez, M.A., Van Cutsem, G., Goemaere, E., Hilderbrand, K., Schomaker, M., Mantangana, N., … Boulle, A. (2013). Effectiveness of Patient Adherence Groups as a Model of Care for Stable Patients on Antiretroviral Therapy in Khayelitsha, Cape Town, South Africa. *PLoS One*, 8(2), e56088.

Medecins Sans Frontieres (MSF): MSF Analysis & Advocacy Unit Brussels with Southern Africa Medical Unit. (2013). *Reaching Closer to Home: Progress implementing community-based and other adherence strategies supporting people on HIV treatment*. Brussels, MSF.

Moher D., Liberati A., Tetzlaff J., Altman D.G., & The PRISMA Group. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*, 6(7), e1000097.

Nakiwogga-Muwanga, A., Katabira, E., Kiragga, A., Kambugu, A., Nakibuuka-Lubwama, E., Manabe, Y.C., … Colebunders, R. (2014). Factors before enrolment are associated with

being removed from a Pharmacy-only Refill Programme at a large urban HIV/AIDS clinic, Uganda. *Int J STD AIDS*, 25(2), 105-12.

Nakiwogga-Muwanga, A., Katabira, E., Sempa, J., Kambugu, A., Nakibuuka-Lubwama, E., Lamorde, M., … Colebunders, R. (2014). A Pharmacy-Only Refill Program at a Large HIV Clinic in Uganda: Experience and Satisfaction of Patients. *Journal Int Assoc Provid AIDS Care*, 13(3), 264-8.

National AIDS and STI Control Programme (NASCOP), Kenya. (2016a). *Guidelines on use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya 2016.* Nairobi: NASCOP.

National AIDS and STI Control Programme (NASCOP), Kenya. (2016b). *Improving the Quality and Efficiency of Health Services in Kenya: A Practical Handbook for HIV Managers and Service Providers on Differentiated Care.* Nairobi, NASCOP.

National AIDS and STI Control Programme (NASCOP), Kenya. (2017). *Differentiated Care: Operational Guide.* Nairobi: NASCOP.

National AIDS Control Council (NACC), Kenya. (2016). *Kenya AIDS Response Progress Report 2016.* Nairobi: NASCOP.

O'Connor, C., Osih, R., & Jaffer, A. (2011). Loss to Follow-Up of Stable Antiretroviral Therapy Patients in a Decentralized Down-Referral Model of Care in Johannesburg, South Africa. *J Acquir Immune Defic Syndr*, 58, 429-32.

Odeny, T.A., Penner, J., Lewis-Kulzer, J., Leslie, H.H., Shade, S.B., Adero, W., … Bukusi, E.A. (2013). Integration of HIV Care with Primary Health Care Services: Effect on Patient Satisfaction and Stigma in Rural Kenya. *AIDS Res Treat*, 2013, 485715.

Pasipamire, L., Kerschberger, B., Zabsonre, I., Ndlovu, S., Sibanda, G., Mamba, S., … Rusch, B. (2016). Implementation of combination ART refills models in rural Swaziland [Abstract]. *J Int AIDS Soc*, 19(6 Suppl 5), 21264.

Selke, H.M., Kimaiyo, S., Sidle, J.E., Vedanthan, R., Tierney, W.M., Shen, C., … Wools-Kaloustian, K. (2010). Task-shifting of antiretroviral delivery from health care workers to persons living with HIV/AIDS: clinical outcomes of a community-based program in Kenya. *J Acquir Immune Defic Syndr*, 55(4), 483-90.

Sethi, A., Bajunirwe, F., Ayebazibwe, N., Mafigin, D., Eng, M., McGrath, J., … Mugyenyi, P. (2010). Feasibility and Effectiveness of a Mobile Antiretroviral Pharmacy in Rural Southwestern Uganda [Abstract]. *J Int Assoc Phys AIDS Care*, 9(4), 261.

The AIDS Support Organization (TASO). (2015). *The TASO Community Drug Distribution Points (CDDP) Model*. Kampala: TASO.

Turan, J.M., Onono, M., Steinfeld, R.L., Shade, S.B., Owuor, K., Washington, S., … Cohen, C.R. (2015). Effects of Antenatal Care and HIV Treatment Integration on Elements of the PMTCT Cascade: Results From the SHAIP Cluster-Randomized Controlled Trial. *J Acquir Immune Defic Syndr*, 69(5), e172-81.

