Article Type: Review Article

Reframing HIV Care: Putting People at the Centre of Antiretroviral Delivery

Chris Duncombe[1], Scott Rosenblum[1], Nicholas Hellmann[2], Charles Holmes[3], Lynne Wilkinson[4], Marc Biot[4], Helen Bygrave[4], David Hoos[5], Geoff Garnett[1]

1 The Bill and Melinda Gates FoundationSaettle, WA, USA

2 Elizabeth Glaser Pediatric AIDS Foundation, place?, country?

3 Centre for Infectious Disease Research in Zambia, place?, Zambia

4 Médecins Sans Frontières, place?, country?

5 Mailman School of Public Health, Columbia University, place?, USA

Summary

The delivery of HIV care in the initial rapid scale-up of HIV care and treatment was based on existing clinic-based models, which are common in highly resourced settings and largely undifferentiated for individual needs. A new framework for treatment based on variable intensities of care tailored to the specific needs of different groups of individuals across the cascade of care is proposed here. Service intensity is characterized by four delivery components: (1) types of services delivered, (2) location of service delivery, (3) provider of health services, and (4) frequency of health services. How these components are developed into a service delivery framework will vary across countries and populations, with the intention being to improve acceptability and care outcomes. The goal of getting more people on treatment before they become ill will necessitate innovative models of delivering both testing and care. As HIV programs expand treatment eligibility, many people entering care will not be "patients" but healthy, active and productive members of society.[1] In order to take the framework to scale, it will be important to: (1) define which individuals can be served by an alternative delivery framework; (2) strengthen health systems that support decentralization, integration and task shifting; (3) make the supply chain more robust; and (4) invest in data systems for patient tracking and for program monitoring and evaluation.

Keywords: HIV; AIDS; antiretroviral treatment, highly active; optimized care; patient-centered care; decentralization; task-shifting; cascade

Introduction

The widespread devastation caused by the HIV pandemic has led to unprecedented increases in overseas development aid for health, much of it earmarked for care and treatment-related services in low and middle income countries.[2] The magnitude of HIV funding allowed for rapid strengthening of under-resourced health systems unaccustomed to providing chronic care and enabled the successful expansion of care and treatment services that have averted an estimated 5.5 million deaths since 1996.[3,4] Further expansion of the emergency scale-up, as currently constituted, is constrained by the donor funding environment [5,6] and subsequent increases in donor resources are unlikely.

A sequel of this success story, however, is that health systems have become even more overburdened. The models of delivery for HIV care developed for the initial rapid scale-up of HIV services were based on traditional clinic-based service models, common in highly resourced settings, and largely not modified to reflect individual needs. Even as the number of people on ART has grown to almost 12 million in low and middle income countries, protocols for frequent clinic follow-up have been perpetuated with very few changes, regardless of how long an individual has been on antiretroviral treatment (ART) or their clinical status. After the early rapid growth in clinic sites, expansion has slowed and ever-growing numbers of people receive care in clinics often with insufficient numbers of doctors, clinical officers and nurses.[7] As a result of traditional care models, HIV clinics are crowded and waiting times are long with many people waiting solely to pick up drug refills. Health care workers are over-taxed due to this high workload and, due to weak infrastructure, face challenges to provide care and follow-up according to the guidelines on which they have been trained.

These challenges have led to a mixed picture of effectiveness among the HIV care and treatment systems. On the one hand individuals who have been linked to care and retained on ART achieve high rates of viral suppression.[8–10] However, studies report substantial loss to follow up across all steps of the care cascade.[6,11] Overburdened health systems, lack of patient-focused services, resource limitations, and mixed quality of care have led to efforts to modify the delivery of HIV care in a framework that addresses the causes of poor retention. Task shifting is one of the most common approaches.[12] WHO has included task shifting in the 2013 Consolidated Guidelines as a way of providing care to a greater number of people at reduced cost or when there are insufficient health care workers in the public sector.[13] Other programs have focused on decentralization, shifting care to primary health clinics and to the communities in which people live.[14]

We describe a delivery framework which provides differential care and treatment services for specific, well-defined groups of people in an effort to improve service quality and access, adherence and retention, outcomes, efficiency, and cost of services. The framework has been variously termed optimized care, patient-centered/focused care, needs-based care or tiered care.

PROBLEM STATEMENTS

1. **The scale up of ART in low and middle income countries has led to overburdened health systems**
   - HIV clinics are overcrowded and waiting times are long
   - Many countries lack sufficient clinical personnel to treat the increasing numbers of patients eligible for ART
   - Health systems are geared to acute disease response rather than to providing chronic care

2. **The needs of people who are stable on and adherent to ART are different to those of people who are unwell or non-adherent**
   - Current models of care are not patient centered
   - People with widely divergent needs have only one access point to the clinic to receive care
   - Stable people do not need regular contact with the health care facility

