Review of differentiated approaches to antiretroviral therapy distribution

Nicole Davis, Natasha Kanaga, Melissa Sharer, Sabrina Eagan, Jennifer Pearson and Ugochukwu “Ugo” Amanyeiwe

ABSTRACT
In response to global trends of maximizing the number of patients receiving antiretroviral therapy (ART), this review summarizes literature describing differentiated models of ART distribution at facility and community levels in order to highlight promising strategies and identify evidence gaps. Databases and gray literature were searched, yielding thirteen final articles on differentiated ART distribution models supporting stable adult patients. Of these, seven articles focused on facility level and six at community level. Findings suggest that differentiated models of ART distribution contribute to higher retention, lower attrition, and less loss to follow-up (LTFU). These models also reduced patient wait time, travel costs, and time lost from work for drug pick-up. Facility- and community-level ART distribution models have the potential to extend treatment availability, enable improved access and adherence among people living with HIV (PLHIV), and facilitate retention in treatment and care. Gaps remain in understanding the desirability of these models for PLHIV, and the need for more information on the negative and positive impacts of stigma, and identifying models to reach traditionally marginalized groups such as key populations and youth. Replicating differentiated care so efforts can reach more PLHIV will be critical to scaling these approaches across varying contexts.

Introduction
In order to maximize the number of patients receiving ART, low- and middle-income countries (LMICs) are beginning to implement treatment delivery models that are “decentralized” (where services are shifted from higher- to lower-level facilities) or “differentiated” (where services are adapted to the needs of individuals on ART) (WHO, 2013). There is no one-size-fits-all approach to delivering ART, and this review categorizes models into two broad categories: facility- and community-level. This review deepens the understanding of the current evidence, identifies gaps, and highlights promising strategies for potential replicability and scale-up by presenting successes and challenges associated with adopting a client-centered approach at each level of service delivery across varying contexts.

Methods
PubMed, Google Scholar and gray literature, including project documents and conference abstracts, published in English from 2000–2015 were searched using a combination of key terms (Table 1). Results were further refined to include only gray and peer reviewed literature published since 2006 when new funding increased HIV treatment availability. The study population of focus was limited to stable adults (18 years and older) on ART, who are the main target of most differentiated models currently being implemented. Articles focused on pregnant or post-partum women, adolescents, patients with comorbidities (such as tuberculosis), or key populations were excluded as they have specific needs beyond the scope of this review. Articles were categorized by ART distribution approach: distribution at either facility or community level.

Searches identified 416 published articles and 27 gray literature documents by three reviewers. Abstracts were reviewed independently via two lead authors and then ranked by a subject matter expert. Each reviewer used inclusion and exclusion criteria to identify articles detailing models at facility or community level, resulting in 138 articles receiving a full review by the two lead authors (see Figure 1).

Results
Thirteen articles were included in this review: seven focused on approaches at the facility level and six focused on community-level approaches (Figure 2). The study
Table 1. Search terms.

<table>
<thead>
<tr>
<th>Search term base</th>
<th>Addition terms for search combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiretroviral therapy AND</td>
<td>[Adherence OR Attrition OR Clubs OR Decentralization OR Delivery OR Differentiated OR Dispensing OR Enablers OR Innovative OR Scale up OR Task Shifting OR Technology]</td>
</tr>
<tr>
<td>HIV treatment AND</td>
<td>[Adherence OR Attrition OR Clubs OR Decentralization OR Delivery OR Differentiated OR Dispensing OR Enablers OR Innovative OR Scale up OR Task Shifting OR Technology]</td>
</tr>
<tr>
<td>ARV AND</td>
<td>[Adherence OR Attrition OR Clubs OR Decentralization OR Delivery OR Differentiated OR Dispensing OR Enablers OR Innovative OR Scale up OR Task Shifting OR Technology]</td>
</tr>
</tbody>
</table>

design, approach type, and effects reported in each article are presented in Table 2.