Umar, N.A., Hajara, M.J., & Khalifa, M. (2011). Reduction of client waiting time using task shifting in an anti-retroviral clinic at Specialist Hospital Bauchi, Nigeria. *J Public Health Afr*, 2, e2.

United Nations Programme on HIV/AIDS (UNAIDS). (2016). *Kenya Country Factsheet 2016.* Accessed at: www.unaids.org.

Uzodike, N., Ross, A., & Harbor, O. (2015). Adherence by a primary healthcare clinic in KwaZulu-Natal to the national HIV guidelines. *South African Family Practice*, 57(3), 198-202.

Vandendyck, M., Motsamai, M., Mubanga, M., Makhakhe, S., Tunggal, S., Jonckheree, S., … Decroo, T. (2015). Community-Based ART Resulted in Excellent Retention and Can Leverage Community Empowerment in Rural Lesotho, A Mixed Method Study. *HIV/AIDS Res Treat*, 2(2), 44-50.

Waldrop, G., Doherty, M., Vitoria, M., & Ford, N. (2016). Stable patients and patients with advanced disease: consensus definitions to support sustained scale up of antiretroviral therapy. *Trop Med Int Health*, 21(9), 1124-30.

Wanyenze, R.K., Wagner, G., Alamo, S., Amanyire, G., Ouma, J., Kwarisima, D., … Kamya, M. (2010). Evaluation of the Efficiency of Patient Flow at Three HIV Clinics in Uganda. *AIDS Patient Care STDs*, 24(7), 441-6.

Wools-Kaloustian, K.K., Sidle, J.E., Selke, H.M., Vedanthan, R., Kemboi, E.K., Boit, L.J., … Kimaiyo, S. (2009). A model for extending antiretroviral care beyond the rural health centre. *J Int AIDS Soc*, 12, 22.

World Health Organization (WHO). (2015). *HIV Treatment and Care: What's New in Service Delivery.* Geneva: WHO.

Wouters, E., Van Damme, W., Van Rensburg, D., Masquillier, C., & Meulemans, H. (2012). Impact of community-based support services on antiretroviral treatment program delivery and outcomes in resource-limited countries: a synthetic review. *BMC Health Serv Res*, 12(1), 194.

Figure 1. Differentiated Care Models. Depiction of novel models of differentiated care for stable patients presented in scoping review compared with the standard of care ("traditional ART care").