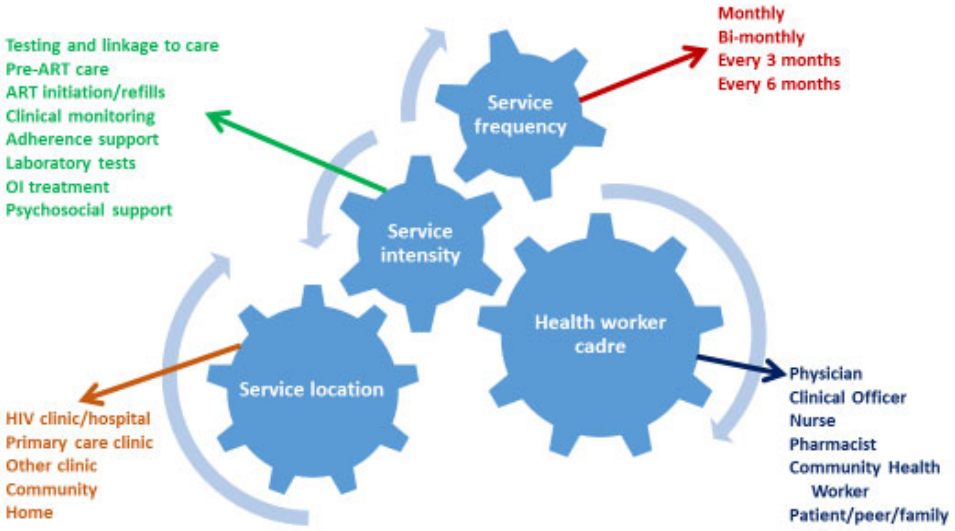
3. **Alternative care models implemented in resource limited settings have not been taken to scale**
   - There are limited robust measures of impact and outcomes of alternative delivery frameworks

A framework for delivering HIV care and treatment

Driven by a desire to provide care which people will use and to increase the efficiency and effectiveness of HIV care delivery, this framework aims to vary the intensity of both ART and pre-ART care based on individual need and to create more flexible, convenient, and acceptable models of service delivery for patients, health care workers, and health systems. In simple terms, the framework describes delivery of the right care at the right frequency to the right individuals by the right care providers in the right location at the right time. Although this concept is not new, it has not been extensively used by HIV care and treatment programs in low and middle income countries to date.

The framework involves providing **differential intensity** of care and treatment services across **defined patient strata**. Service intensity is characterized by four components, all centered on the needs of individuals: (1) types of services delivered; (2) location of service delivery; (3) provider of health services; and (4) frequency of health services.

Figure 1: Four levers to tailor or adapt care to people's needs (service frequency, location, intensity and cadre**)**



Each of these components represents a flexible lever for adjusting or modifying a model of care to serve a specific patient stratum in a given geographic or health system setting. Health system variables, such as geography, level of health facility, available cadres of health workers, and individual variables (distance to the health facility, clinical condition, social and economic situation, education level, rural/urban context, and mobility pattern) determine how levers are applied in a given location. How the framework is implemented will vary across countries and populations in order to best serve the needs of individuals. Similarly, individual eligibility criteria will vary by heath setting, with the intention being to improve patient acceptability and care outcomes.

Different intensities of service can be delivered within a single location or between locations. Distribution of individuals into strata for optimized care is determined by the needs and preferences as defined by specific characteristics (Table 1). The distribution of individuals across care strata is dynamic due to the need for periodic up-referral or down-referral to more or less intensive care based on their current needs.

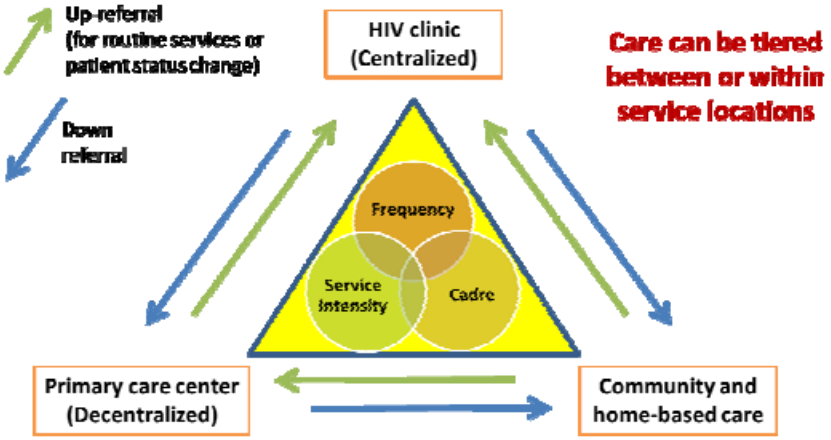
Table 1: Key determinants of stratification into different levels of care

Clinical determinants	**Social/cultural determinants**
Knowledge of HIV status	Individuals' support network
HIV disease severity and current health status	Individuals' preference for specific model of care
Duration of care or treatment	Distance from home to healthcare facility

Treatment tolerance and adherence	Socio-cultural factors (family, work, or community barriers to care)

Models of care can be organized into three categories based on the location at which people receive services. **Centralized, facility based models** can provide differential care within a single health facility, such as reduced frequency of visits or substitution of a clinical assessment visit by a pharmacy only medication refill visit. **Decentralized models** of care provide pre-ART and ART services either by down-referring stable people or initiating and managing people at more peripheral health facilities.[15,16] Other models decentralize care even further by providing care directly in the **community or in the home**.