Facility-level models

At the facility level, differentiated approaches to ART distribution include shifting ART responsibility to lower-level facilities and cadres, strengthening the pharmaceutical system and tailoring pharmacy services using technology.

Benefits

A study in Malawi demonstrated that involving non-physician clinicians in ART initiation could double ART enrollment (Bemelmans et al., 2010). Furthermore, a computerized dispensing system shifts ART dispensing to primary health facilities and community distribution points for stable patients in South Africa, with patients reporting significantly reduced waiting times (Mabirizi, Embrey, Saleeb, & Aboagye-Nyame, 2015). Similarly, South Africa’s Chronic Dispensing Unit (CDU) was introduced as an outsourced, centralized service dispensing prepackaged medications to stable clients via facilities and community sites including mobile clinics, clubs, and private pharmacies. Findings show ART patients saved money and time by accessing their medication at local facilities (Magadzire, Marchal, & Ward, 2015).

Figure 1. PRISMA diagram of literature review process.
In Ethiopia and Kenya, strengthening pharmaceutical systems led to improved efficiency of ART distribution. Models in South Africa and Malawi showed stable clients enrolled in “fast track” pick-up lanes saved time by collecting prepackaged ART (Mabirizi et al., 2015). Automated pharmacy dispensing units in South Africa allowed clients to avoid queues for ART refills. Although a formal evaluation has not been published, reports from one clinic indicated improvements in patient wait times, increased time for counseling, and adherence (Turquoise PR Communications, 2014).

In Namibia, pharmacists using the mobile Electronic Dispensing Tool (EDT), which enabled health workers to monitor the adherence of each patient through pill count and time of prescription refill, have reported reduced burden of dispensing ART and increased pharmacy efficiency and availability to provide care (Sumbi et al., 2013).

**Challenges**

Reported challenges with facility-level differentiation of ART distribution included increased patient loads, reducing patient attention and decreased quality of care, potentially leading to LTFU and treatment failure (Fatti, Grimwood, & Bock, 2010).

**Community-level models**

Differentiated models of community-level ART distribution include ART adherence support groups, the use of “expert patients” for peer support involving community health workers (CHWs) in treatment, and community drug distribution points (Bemelmans et al., 2014).

**Benefits**

Community-based ART distribution may significantly reduce the frequency at which clinically stable clients are required to attend a health center, which decreases clinicians’ workload, resulting in time savings for the client and for facility staff and allowing health center resources to be applied to improved management of complex clinical cases (Bemelmans et al., 2014).
Table 2. Description of reviewed documents and associated reported outcomes.