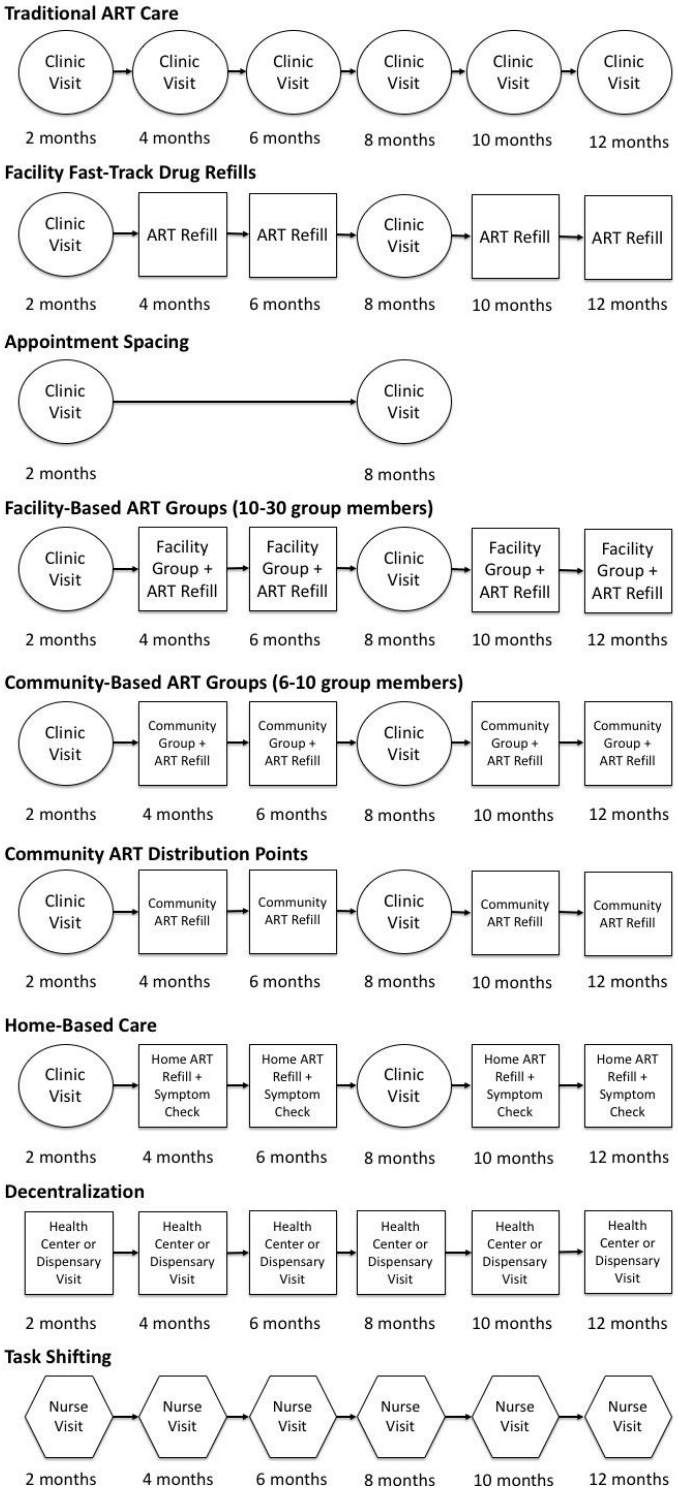

Figure 1. PRISMA Chart. Study selection flowchart for final inclusion in analysis of scoping review on differentiated ART delivery for stable patients.
*SSA: Sub-Saharan Africa