Figure 2: Categories of Care Models



There are critical enabling services that are levers for successful HIV health delivery regardless of location, intensity, and frequency of care and who delivers that care. The need for psycho-social support, transportation, child care, nutrition, legal and other services may be as important as how long people wait in clinic.

Examples and evidence from the literature

Application of individual elements of this care framework, notably decentralization and task shifting, has increased significantly during the past few years and has been widely endorsed by the WHO and other agencies. However, there are few models that represent differential HIV care intensity across patient strata in either the peer reviewed literature or the grey/conference literature. While not a systematic review, the examples presented in Table 2 illustrate the key dynamics and outcomes of innovative models of care in the real world. The studies included in this analysis reported results from approximately 68,000 HIV-positive individuals in eight countries (Democratic Republic of the Congo, Kenya, Malawi, Mozambique, South Africa, Swaziland, Thailand, and Uganda). See Table 2 in the annex for a detailed listing of studies and results.

All of the models analyzed differentiated individuals on the basis of clinical stability on treatment to determine eligibility for an alternative framework of care. Eligibility was generally restricted to adults with CD4 count above a certain threshold (ranging from ≥50 to ≥350), a certain length of time on ART (from ≥4 weeks to ≥18 months and adherent), undetectable viral load and/or other clinical considerations (no oppor-

tunistic infections, no adverse reactions, not pregnant). The studies generally reported on outcomes (including loss to follow-up, mortality and adherence), and some studies reported changes in resource use (health system and/or cost per person per year, number of clinic visits).

Examples of models and evidence of impact

One study examined the cost-effectiveness of the **centralized, facility-based model** in an urban HIV clinic.[17] At the Infectious Diseases Institutes (IDI) in Kampala, Uganda, stable individuals are offered 3 monthly nurse visits, 6 monthly physician visits and monthly pharmacy only ART refills. Individual outcomes were similar between those managed with monthly refill visits and standard monthly physician/nurse visits but the cost per person per year fell from $610 per year to $496 for monthly refill-only visits, a decrease of nearly 20%.[17]

A clinic-based model that used a six monthly clinical appointments (SMA) program was initiated at the Chiradzulu District Hospital in rural Malawi and supported by Médecins Sans Frontières (MSF) to reduce waiting times and clinic staff workload using visit spacing and pharmacy only visits.[18] This program enrolled people stable on ART to receive 6-monthly clinical appointments with nurses and 3-monthly drug refill visits. Between January 2008-mid-2013, 8,528 adults were enrolled in SMA. Cohort retention at 36 months after SMA start was 94%, however 2722 (33%) people had returned to standard clinical follow-up status. Reasons for SMA discontinuation and long-term treatment outcomes are being evaluated.[18]

A number of studies evaluated the impact of a **decentralized, facility based model** in which stable individuals were down-referred from the HIV clinic (where care was generally provided by a doctor or clinical officer) to a primary care health center (where the care was generally provided by a nurse). Among the 39,000 individuals included in a meta-analysis of this approach, loss to follow up per 100 patient years was 7.4 (95% CI 6.0 – 9.3) in the primary care center group compared to 13.4 in the HIV clinic group and mortality per 100 patient years was 2.8 (95% CI 1.1 to 7.3) in the primary care center group compared to 8.4 in the HIV clinic group.[14]

At the Themba Lethu Clinic in Johannesburg, South Africa, stable individuals were down referred to nurse-managed primary care clinics for treatment maintenance rather than being maintained at the HIV clinic.[19–21] More than 2,000 individuals were down-referred as of 2011, and a matched cohort analysis found that down-referred people were less likely to die (HR 0.2; 95% CI 0.04-0.8), or be lost to follow-up (HR 0.3; 95% CI 0.2-0.6) or experience viral rebound (RR 0.6; 95% CI 0.4-0.9).[19] The cost of care in primary clinics was 11% less than in the HIV clinic.[20] Similar care models have been introduced in rural areas of South Africa with similar outcomes.[21]

A number of different approaches have **decentralized care** to the **community or to the home**. These models minimize the number of required clinic visits by utilizing community health workers or peers to deliver care or treatment either at home or at a community meeting point. The community

health workers ranged in education and training, and the qualifications and pay for community health care workers varied throughout the models. Some models used volunteers with few education requirements[22] while others recruited paid staff with college degrees[23]. One model provided decision support tools to the community health workers.[24] Two models used groups of people living with HIV (PLHIV) [25,26] while others used community health workers to deliver medication directly to the house[22,24,27] or distributed treatments in community meeting points[18]. All models reported reduced loss to follow-up and reduced number of clinic visits among patients managed in the community or at home.