<table>
<thead>
<tr>
<th>Study and site</th>
<th>Type of differentiated approach</th>
<th>Study design</th>
<th>Limitations to study design</th>
<th>Effects reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facility-Level Interventions (7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedelu et al., 2007 South Africa</td>
<td>Task Shifting Decentralization of care</td>
<td>Case Study / Program description</td>
<td>Limited generalizability</td>
<td>Improved geographic access for patients, Reduced loss to follow up, Reduced workload for health facility staff, Improved retention</td>
</tr>
<tr>
<td>Bemelmans et al., 2010 Malawi</td>
<td>Task Shifting Decentralization of care</td>
<td>Case Study / Program description</td>
<td>Limited generalizability</td>
<td>Improved geographic access for patients, Improved enrollment into ART treatment, Better efficiency of ART services, Improved retention</td>
</tr>
<tr>
<td>Fatti et al., 2010 South Africa</td>
<td>Decentralization of Care</td>
<td>Retrospective cohort study</td>
<td>Potential for poor data quality or limited data availability</td>
<td>Improved geographic access for patients, Lowered time and/or costs for patients attending clinics, Improved retention, Improved virological suppression</td>
</tr>
<tr>
<td>Mabirizi et al., 2015 Ethiopia &amp; Kenya</td>
<td>Pharmaceutical System Strengthening</td>
<td>Program Report</td>
<td>Descriptive program reports</td>
<td>Increased availability of ART, Better efficiency of ART services</td>
</tr>
<tr>
<td>Magadzire et al., 2015 South Africa</td>
<td>Automated Pharmacy Dispensing Community ART distribution points</td>
<td>Case Study</td>
<td>Limited availability of data, Limited generalizability</td>
<td>Improved geographic access for patients, Reduced client waiting times, Improved patient autonomy, agency and resilience</td>
</tr>
<tr>
<td>Sumbi et al., 2013 Namibia</td>
<td>Task Shifting Pharmaceutical System Strengthening</td>
<td>Program Report</td>
<td>Limited description of analysis, Limited generalizability</td>
<td>Reduced client waiting times, Reduced workload for health facility staff</td>
</tr>
<tr>
<td>Community-Level Interventions (6)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bemelmans et al., 2014 DRC, Malawi, Mozambique, South Africa</td>
<td>Adherence clubs Community ART distribution points Appointment Spacing</td>
<td>Case Study Series</td>
<td>Program reporting, Limited generalizability</td>
<td>Lowered time and/or costs for patients attending clinics, Improved social support for patients, Improved patient autonomy, agency and resilience, Reduced workload for health facility staff, Improved retention</td>
</tr>
<tr>
<td>Decroo et al., 2011 Mozambique</td>
<td>Adherence clubs</td>
<td>Case Study</td>
<td>Program reporting, Limited generalizability</td>
<td>Lowered time and/or costs for patients attending clinics, Improved social support for patients, Reduced workload for health facility staff, Improved retention</td>
</tr>
<tr>
<td>Dudhia &amp; Kagee, 2015 South Africa</td>
<td>Adherence clubs</td>
<td>Case Study</td>
<td>Qualitative data, Small sample size, Limited generalizability</td>
<td>More time for staff interaction with patients</td>
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</tbody>
</table>

(Continued)
Table 2. Continued.

<table>
<thead>
<tr>
<th>Study and site</th>
<th>Type of differentiated approach</th>
<th>Study design</th>
<th>Limitations to study design</th>
<th>Effects reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grimsrud et al., 2015</td>
<td>Adherence clubs within 500 ft of facility</td>
<td>Case Study/ Program description</td>
<td>• No comparison group • Limited generalizability</td>
<td>• Lowered time and/or costs for patients attending clinics • Improved social support for patients • Improved geographic access for patients • Reduced workload for health facility staff • Lowered time and/or costs for patients attending clinics • Improved virological suppression</td>
</tr>
<tr>
<td>South Africa</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>“MSF,” 2012. DRC, Lango</td>
<td>Adherence clubs Community ART distribution points Appointment Spacing</td>
<td>Case Study (cross case study)/ program description</td>
<td>• Limited generalizability</td>
<td>• Lowered time and/or costs for patients attending clinics • Reduced workload for health facility staff • Improved social support for patients • Improved retention • Reduced workload for health facility staff • Improved social support for patients • Improved patient autonomy, agency and resilience</td>
</tr>
<tr>
<td>Mozambique</td>
<td>Adherence clubs</td>
<td>Program evaluation</td>
<td>• Limited generalizability</td>
<td></td>
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</tbody>
</table>

ART distribution at community levels was found to reduce patient costs related to transport, time and work lost due to frequent clinic visits (Bedelu, Ford, Hilderbrand, & Reuter, 2007; Bemelmans et al., 2010; MSF, 2012). One study indicated that a patient’s departure from the “sick” role to that of a participant or leader of a community group may improve both self-efficacy and self-management skills. This shift in perception may contribute to their sense of empowerment, and increase their agency and ability to self-manage their care (Dudhia & Kagee, 2015).

Models like adherence clubs or community-distribution-points include a component of peer support/education that can increase access and reduce time/travel needed to collect ART (MSF, 2012).

Studies in South Africa and Mozambique found that stable patients receiving ART via community groups had higher rates of viral suppression and higher CD4+ counts compared to those who collected ART at health facilities (Bemelmans et al., 2014). Decroo et al. (2011) found patients enrolled in community-based delivery methods or using community distribution points have higher rates of retention, lower rates of attrition, and less LTFU.

