Roundtable discussion report

Accelerating access to long-acting HIV prevention and treatment formulations and delivery platforms: Challenges and opportunities

Session 2
Delivering differently: Service delivery optimization to ensure sustainability of the HIV response
25 May 2022, 120 mins, 17:30–19:30 CET

IAS – the International AIDS Society – in collaboration with the Medicines Patent Pool (MPP)

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Delivering differently: Service delivery optimization to ensure sustainability of the HIV response

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The second session in the series:

- Presented the landscape of widely implemented differentiated service delivery models for HIV prevention and treatment
- Discussed current challenges in service delivery differentiation and integration that could be addressed by long-acting formulations and delivery platforms
- Outlined key aspects from a service delivery perspective that should be considered in the development and implementation of long-acting formulations and delivery platforms

The following speakers presented at the roundtable discussion:

1. **Welcome and introduction** – led by Industry Liaison Forum Co-Chairs Anton Pozniak, Chelsea and Westminster Hospital and LSHTM, and Helen McDowell, ViiV Healthcare (UK)
2. **Recap of session 1** - Wim Vandevelde, GNP+, South Africa
3. **An overview of differentiated service delivery (DSD) for HIV prevention and treatment: Current landscape and challenges** - Anna Grimsrud, IAS, South Africa
4. **Rapid fire key service delivery considerations in the development and implementation of long-acting formulations and delivery platforms** - Marco Vitoria, WHO, Switzerland; Kimberly Green, PATH, Vietnam; Nelson Otwoma, NEPHAK, Kenya; Peter Ehrenkranz, BMGF, United States
5. **What are the enablers and implementation challenges that new long-acting prevention technologies should consider?** - Nittaya Phanuphak, IHRI, Thailand
6. **Panel discussion** - Maurine Murenga, Global Fund Advocates Network, Kenya; Sinead Delany-Moretlwe, University of the Witwatersrand, South Africa; Kenneth Ngure, Jomo Kenyatta University of Agriculture and Technology, Kenya; Helen Bygrave – IAS DSD consultant, UK; Nittaya Phanuphak, IHRI, Thailand

Find the summary of the presentations in Annex 1.

The panel discussion raised the following prominent themes:

WHO:

1. Person-centred commodity: Clients and healthcare providers must be involved in the design of the product and provide input into preferred service delivery modalities. The product must be discrete and fit the preferences and lifestyle of the client.
2. Populations: Who are we aiming to offer the long-acting formulations to? Are they selected based on viral suppression? Are the long-acting formulations going to be added to the "menu" of options for somebody starting ART?
3. Provider training: Healthcare providers need to be trained on how to administer the new technologies even before they are released and receive support through the process (in case they have any questions, do refresher courses, and so on).

WHERE:

4. Administration: Are the health facilities equipped to administer and shift the clients to this new product?
5. Uniqueness of the healthcare systems: We must remember that the healthcare system is as strong as its weakest link when we consider products to use. We should make sure that long-acting formulations will work in all types of healthcare systems.

WHEN:

6. Can we be visit neutral? How can we make sure that we do not "re-burden" our health system and clients?
7. Could there be multiple points of delivery (to cater for different client needs)? If the current regimens allow fewer clinical visits and long-acting technologies require more frequent visits, it is unlikely that the client will shift to the new product.

OTHER CONSIDERATIONS:

8. Some countries have strict regulations on who can administer injectables. This will require an advocacy shift from clinicians to other healthcare provider cadre. We need to overcome policy blockers to enable task sharing to enable decentralization.
9. Could long-acting formulations be used safely with contraceptives and other treatments like TB medication?
10. The product must be affordable in low- and middle-income countries.
11. Would we need different testing approaches? It should not become a barrier to use.
12. It is important to define the implementation science agenda. We need to go beyond the African region, from trials to implementation. The industry fully supports the implementation science agenda and the need to collect data and fill gaps related to implementation before countries and donors can support roll out. The industry wants to make sure that the way those are conducted informs guidelines and policies and addresses a lot of the issues highlighted in this roundtable (effective service delivery models, adherence, persistence, task shifting and demand creation and destigmatization). To read about the implementation science questions for CAB, presented at a BioPIC meeting convened by AVAC and WHO in April 2022, please click here. The AVAC CAB for PrEP Implementation Study Tracker is also available here.