One decentralized model is of particular interest in urban, high-density areas due to the degree it has been scaled and evaluated. In the Western Cape of South Africa, MSF, driven by the need to provide better patient-centered care and to decongest over crowded HIV clinics, developed a model in which care, including ART drug refills, is provided either at the clinic or in community venues in a group setting.[26] These groups, referred to as ART adherence clubs, are facilitated by a community health care worker. Forty-month retention in the clubs in Khayelitsha is 97% (club) versus 83% (clinic) with a 67% reduction in virological rebound among those in clubs compared to clinics.[26] While there is selection bias since those eligible for club care are, by definition, stable and adherent, adherence and retention have remained high despite a reduction in clinic visits. This model has been adopted by the Metro District Health Services[i] from the initial MSF project in Khayelitsha to include 27,800 people (1/4 of total individuals in care by end June 2014) in the Cape Town metropolitan region.[26] Roll out of the same care model has commenced in some districts in Gauteng and Free State provinces, while Swaziland is likely to implement the model in 2015.

In Mozambique, MSF has collaborated with the Health Ministry to implement and scale Community ART Groups (CAGs) throughout the country.[25] CAGs are groups of six individuals from which one rotating person in the group acts as the monthly ART collector for all members. Thus, each CAG member visits the clinic every six months. Eligible people must be stable on ART for >6 months and a CD4 count >200. Retention at 12, 24, 36, 48 months, respectively, has been 97.7%, 96%, 93.4%, and 91.8% and mortality has been 2.1 per 100 person years.[25] CAGs are being implemented at varied degrees of scale in Lesotho, Zimbabwe, Malawi, and South Africa.

Limitations of the studies

The field of research on alternative delivery frameworks is nascent and a number of important questions remain. The articles we found did not discuss the impact on people who remained in standard clinic care or the impact on care providers. Only two studies were randomized and most were retrospective cohort studies. While models have been implemented in a number of countries, 6 of the 16 models and approximately 48,000 of the 68,000 people who were delivered care in this framework were in South Africa, often in ur-

[i] Metro District Health Services provides comprehensive primary health service, mainly to lower income groups in the Cape Town metropolitan region.

ban settings. A model that is effective in urban South Africa, where resources and infrastructure are generally better, may not be reproducible with similar results in more resource-limited settings, such as Malawi, Mozambique, Zambia, or even rural South Africa.

Implementation challenges

Challenges to implementing this framework include defining the most appropriate selection criteria for reduced intensity or non-clinic care, national and local regulatory and policy frameworks around reduced intensity of services, supply chain management and data systems for patient tracking and program monitoring and evaluation.

Each country has their own regulatory frameworks that establish the scope of work for each cadre of health care worker. These regulations determine which cadre can initiate and/or manage antiretroviral therapy, dispense medications, and perform laboratory tests. Further, regulations stipulate the frequency at which medications may be dispensed. These regulations significantly impact the ability to decentralize or temporally space care. For example, ARV dispensing for individual patients in Western Cape was maintained centrally at pharmacy level, while distribution of pre-packed and labeled ART was permitted at lower level facilities and through community-based adherence clubs. At present in many clinics in eastern, central, and southern Africa, nurses cannot initiate ART , though WHO guidelines support it.[28]

Supply chains and stock management must be sufficiently robust to ensure stable ART distribution for decentralized primary health centers and community-delivered ART along with longer durations of refills (ideally three monthly).

Robust data systems are necessary to track individuals across care sites as well as monitor overall program effectiveness, in particular to ensure that retention in care can be tracked as patients move between care facilities or settings. Community delivered ART requires simple and robust data collection. Unique identifiers, referral tools and data management systems are needed.

Conclusions

We believe this framework can guide policy makers into introducing and scaling up new approaches to delivery across the HIV cascade of care. The framework is driven by two needs. First, care that better meets the needs of people and assisting them to access care and remain in care for life. Second, with donor funding for HIV expected to remain constant or decline in the coming years, this framework may provide a tool to provide this care more economically. The cost and cost effectiveness of innovative models delivery of care needs further evaluation.

The framework, with its levers and patient centeredness, addresses the losses described by others across the cascade of testing, linkage and retention in care.[6] Differentiated testing and linking strategies using new testing technologies such as oral self-test may hold promise in helping hard-to-reach populations know their HIV status.[28–30]The framework is equally applicable to pre-ART care as it is to ART care.

Scale-up of innovative models of care should be monitored and evaluated through a robust implementation science framework targeting critical questions about most effective and efficient approaches to providing care in varied settings. As best practices are identified, normative bodies and lead implementers should continue to develop toolkits[ii] and guidelines to help countries and providers to implement these approaches.