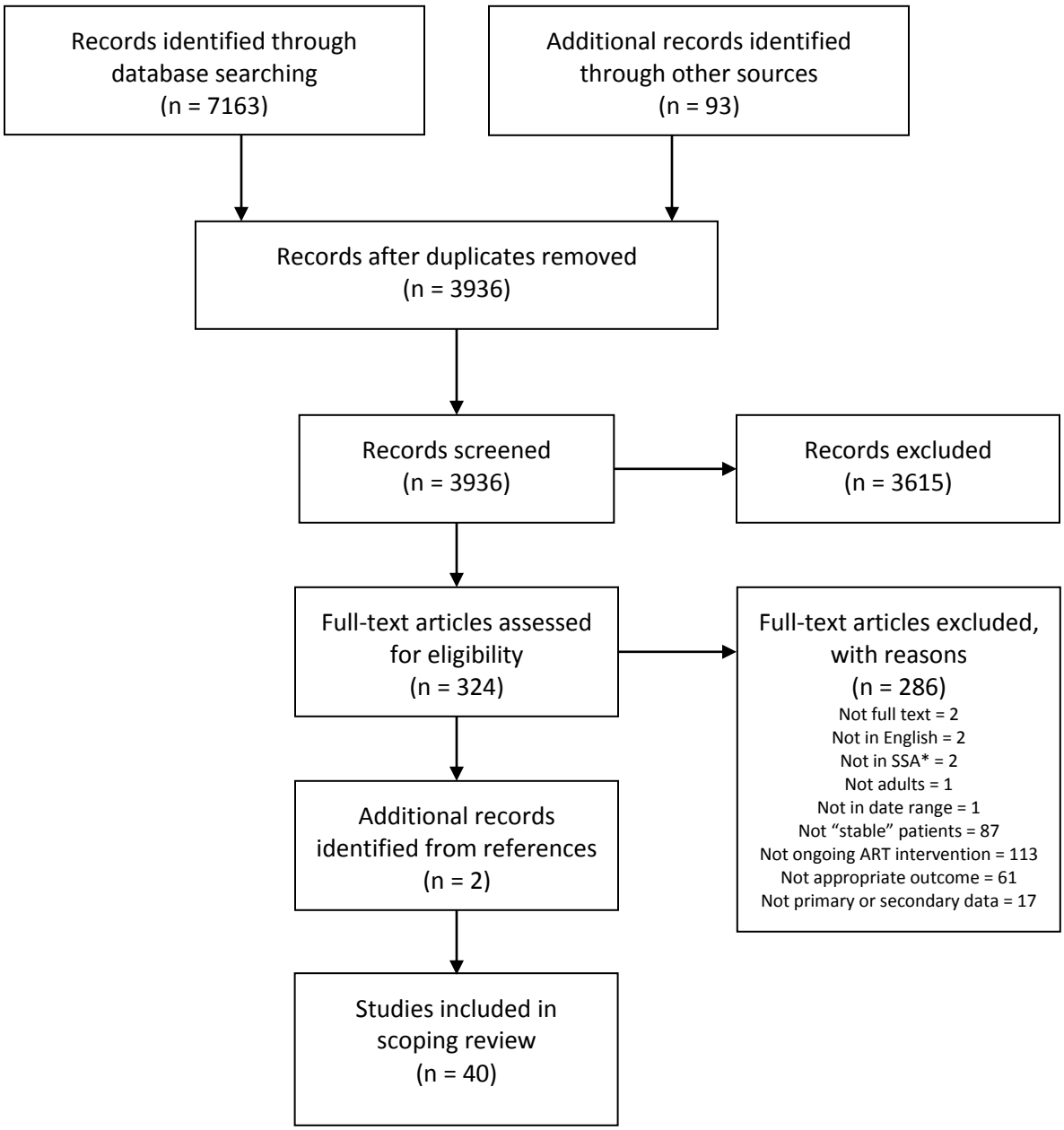

Table 1. Study Characteristics. Characteristics of articles included in scoping review on differentiated ART delivery for stable patients.

Characteristic	N (%)[§, *]
Study Type	
- Randomized controlled trial	4 (8.3%)
- Cohort study	14 (29.2%)
- Cross-sectional study	8 (16.7%)
- Descriptive study	18 (37.5%)
- Costing study	4 (8.3%)
Study Location	
- South Africa	18 (35.3%)
- Uganda	13 (25.5%)
- Mozambique	6 (11.8%)
- Malawi	3 (5.9%)
- Swaziland	3 (5.9%)
- Lesotho	3 (5.9%)
- Kenya	2 (3.9%)
- Nigeria	2 (3.9%)
- Democratic Republic of Congo	1 (2.0%)
Urban/Rural	
- Urban	23 (47.9%)
- Rural	21 (43.8%)
- Both	4 (8.3%)
Intervention Type	
- Facility Fast-track drug refill or appointment spacing	7 (13.2%)
- Facility or community-based ART groups	22 (41.5%)
- Community ART distribution points or home-based	5 (9.4%)
care	19 (35.8%)
- Decentralization or task-shifting	
Outcome Types	
- Clinical outcome	37 (54.4%)
- Acceptability outcome	16 (23.5%)
- Cost outcome	15 (22.1%)

[§] Number of studies may add up to more than 40 in characteristics because some publications described multiple interventions.

*Sum may not add to 100% due to rounding.

Additional file 1: Search Strategy Details

Database	Search Strategy	Number of Results
PubMed	(("HIV Infections/drug therapy"[MeSH] OR "Anti-Retroviral Agents/therapeutic use"[MeSH] OR "Anti-HIV Agents/therapeutic use"[MeSH] OR "Anti-Retroviral Agents/administration and dosage"[MeSH] OR "Antiretroviral Therapy, Highly Active"[MeSH] OR antiretroviral[tiab] OR antiretrovirals[tiab] OR "ART") AND (Differentiated[tiab] OR differentiating[tiab] OR differentiate[tiab] OR care[tiab] OR integration[tiab] OR integrated[tiab] OR integrating[tiab]) AND (africa[tiab] OR uganda[tiab] OR kenya[tiab] OR mozambique[tiab] OR swaziland[tiab] OR zambia[tiab] OR tanzania[tiab] OR nigeria[tiab] OR cameroon[tiab] OR malawi[tiab] OR ethiopia[tiab] OR congo[tiab] OR lesotho[tiab] OR botswana[tiab] OR angola[tiab] OR burundi[tiab] OR "central african republic"[tiab] OR chad[tiab] OR guinea[tiab] OR gabon[tiab] OR rwanda[tiab] OR sudan[tiab] OR djibouti[tiab] OR eritea[tiab] OR somalia[tiab] OR comoros[tiab] OR madagascar[tiab] OR mauritius[tiab] OR namibia[tiab] OR seychelles[tiab] OR benin[tiab] OR mali[tiab] OR "burkina faso"[tiab] OR "cape verde"[tiab] OR gambia[tiab] OR ghana[tiab] OR liberia[tiab] OR niger[tiab] OR senegal[tiab] OR "sierra leone"[tiab] OR togo[tiab] OR mauritania[tiab] OR ivoire[tiab] OR ivory[tiab] OR "sao tome"[tiab]) AND (Retention[tiab] OR adherence[tiab] OR follow-up[tiab] OR “follow up”[tiab] OR LTFU[tiab] OR suppression[tiab] OR maintenance[tiab] OR stable[tiab] OR decentralize[tiab] OR decentralized[tiab] OR decentralizing[tiab] OR decentralization[tiab] OR decentralise[tiab] OR decentralised[tiab] OR decentralising[tiab] OR decentralization[tiab])) NOT (pmtct[tiab] OR mtct[tiab] OR mother[tiab] OR pregnant[tiab] OR pregnancy[tiab])	1151
Embase	((antiretroviral OR antiretrovirals OR ‘antiretrovirus agent’/exp OR ART) AND (Differentiated OR differentiating OR differentiate OR care OR integration OR integrated OR integrating) AND (africa OR uganda OR kenya OR mozambique OR swaziland OR zambia OR tanzania OR nigeria OR cameroon OR malawi OR ethiopia	2619