Annex 1: Presentations summary session 2

Recap of session 1 – Wim Vandevelde, GNP+, South Africa
Wim presented a recap of Session 1, which is available in the following report. Wim mentioned the ongoing advocacy campaign, led by AfroCAB (which was represented on the panel in Session 1 by Kenly Sikwese). The campaign is calling for ViiV to licence CAB-LA to generic manufacturers to ensure that it is affordable and accessible in low- and middle-income countries. ViiV is asked to urgently update the access plans for CAB-LA using the dolutegravir licence agreement and geographic scope as the absolute minimum while ensuring that the licencing process for generic manufacturers is open and transparent.

Note: The day after the second roundtable discussion, ViiV Healthcare announced that it would enter negotiations with MPP over the voluntary licencing of cabotegravir long-acting (LA) for HIV pre-exposure prophylaxis (PrEP). Press releases on this can be found on ViiV Healthcare, MPP and Financial Times websites.

An overview of differentiated service delivery (DSD) for HIV prevention and treatment: Current landscape and challenges – Anna Grimsrud, IAS, South Africa
What is DSD for HIV treatment?
Anna explained that DSD puts the person at the centre and acknowledges that we need to simplify and adapt HIV services across the cascade, which can have benefits for people living with or vulnerable to HIV while reducing unnecessary burdens on the healthcare system.

Service delivery should be adapted beyond clinical characteristics and consider the context and needs of specific populations (called the elements). Different DSD models are adapted using the building blocks – when (frequency), where (location), who (provider) and what (package) – of service delivery. The building blocks are different for ART refills, clinical consultations and psychosocial support.

There are four models of DSD for HIV treatment: 1) group models managed by healthcare workers (lay provider or clinical); 2) models managed by clients (people living with HIV in the group); 3) individual models based at facilities; and 4) models not based in facilities but in communities. The diversity of individual models not based at facilities includes home delivery, private pharmacies, community pharmacies, community-based organizations, drop-in centres and mobile or outreach services.

What are the DSD guidelines for treatment?
In 2016, WHO guidelines added a new service delivery chapter that included what to start, when to start and how to deliver treatment. It acknowledged the diverse needs of people living with HIV and divided them into four groups that required specific clinical packages of care (moving away from the one-size-fits-all approach). The guidelines gave recommendations to support further task shifting and decentralization of services and outlined who could qualify for being "stable" or virally suppressed and established on treatment and access DSD. In March 2021, WHO updated its consolidated guidelines and revised the eligibility criteria for determining whether a person is established on treatment. See the table below on the difference between the 2016 and 2021 guidelines.

"The definition of being established on ART (stability) should be applied to all populations, including those receiving second- and third-line regimens, those with controlled comorbidities, children, adolescents, pregnant and breastfeeding women and key populations." – World Health Organization, *Updated recommendations on service delivery for the treatment and care of people living with HIV*. April 2021.

	2016	2021
Term	Stable	Established on ART
Time on ART	12 months on ART	6 months on ART
Inclusion of pregnant women	Pregnant women excluded	Pregnant women included
Inclusion of children and adolescents	Children and adolescents included	Children and adolescents included
Regimen	Second and third line not explicitly stated	Any ART line included
Viral load/evidence of treatment success	Two consecutive viral loads <1000 copies/ml	At least one viral load <1000 copies/ml in past 6 months

PEPFAR went beyond WHO's recommendations regarding multi-month dispensing (MMD) to ensure uninterrupted access during COVID-19. The following populations were identified as eligible for three-six-month refills: people new to ART; children and adolescents; pregnant and breastfeeding women; people with advanced HIV disease who are not virally suppressed; and people living with co-morbidities. From October 2019 to September 2021, the percentage of ART clients receiving MMD increased from 49% to 79% (almost 10 million). MMD scale up did not have a negative impact on viral load coverage or suppression.