References

1. Eaton, J. W. *et al.* Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models. *Lancet Glob. Health* **2,** 23–34 (2013).
2. Kates, J., Wexler, A. & Kaiser Family Foundaiton. Financing the Response to AIDS in Low- and Middle-Income Countries: International Assistance from Donor Governments in 2013. at <https://kaiserfamilyfoundation.files.wordpress.com/2014/07/7347-10-financing-the-response-to-hiv-in-low-and-middle-income-countries.pdf>
3. El-Sadr, W. M. *et al.* Scale-up of HIV treatment through PEPFAR: a historic public health achievement. *J. Acquir. Immune Defic. Syndr. 1999* **60 Suppl 3,** S96–104 (2012).
4. UNAIDS. Global Report: UNAIDS report on the global AIDS epidemic 2013. (2013). at <http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf>
5. Katz, I. T., Bassett, I. V. & Wright, A. A. PEPFAR in transition--implications for HIV care in South Africa. *N. Engl. J. Med.* **369,** 1385–1387 (2013).
6. Rosen, S. & Fox, M. P. Retention in HIV Care between Testing and Treatment in Sub-Saharan Africa: A Systematic Review. *PLoS Med.* **8,** (2011).
7. Boyd, M. A. & Cooper, D. A. Optimisation of HIV care and service delivery: doing more with less. *The Lancet* **380,** 1860–1866 (2012).
8. Barnabas, R. V. *et al.* Initiation of antiretroviral therapy and viral suppression after home HIV testing and counselling in KwaZulu-Natal, South Africa, and Mbarara district, Uganda: a prospective, observational intervention study. *Lancet HIV* **1,** e68–e76 (2014).
9. McMahon, J. H., Elliott, J. H., Bertagnolio, S., Kubiak, R. & Jordan, M. R. Viral suppression after 12 months of antiretroviral therapy in low- and middle-income countries: a systematic review. *Bull. World Health Organ.* **91,** 377–385E (2013).
10. Elul, B. *et al.* High Levels of Adherence and Viral Suppression in a Nationally Representative Sample of HIV-Infected Adults on Antiretroviral Therapy for 6, 12 and 18 Months in Rwanda. *PLoS ONE* **8,** (2013).
11. Fox, M. P. & Rosen, S. Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007–2009: systematic review. *Trop. Med. Int. Health* **15,** 1–15 (2010).

[ii] MSF has already developed a toolkit for the Khayelitsha ART adherence clubs and a toolkit for the CAGs.

12. Kredo, T., Bateganya, M., Pienaar, E. D. & Adeniyi, F. B. in *Cochrane Database of Systematic Reviews* (John Wiley & Sons, Ltd, 2012). at <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007331.pub2/abstract>
13. Holmes, C. *et al.* Health systems implications of the 2013 WHO consolidated antiretroviral guidelines and strategies for successful implementation. *AIDS Lond. Engl.* **28 Suppl 2,** S231–239 (2014).
14. Kredo, T., Ford, N., Adeniyi, F. B. & Garner, P. in *Cochrane Database of Systematic Reviews* (John Wiley & Sons, Ltd, 2013). at <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009987.pub2/abstract>
15. Fatti, G., Grimwood, A. & Bock, P. Better Antiretroviral Therapy Outcomes at Primary Healthcare Facilities: An Evaluation of Three Tiers of ART Services in Four South African Provinces. *PLoS ONE* **5,** (2010).
16. Decroo, T. *et al.* Lessons learned during down referral of antiretroviral treatment in Tete, Mozambique. *J. Int. AIDS Soc.* **12,** 6 (2009).
17. Babigumira, J. B. *et al.* Potential impact of task-shifting on costs of antiretroviral therapy and physician supply in Uganda. *BMC Health Serv. Res.* **9,** 192 (2009).
18. Bemelmans, M. *et al.* Community-supported models of care for people on HIV treatment in sub-Saharan Africa. *Trop. Med. Int. Health* n/a–n/a (2014). doi:10.1111/tmi.12332
19. Brennan, A. *et al.* Outcomes of stable HIV-positive patients down-referred from doctor-managed ART clinics to nurse-managed primary health clinics for monitoring and treatment. *AIDS Lond. Engl.* **25,** (2011).
20. Long, L. *et al.* Treatment Outcomes and Cost-Effectiveness of Shifting Management of Stable ART Patients to Nurses in South Africa: An Observational Cohort. *PLoS Med* **8,** e1001055 (2011).
21. Fairall, L. *et al.* Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial. *Lancet* **380,** 889–898 (2012).
22. Kipp, W. *et al.* Antiretroviral Treatment for HIV in Rural Uganda: Two-Year Treatment Outcomes of a Prospective Health Centre/Community-Based and Hospital-Based Cohort. *PLoS ONE* **7,** (2012).
23. Jaffar, S. *et al.* Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. *Lancet* **374,** 2080–2089 (2009).
24. Selke, H. M. D. *et al.* 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. Dec. 1* **55,** 483–490 (2010).
25. Decroo, T. *et al.* Four-year retention and risk factors for attrition among members of community ART groups in Tete, Mozambique. *Trop. Med. Int. Health* **19,** 514–521 (2014).
26. Luque-Fernandez, M. A. *et al.* 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,** (2013).
27. Amuron, B. *et al.* Mortality in an antiretroviral therapy programme in Jinja, south-east Uganda: a prospective cohort study. *AIDS Res. Ther.* **8,** 39 (2011).