Additionally, community-based models exhibited flexibility – including across different regions/countries or populations (Grimsrud, Sharp, Kalombo, Bekker, & Myer, 2015). These models’ adaptability makes them desirable for implementation and scale-up given their potential to adapt to ever-changing needs and contexts (Rasschaert et al., 2014).

Challenges

Reported challenges with community based ART distribution included: low enrolment in community adherence clubs (MSF, 2012); low uptake of community services due to stigma (Bemelmans et al., 2014) and poor coordination and management (Rasschaert et al., 2014).

Discussion

Evidence shows decentralization of ART distribution mechanisms to the facility level can lead to better outcomes and increased accessibility, which is reinforced by similar findings in South Africa, Kenya, and Malawi (Chan et al., 2010; Fatti et al., 2010; Massauquoi et al., 2009; Reidy et al., 2014). Similarly, community-level distribution mechanisms reduced patient waiting times (Mabirizi et al., 2015) as well as transport costs and time lost from work (Bedelu et al., 2007; Bemelmans et al., 2010; IAS, 2016; Decroo et al., 2013; MSF, 2012).
Furthermore, models such as adherence clubs offered the additional benefit of peer support (MSF, 2012; Reda & Biadgilign, 2012). Results revealed the importance of CHWs’ role in facilitating access to ART for rural and underserved populations (Arem et al., 2011; Gusdal et al., 2011; Mukherjee & Eustache, 2007; Torpey et al., 2008).

Our findings have shown the benefits and challenges associated with various ART delivery models and highlighted the importance of understanding which individuals are most suited to community- or facility-based decentralized ART delivery mechanisms. The review reinforces that community ART distribution can complement health facility/provider-driven service delivery and enhance patients’ ability to manage HIV. Findings further reinforce that efforts driven, owned by, and embedded in the communities themselves are sustainable (Decroo et al., 2009).

There is a need for more in-depth information on positive and negative effects related to stigma and ART distribution. Future efforts should focus on determining if the models explored in this review are translatable to individuals who are not clinically stable and struggle with retention and adherence. Finally, more attention is needed on effective coordination and structured supervision as ART distribution moves from facility to community level. It remains critical that PLHIV must still be linked to the health care system and able to access more advanced care when needed in order to ensure that these approaches continue to represent an effective, convenient, and supportive alternative for ART distribution.

**Limitations**

Widespread implementation of ART distribution models is relatively new, and the breadth of results likely will continue to emerge. Further, the risk of bias is a challenge to assess as most of the studies did not employ randomization, were observational, and have small sample sizes. Finally, due to the heterogeneity of outcome measures, it was not feasible to conduct meta-analysis.

**Conclusions**

The evidence shows differentiated models of care have the potential to extend the reach of treatment, and reduce barriers to accessing ART, and this review broadens the knowledge base and understanding of the models that do exist. Additionally, emerging evidence describes the potential of health and pharmaceutical systems strengthening and community-based mechanisms to distribute ART which may lead to more innovation. Much of the literature available focused on reporting results of the specific interventions carried out; however, there were few details on the specific enablers and barriers that are key to replication and scale-up. Additionally, all models focused on stable populations and did not provide in-depth information any positive or negative impacts on self-perceived stigma. It is therefore important to consider the expansion and variety of differentiated models to serve the different contextual needs of those living with HIV (Brinkhof et al., 2008) as no one model will suit all.

**Authors’ contributions**

Natasha Kanagat, Nicole Davis, Melissa Sharer, and Sabrina Eagan conceived the study design; Nicole Davis and Natasha Kanagat carried out the review; Sabrina Eagan and Melissa Sharer double-screened most included papers; Nicole Davis, Natasha Kanagat, and Melissa Sharer wrote the first draft; and Sabrina Eagan commented on all subsequent drafts. Jennifer Pearson critically read and revised the manuscript. Ugochukwu “Ugo” Amanyeiwe critically read and provided comments on the manuscript. All authors reviewed and approved the final version.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

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