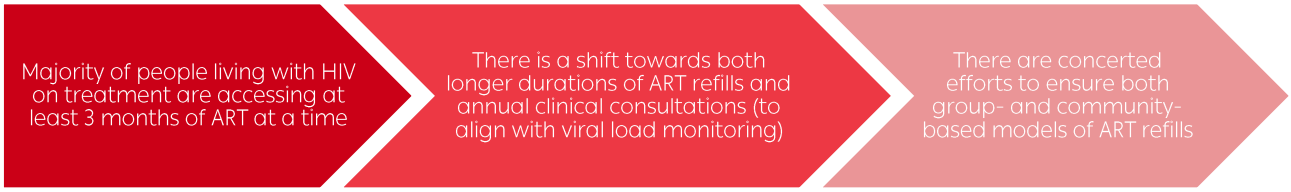
Country policies related to DSD for HIV treatment
A lot of countries are aligned with WHO guidelines on three- to six- or six-month dispensing. A few countries are recommending annual clinical consultants for clients established on treatment. More countries are supporting group models and the majority of the countries have facility- and community-based DSD models endorsed in their national policies.

To access the national policy dashboards, please visit here.

For long-acting treatment, the following service delivery considerations should be made:

- Is long-acting about a new standard of care, given that people have MMD and long spacing between clinical consultations?
- Or is long-acting more about reaching and supporting specific groups (those who are interrupting treatment, not virally suppressed or those with challenges)? And can long-acting address some of these challenges with different first-line options depending on choice of formulation (oral, injectable, implant)?

In summary, for treatment



DSD for prevention

The differentiation of PrEP services was catalysed by COVID-19. In recent years, we have seen:

1. Longer PrEP refills, particularly for those in the PrEP continuation phase
2. Decentralized PrEP refills, including home delivery, through community groups and mobile services complemented by virtual support
3. A shift towards de-medicalization with nurse-provided and peer-supported PrEP
4. An expansion and innovation in what has been offered as part of PrEP delivery to ensure comprehensive and person-centred services

There are analogous building blocks from treatment that are applicable for PrEP (looking at PrEP refills separately from clinical consultations and psychosocial support).

For long-acting PrEP, the following service delivery considerations should be made:

<u>When</u>

- How can we reduce unnecessary visits to health facilities?
  - For injections – and also for multiple rings and longer oral refills
- Can we "fast track" injection-only visits?

<u>Where</u>

- Can injections be done outside of health facilities – as well as oral refills and ring distribution

<u>Who</u>

- Who can do injections?
  - Community health workers?
  - Self-injections?
- Reducing volume and complexity of administration

<u>What</u>

- How can we ensure long-acting does not add clinical complexity?
- Can long-acting be co-formulated with contraceptives?
- Can we integrate care with family planning and gender-affirming hormone therapy?
- mHealth can facilitate support (and adherence to injection schedule).

What are the DSD guidelines for prevention?

Current WHO PrEP guidelines include oral PrEP, as well as the dapivirine vaginal ring, as additional prevention choices for those at substantial risk of HIV acquisition.

WHO is working on guidance for CAB-LA, as well as a technical brief on differentiated and simplified PrEP for HIV prevention, that will be released at AIDS 2022. The IAS is also working with several countries to update their guidance on PrEP, within either their clinical guidance or DSD operational guidance.

Where to from here?
The realities of HIV treatment versus PrEP are different.

HIV treatment	PrEP
Large numbers – 28+ million people on ART (73% of people living with HIV) *Specific populations that could benefit*	Small numbers – around 1 million, behind global targets
Treatment is lifelong	PrEP depending on risk and need – changes over time
Already differentiated – and lots of experience	Still very clinical – need for simplification, de-medicalization and decentralization, integration into other service points (e.g., family planning) but recognition that it's critical
Globally, one first-line therapy	Choice is important – has the potential to increase uptake

Rapid fire key service delivery considerations in the development and implementation of long-acting formulations and delivery platforms
Marco Vitoria, WHO, Switzerland
Marco highlighted several expected benefits and potential challenges with the transition to long-acting ARV regimens in the future, both from the perspective of innovative service delivery strategies and optimized drug characteristics (including treatment durability, convenience, simplicity, low toxicity, use across all populations and equitable access).