28. Zuber, A., McCarthy, C. F., Verani, A. R., Msidi, E. & Johnson, C. A Survey of Nurse-Initiated and -Managed Antiretroviral Therapy (NIMART) in Practice, Education, Policy, and Regulation in East, Central, and Southern Africa. *J. Assoc. Nurses AIDS Care* **25,** 520–531 (2014).
29. Babigumira, J. B. *et al.* Cost Effectiveness of a Pharmacy-Only Refill Program in a Large Urban HIV/AIDS Clinic in Uganda. *PLoS ONE* **6,** e18193 (2011).
30. Humphreys, C. P. *et al.* Nurse led, primary care based antiretroviral treatment versus hospital care: a controlled prospective study in Swaziland. *BMC Health Serv. Res.* **10,** 229 (2010).

Corresponding author: Chris James Duncombe, Bill and Melinda Gates Foundation, Saettle, WA, USA. Email chrisduncombe@gatesfoundation.org

Annex: Table2

Location, Dates, Summary (Source)	cale; Rural/Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
Centralized Models									
Kampala, Ugan da. [29] 6/2006 – 7/2007 Monthly pick-up of medication at pharmacy, where routine screening is completed. SOC is monthly visit to clinic with physician.	78 in the intervention group. Urban	Health Service Provider	CD4≥200; ≥12 months of ART; self-reported adherence ≥95%; adherence to scheduled clinic visits for last six months; disclosed status to spouse; not pregnant; no substantial clinical event in last 6 months.	Monthly in the pharmacy by a pharmacy-based nurse	Pharmacy-based nurse asked screening questions; Physician visit every 6 months	**Favorable immune response after one year (CD4≥500):** 18.9% vs 19.6%; comparison group was a matched sample before PRP who were followed for at least one year after initiating ART.		$496 per year vs $610 per year Costs include: ART, other drugs, radiology, labs, health personnel, and overhead and capital.	
Decentralized Mo									
Free State, South Africa [21] January 2008 – June 2010 In one cohort (top row) ART initiation and management	d management 5,290 Rural a d Ur-	Health Service Provider, Location	CD4 between 51 and 200; no Stage IV infection; no previous ART ≥1 month; no drugs other than	Monthly in the primary care clinic by a nurse	Routine, not discussed in article; care provided in health center by nurse.	**Mortality per 100 person years:** 1.34 vs 1.44 **Program retention**: 63% vs 58%* Random as-	Shorter commute to community clinic, not quantified in study.		Significant training for nurses and nurse managers (4 sessions), plus 2.5 day train the trainer session

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
was completed in nurse-led primary care clinic. In the other cohort (bottom row) ART management provided in nurse-led primary care clinic. SOC is initiation and management at physician-led HIV clinic.			cotrimoxazole or vitamins, not bed-or wheelchair bound; Weight>40kg; BMI<28			signment by primary care clinic.			
	Management Rural and Urban	Health Service Provider, Location	Undetectable VL; no severe side effects; no new opportunistic infections	Monthly in a primary care clinic by a nurse	Routine, not discussed in article; care provided in health center by nurse.	**Suppressed VL**: 71% vs 70% **Program retention:** 90% vs 91% Random assignment by primary care clinic.	Shorter commute to community clinic, not quantified in study.		Significant training for nurses and nurse managers (4 sessions), plus 2.5 day train the trainer session
South Africa (3), Malawi (1), Swaziland (1), Thailand (1) [14] Study data range from 2004 through 2009 Partial decentralization –	Individuals decentralized; 15,980 in control; three studies focused only on adults, two on children, one	Health Service Provider, Location	Varies, one study included only treatment naïve patients, three on stable patients with minimum time on ARV between 4 weeks	Studies did not vary frequency of care/ART distribution. Initiation was at the hospital by a doctor or	Varies, but generally by nurse at health center	**Lost to care per 100 patient years:** 7.4 vs 13.4* **Mortality per 100 patient years:** 2.8 vs 8.4* Note: these			

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
treatment initiation in a hospital with follow-up care provided by a health center	on both Rural, peri-urban, and urban		and 11 months, and one with limited requirements.	clinical officer, while follow-up care provided at health centers by a nurse.		amounts are for 12-month follow-up of four of six studies. Account for nearly all participants. Two excluded studies are small and excluded b/c they don't provide 12-month time point.			
South Africa(1), Malawi (2), Ethiopia(2), Kenya, Mozambique, Rwanda, Tanzania, Lesotho [14] Study data range from 2004 through 2010 Full decentralization – treat-	20,448 individuals fully-decentralized; [illegible] control; four studies focused only on adults, one only on children, and one on both All studies include rural pa-	Task shifting, location	Varies, most studies do not note exclusion criteria, one study required individuals to be on treatment for less than 6 months, another required treatment naïve pa-	Studies did not vary frequency of care/ART distribution. Initiation and follow-was done at a primary health centers. All studies	Varies, but generally by nurse at health center	**Lost to care per 100 patient years:** 8.1 vs 27.0* **Mortality per 100 patient years:** 10.6 vs 9.7 Note: these amounts are for 12-month follow-up of			