	OR congo OR lesotho OR botswana OR angola OR burundi OR "central african republic" OR chad OR guinea OR gabon OR rwanda OR sudan OR djibouti OR eritea OR somalia OR comoros OR madagascar OR mauritius OR namibia OR seychelles OR benin OR mali OR "burkina faso" OR "cape verde" OR gambia OR ghana OR liberia OR niger OR senegal OR "sierra leone" OR togo OR mauritania OR ivoire OR ivory OR "sao tome") AND (retention OR adherence OR follow-up OR “follow up” OR LTFU OR suppression OR maintenance OR stable OR decentralize OR decentralise OR decentralized OR decentralised OR decentralizing OR decentralising OR decentralization OR decentralisation)) NOT (pmtct OR mtct OR mother OR pregnant OR pregnancy)	
Web of Science	((antiretroviral OR antiretrovirals OR ART) AND (Differentiated OR differentiating OR differentiate OR care OR integration OR integrated OR integrating) AND (africa OR uganda OR kenya OR mozambique OR swaziland OR zambia OR tanzania OR nigeria OR cameroon OR malawi OR ethiopia OR congo OR lesotho OR botswana OR angola OR burundi OR "central african republic" OR chad OR guinea OR gabon OR rwanda OR sudan OR djibouti OR eritea OR somalia OR comoros OR madagascar OR mauritius OR namibia OR seychelles OR benin OR mali OR "burkina faso" OR "cape verde" OR gambia OR ghana OR liberia OR niger OR senegal OR "sierra leone" OR togo OR mauritania OR ivoire OR ivory OR "sao tome") AND (retention OR adherence OR follow-up OR “follow up” OR LTFU OR suppression OR maintenance OR stable OR decentralize OR decentralise OR decentralized OR decentralised OR decentralizing OR decentralising OR decentralization OR decentralisation)) NOT (pmtct OR mtct OR mother OR pregnant OR pregnancy)	1651
Popline	((antiretroviral OR antiretrovirals OR ART) AND (Differentiated OR differentiating OR differentiate OR care OR integration OR integrated OR integrating) AND (africa OR uganda OR kenya OR mozambique OR swaziland OR zambia OR tanzania OR nigeria OR cameroon OR malawi OR ethiopia OR congo OR lesotho OR botswana OR angola OR burundi OR "central african republic" OR chad	1526