The impact of the transition to long-acting ARVs on the building blocks of DSD for HIV treatment is expected to be as follows:

DSD building block	Current DSD model (oral cART - TLD)	Current LAI management (injectable CAB/RPV)	Optimized DSD model (future LAIs)
WHEN: Frequency of treatment refills and clinical appointment	3-6-monthly drug pickup 6-monthly clinical visits	**1-2-monthly IM injections and clinical visits** (need of oral lead dosing, 2 separate injections, not self-administered)	6-12-monthly injections (SC self-injections or implants) 6-12-monthly clinical visits
WHERE: Where the service is provided	HIV clinic/hospital (decentralizing to primary care/outreach services)	**HIV clinic/hospital** (infrastructure for IM injecting, cold chain for RPV, management of syringes and needles)	Use of non-traditional healthcare models (e.g., pharmacies, minute clinics, community-based organizations, mobile vans, home visits)

WHO: Who can provide the services	ART prescription by trained healthcare workers (HCWs); ART dispensing by HCWs task sharing with trained primary health/community healthcare workers	ART prescription and dispensing (IM injection) by **trained HCW**	ART prescription in HIV clinic, primary care, community, mobile and/or home services (with referral system) SC self-injection or implant
WHAT: What the services are	ART prescription & refills, clinical & lab monitoring, management of opportunistic infections/co-morbidities, and psychosocial & adherence support	Same as current DSD +IM **injecting sites (+logistics)**	Same as current DSD + SC self-injection or implant (strong community support)

New LA formulations hold promise, but service delivery models remain to be developed and tested, triggering a call for implementation science, particularly in low- and middle-income countries. There is a need to begin developing programmatic experience in delivering LA drugs in parallel with development of these regimens.

Kimberly Green, PATH, Vietnam
Kim pointed out that there are indications from preliminary real-world product introduction and acceptability studies that demand is strong for the long-acting products and that supply-side issues may present more of a challenge. Given the novelty of long-acting innovations, there are several potential challenges of "being first" that we would need to work through. The following table shows the top 10 innovations that are believed to be important and how they reflect across different types of long-acting products:

Challenges of LA-ART & LA-PrEP introduction and scale-up	Shorter-duration LA injectables or devices (1-2 months)	Longer-duration LA injectables/ devices (3 months or longer)	Ring, LA oral	bnAbs
1. $$$$	LAI currently far too expensive for most LMICs – $$$$	Cost savings with longer LA options? $$$	Less expensive? $	$$?
2. More clinic visits (versus current DSD models with 3-6-month dispensing)	Yes, every 1 to 2 months; "tethered" to clinic; robust scheduling & f/u	NA	NA	Yes
3. Additional provider training, approvals	Yes, significant; IM certification	Yes, significant	Yes, minimal	Yes, significant

4. Space for injection or transfusion	Yes	Yes	NA	Yes
5. Supply chain, storage (cold chain: LAI rilpivirine)	Yes	Yes?	No	Yes?
6. Oral lead-ins, managing the "tail"	Yes	Yes?	No	No
7. Specific population acceptability issues (injection site)	Yes	Yes?	No	Yes
8. Inter-individual variability in LA-ART pharmacokinetics	Yes for LAI-ART	Yes for LAI-ART	NA	NA
9. Managing adverse events, TB interactions	More complex for current LAI-ART and LAI in general	More complex for LAI in general	No	Maybe?
10. Increased risk of resistance	Yes, potentially	Yes, but less likely?	Yes, but less likely	Yes, potentially

A decade of progress in differentiating ART services enables effective community-based service delivery and dispensing (for example, via fast tracking, peer led, mobile, pharmacy based, home delivery and tele-med).

The fundamental questions are:

1. For treatment, how do we integrate different LA-ART products into existing client-preferred service models? How do we address additional training or certifications, cold-chain requirements, effective scheduling and follow-up, and track potential resistance and other issues?
2. For prevention, how do we build new products into existing service delivery platforms to optimize client choice and efficiencies, or inform new models of care (such as mobile services and engaging pharmacies)?