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
ment initiation and management provided by health center	tients, two included urban patients as well		tients.	used nurses, two also used physicians, three used medical officers, and two used medical assistants.		four of six studies. Account for nearly all participants. Two excluded studies are small and excluded b/c they don't provide 12-month time point.			
Chiradzulu District, Malawi [18] 1/2008 – 6/2013 Intervention group could pick up medication at health center every three months. Clinic visits every 6 months. Care at health center provided by CHW. SOC is clinic visit every	3,869 received [illegible] tion, which was 21% of active [illegible] cohort; 2,722 (33% of [illegible] enrollees) returned [illegible] clinical follow-up status. Rural	Health Service Provider, Frequency, Location	Stable adult patients - ≥15 on first-line ART for ≥12 months; CD4 ≥300; no OI or side effects; no pregnancy or breastfeeding	Clinic every 6 months vs 1-2 months; 3-month ART refills at health centers by a community health worker	Monitored via standardized assessment tool at each visit; Clinic visits every 6 months.	**36-month Retention**: 94% vs 83% **Lost to follow-up (1, 2, 5 yrs.):**– 1.3%, 2.98%, 7.8%; **Mortality (1, 2, 5 yrs.)** - .4%, .9%, 2.8%. Comparison with those eligible for but not enrolled in			Paid community health workers; supply chain that can accommodate 3-month prescriptions

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
1-2 months.						intervention.			
Lubombo, Swaziland[30] January 2007 – November 2007 Intervention group received care in primary care health clinic by nurse. SOC is monthly visit to central HIV clinic and receiving care from clinical officer.	315 were included in the study of the 425 invited from the intervention clinic	Health Service Provider, Location	≥14; on ART for ≥4 weeks; CD4≥100; clinically suitable	Monthly at primary care clinic by a counsellor and nurse evolving to primary care nurse and staff	Blood test, clinical questionnaire; care provided at health center by nurses	**No missed appointments** - 89.6% vs 72%* **Loss to follow-up**: 2.8% vs 1.3% **Mortality**: 0 vs 2.5%* Comparison population were individuals who would have been eligible for the study, but receive care from a different clinical area.	Average cost of round trip transportation was halved ($.74 vs $1.5); 53% of intervention group said transportation cost was lowered. Other benefits reported include being nearer to home, shorter waits, better treatment by staff, better care.		Initial training of primary care team
South Africa [19,20] February 2008 through January 2009 (Study timeline, initiation interven-	693 in study, 2,000 in total referred. Urban	Health Service Provider, Location	ART≥11 months; no opportunistic infections; CD4>200; stable weight as	Every two months at the primary care clinic by a primary care	Weight loss; symptoms other visit to medical facility; blood test every 6	**Mortality per 100 patient years**: .3 vs 1.6*; **Lost to follow-up**: 1.4% vs		Costs reduced by 11% - $492 pppy vs 551. Cost effectiveness in-	EHR system that enables communication between clinic and initiation site; 6 week

Location, Dates, Summary (Source)	Scope/Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
tion began in 2007) Care and medication distribution provided at nurse-led primary care clinic every two months. SOC is bi-monthly visits to HIV clinic with physician.			reflected by <5% weight loss between the last three visits; VL undetectable	nurse	months; care provided at primary care health center by nurse	4.2%* Matched cohort using propensity scores based on gender, age, months on ART, ARV regimen, BMI, CD4 count		creased: $509 to $602 per person in care and responding to treatment Costs included: ARVs, other drugs, labs, outpatient visits, fixed costs	ART specific training for primary care health nurses.
Community and H…-ba…ed models									
Khayelitsha, South Africa [18,26] 11/2007 – 6/2013 Medications distributed via community health worker-led 30 person support groups bi-monthly. SOC is monthly visits with medi-	…s have formed as of …ublica…ion. 18,719 receiving care …roug… the …terve…tio…, which is 19% of active ART cor…ort	Health Service Provider, Location	Adult on 1st line for ≥18 months; two undetectable VL; CD4>200; Criteria for return to clinic care: Missed club visit (5 day grace) or clinically unstable including high VL	Every two months at meetings which take place either at clinic or community location, provided by community health workers.	Bi-monthly weight, symptom based general assessments; attendance; nurse review twice per year (1 clinical, 1 blood test). Nurse attends meetings only during these sessions.	**Lost to care (including death, per 100 person years:** 2.98 vs 11.69* **Virological rebound per 100 person years:** 3.18 vs 9.04* Comparison population had been on	Shorter waiting times; higher acceptability of services; fewer missed appointments	$58 per year vs $109 in SOC (unclear what is included, citation to a conference abstract)	Pharmacy staff to pre-package drugs for groups, well-trained lay-workers and support for lay-workers, registries