	OR guinea OR gabon OR rwanda OR sudan OR djibouti OR eritea OR somalia OR comoros OR madagascar OR mauritius OR namibia OR seychelles OR benin OR mali OR "burkina faso" OR "cape verde" OR gambia OR ghana OR liberia OR niger OR senegal OR "sierra leone" OR togo OR mauritania OR ivoire OR ivory OR "sao tome") AND (retention OR adherence OR follow-up OR “follow up” OR LTFU OR suppression OR maintenance OR stable OR decentralize OR decentralise OR decentralized OR decentralised OR decentralizing OR decentralising OR decentralization OR decentralisation)) NOT (pmtct OR mtct OR mother OR pregnant OR pregnancy)	
Cochrane Library: DARE	((antiretroviral OR antiretrovirals OR ART) AND (Differentiated OR differentiating OR differentiate OR care OR integration OR integrated OR integrating) AND (africa OR uganda OR kenya OR mozambique OR swaziland OR zambia OR tanzania OR nigeria OR cameroon OR malawi OR ethiopia OR congo OR lesotho OR botswana OR angola OR burundi OR "central african republic" OR chad OR guinea OR gabon OR rwanda OR sudan OR djibouti OR eritea OR somalia OR comoros OR madagascar OR mauritius OR namibia OR seychelles OR benin OR mali OR "burkina faso" OR "cape verde" OR gambia OR ghana OR liberia OR niger OR senegal OR "sierra leone" OR togo OR mauritania OR ivoire OR ivory OR "sao tome") AND (retention OR adherence OR follow-up OR “follow up” OR LTFU OR suppression OR maintenance OR stable OR decentralize OR decentralise OR decentralized OR decentralised OR decentralizing OR decentralising OR decentralization OR decentralisation)) NOT (pmtct OR mtct OR mother OR pregnant OR pregnancy)	175
African Index Medicus	(ART OR antiretroviral OR antiretrovirals) AND (care)	41
Total before duplicates		7163
Number of duplicates		3257
Total after de-duplication		3906

Additional File 2: Full Text Articles for Scoping Review

Intervention Type	**Outcome Type**	**Studies Investigated**
Facility fast-track drug refills	Clinical Outcomes	Babigumira et al, 2011; MSF, 2013; Nakiwogga-Muwanga et al, 2014a
	Acceptability Outcomes	Nakiwogga-Muwanga et al, 2014b
	Cost Effectiveness Outcomes	Babigumira et al, 2011
Appointment spacing	Clinical Outcomes	Cawley et al, 2016; Grimsrud et al, 2014
	Acceptability Outcomes	Alamo et al, 2013
	Cost Effectiveness Outcomes	N/A
Facility-based ART groups	Clinical Outcomes	Bango, Ashmore, Wilkinson, Van Cutsem & Cleary 2016; Hanrahan et al, 2016; Khabala et al, 2015; Luque-Fernandez et al, 2013; MSF, 2013; Pasipamire et al, 2016
	Acceptability Outcomes	Bango et al, 2013; Bango et al, 2016
	Cost Effectiveness Outcomes	Bango et al, 2013; MSF, 2013
Community-based ART groups	Clinical Outcomes	Decroo et al, 2011; Decroo et al, 2014; Decroo et al, 2016; Grimsrud et al, 2014; Grimsrud, Lesosky, Kalombo, Bekker & Meyer 2015, 2016; Grimsrud, Sharp, Kalombo, Bekker & Meyer, 2015; Jobarteh et al, 2016; MSF, 2013; Pasipamire et al, 2016; Vandendyck et al, 2015
	Acceptability Outcomes	Decroo et al, 2011; Vandendyck et al, 2015
	Cost Effectiveness Outcomes	N/A
Community ART distribution points	Clinical Outcomes	Kalibala et al, 2016; MSF, 2013; Pasipamire et al, 2016; TASO, 2015
	Acceptability Outcomes	Kalibala et al, 2016; MSF, 2013; Sethi et al, 2010
	Cost Effectiveness Outcomes	Kalibala et al, 2016; MSF, 2013; Sethi et

		al, 2010
Home-based care	Clinical Outcomes	Kalibala et al, 2016
	Acceptability Outcomes	Kalibala et al, 2016; Wools Kaloustian et al, 2009
	Cost Effectiveness Outcomes	Kalibala et al, 2016
Decentralization	Clinical Outcomes	Igumbor et al, 2014; Johns and Baruwa, 2016; Kipp et al, 2011; Long et al, 2011; O'Connor et al, 2011; Uzodike et al, 2015
	Acceptability Outcomes	Kipp et al, 2011
	Cost Effectiveness Outcomes	Johns and Baruwa, 2016; Kipp et al, 2011; Long et al, 2011
Task shifting	Clinical Outcomes	Barton et al, 2013; Brennan et al, 2011; Fairall et al, 2012; Grimsrud, Kaplan, Bekker & Meyer 2014; Kalibala et al, 2016; Long et al, 2011; Umar et al, 2011; Uzodike et al, 2015
	Acceptability Outcomes	Castelnuovo et al, 2009; Foster et al, 2012; Kalibala et al, 2016; Wanyenze et al, 2010
	Cost Effectiveness Outcomes	Babigumira et al, 2009; Barton et al, 2013; Foster et al, 2012; Kalibala et al, 2016; Long et al, 2011;