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
cal staff.						ARVs for a similar period of time.			
Kinshasa, Democratic Republic of the Congo[18] 12/2010 – 5/2013 Medications distributed at community distribution points by peers every 3 months. SOC is visits to clinic (timing of SOC is not described.)	2,161 referred to community ART distribution sites, which is 43% of ART cohort	Health Service Provider, Frequency (?), Location	On 1st line ART for ≥6 months; CD4≥350; no OI or side effects	Every 3 months at community ART distribution points by peers.	Basic health indicators monitored by peer distributor; annual clinical consultation and blood test (CD4) at clinic	**Retention at 12 months, 24 months:** 89.3%, 82.4%; reported retention of 75-85% reported elsewhere **Lost to follow-up at 24 months**: 7.6%	Reduction from 85 minutes to 14 minutes to refill prescription; Transportation costs cut to 1/3.	HR costs lower, not quantified	Trained PLWH, supply chain that can support 3-month med delivery
Tete Province, Mozambique[18,25] 2/2008 – 12/2012 PLWH form groups of six who share responsibility of picking up medications and dis-	8,181 receiving medication through CAGs [illegible], which is 50% of active ART cohort within demonstration program; Overall	Frequency, Location	On 1st line ART for ≥6 months; CD4≥200; no OI or side effects	Monthly, in the community for 5 of6 members, while one member attends clinic to pick up meds for	Clinic visit every six months , which includes clinical consultation and blood test (CD4); group card record keeping	**Retention at 12, 24, 36, 48 months:** 97.7%, 96%, 93.4%, 91.8%; **Mortality per 100 person years:** 2.1 **LTFU per 100 person years**:	Reduced costs and time burden on patients; 28% of members shared transportation costs	49.6% reduction in clinic visits, 62% reduction of ART refill visits	Lay Health Service Providers to ensure links between community groups and health facilities.

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
tributing them to group monthly. SOC is monthly clinic visits by all.	17,272 receiving [illegible] this study country-wide, including 276 children. Rural			the group.		1.0			
Kosirai, Western Kenya [24] March 2006 – March 2007 CHWs deliver medications, screen, and provide adherence support monthly at home. SOC is monthly clinic visits served by full medical staff.	100, 5% of a[illegible] cohort in [illegible] clinic [illegible] was studied. Rural	Health Service Provider, Location	≥18 years old; clinically stable on ART for ≥3 months; no adherence issues; household members aware of patients' HIV status; no WHO stage 3 or 4 condition; no pregnancy; no hospitalizations	Monthly, in the home by community health workers with secondary education, training and PDA with decision support tools	CCC assessed patient symptoms (using PDA) vital signs, adherence to ART, and opportunistic infection prophylaxis. Clinical consultation every 3 months with nurse, physician, and pharmacist. Blood test every 6 months.	**LTFU:** 5.2% vs 4.5% No significant difference of results as compared to SOC. Comparison population was based on random sample.	6.4 clinic visits vs 12.6	Half the clinic visits	CCCs with secondary education and mobile, computer-based decision support tools
Karabole, Uganda [22]	[illegible]5 enrolled in trial [illegible]rm	Health Service Provid-	Eligible for treatment and	Monthly at home by	Weekly monitoring by	**Mortality:** 17% vs 12%			Clinic staff was trained on ART

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
March 2006-May 2009 Weekly, home-based monitoring and adherence counseling and monthly ARV-delivery by unpaid volunteers with 6-monthly appointments at the clinic vs monthly hospital visits in the standard of care.	Rural	er, Frequency, Location	willing to accept daily treatment support from a family member and weekly visits by a trained community volunteer	trained community volunteers	trained volunteers looking for adverse reactions, adherence (pill counts), and clinical problems. Six-monthly visits to clinic for blood work and clinical review. Health center is staffed by two clinical officers, two nurses, and on mid-wife	**VL suppression (ITT):** 64.9% vs 62.0% In multivariate analysis, the only factor significantly related to viral suppression was enrollment in home-based cohort. Odds ratio: 2.47 (1.02-6.04)			as part of the project; training for volunteers; boots, raincoats, bicycles for volunteers. Report forms for volunteers
Jinja, Uganda[23] February 2005 through January 2009 Home-based, monthly follow-up by trained field officers,	359 enrolled Rural and semi-urban	Health Service Provider, Location	Anyone eligible for treatment within 100 km from the clinic	Monthly at home by trained field officers	Monthly monitoring at home, plus clinic visits at months 2, 6, and every six months thereafter.	**Virological failure, LTFU, or withdrew**: 24% vs 27% **Mortality (24 months)**: 14% vs 14%	**First Year**: 29 vs 60 **Second Year:** 18 vs 54 This includes transportation, lunch, childcare costs, and	$793 vs $838 This includes staff, transport, drugs, labs, sensitization, training, utilities, supervi-	4-weeks of training for field officers over and above a college degree; motorcycles for field staff

Location, Dates, Summary (Source)	Scope, Scale; Urban	Optimization component	Stratification metric	ARV Distribution Frequency, Location, and Provider	Monitoring and Clinical Care	**Clinical Metric:** Intervention vs SOC for similar population * denotes significant at p<.05	Costs	System Costs	Necessary Supports
with six-monthly clinic visits (after visits during months 2 and 6). SOC is 3-monthly visits with monthly ARV pick-up.							lost work time.	sion and overheads, and capital. Main cause of higher costs of facility-based model is increased contacts with staff. Home-based patients had 75% fewer clinic visits.	