Nelson Otwoma, NEPHAK, Kenya

1. Capacity building: Recipients of care are excited by the new technologies coming to the market. However, capacity building is required on what to expect from these new technologies (injection and needle size) and who can administer it (self-administration or healthcare workers).
2. Overcrowding: Strategies to ensure that facilities are not overcrowded and visits are not lengthy would be welcomed. This can be achieved through differentiated service delivery, receiving the technologies in dispensaries or pharmacies, as it will ensure that healthcare facilities are not overcrowded and avoid lengthy travel to the facilities.
3. Stigma: Preference for privacy and confidentiality must be guaranteed when accessing the services (for example, by accessing community pharmacies or administering injectables in the safety of client's home, collecting the services from the group leader, or having the healthcare worker join the community ART group to administer the injection).
4. Interaction with the healthcare worker: This would be to discuss viral load, adherence, how to remain undetectable and any other services that the recipient of care might need.

5. Stock-outs: This might cause a lot of anxiety.
6. Consider client preferences: Provide options for clients to take the long-acting injectable versus other methods of treatment and care.

Peter Ehrenkranz, BMGF, United States
Peter explained that new technologies have to meet the needs of various stakeholders to be successfully launched and delivered to those who will most benefit from them.

The means of delivering the service in a matter that is acceptable, feasible and at reasonable cost, with a potential for scale and sustainability are the outcomes that should be considered from the perspective of the healthcare worker, healthcare system and especially the client.

For treatment, there is an oral daily pill (TLD) that meets most of these needs, costs less than USD 60 per person per year and can be given to clients in bottles that contain up to six months of supply. DSD decreased the required frequency of health system interactions and moved the service closer to the client, reducing the time, energy and money required for a client to access TLD and resources required to deliver the medicine. This theoretically frees up healthcare workers' time to be used for clients who need the care most.

All stakeholders would most likely compare any new treatment product with the known benefits and flexibility of delivering and taking oral TLD. An ideal new product would have to require very little from the healthcare system and the client. It should not cost more than the oral TLD, not require maintenance within a cold chain and be formulated or co-packed into a single-dose product, and the means of administration must be acceptable to clients. Ideally, it should be self-administered (oral, subcutaneous, patch, injectable of as small volume as possible) and as long acting as possible (at least three-monthly so it can be coordinated with other products like injectable contraceptives), with rare adverse events or risk of resistance if the client is not adherent. All these factors will influence the processes of service delivery and determine feasibility, acceptability and potential for scale of the product.

For HIV prevention, the service delivery bar is lower. There is no equivalent to TLD in large-scale use throughout high-risk populations. We must keep the same service delivery considerations: acceptability, feasibility, cost and potential for scale and minimal laboratory testing for client initiation and/or refill. Also, dosing should be infrequent and aligned with other products like injectable contraceptives. A self-administered product might be particularly well-received, but any product should be available in settings where clients who are most in need can easily access it (with minimal engagement with healthcare workers).

What are the enablers and implementation challenges that new long-acting prevention technologies should consider? - Nittaya Phanuphak, IHRI, Thailand

Key population-led PrEP services in Thailand aim to simplify, de-medicalize and differentiate PrEP services through close collaboration with the hospitals. It has been very successful in scaling up oral PrEP programme because of its:

1. Accessibility: Hotspot locations, flexible hours, one-stop service

2. Availability: Needs-based and client-centred services (such as gender-affirming services for trans people, hormone monitoring, STI, legal consultation and harm reduction)
3. Acceptability: Staff from key population communities and services gender-oriented and free from stigma and discrimination
4. Quality: Trained and qualified staff, and strong linkage with and high acceptance by public health sector

The three main components of key population-led PrEP services are:

1. De-medicalization: PrEP offered by lay providers or through healthcare worker task-shifting
2. Simplify: Finding less complex ways to deliver care, to promote increased access and lower cost while retaining efficacy and quality
3. Differentiation: Adapting the when, where, who and what based on a client-centred approach

When thinking about integrating CAB-LA into key population-led PrEP service, the three areas currently look like this:

1. Re-medicalization as product administration task shifted back from key population lay providers to nurses and doctors
    a. Consider thigh injection, reduced volume and subcutaneous route be made possible for self-injection?
2. More complex as HIV testing algorithm will need HIV RNA assay
    a. Can 3rd/4th-generation rapid test, 3rd/4th-generation self-testing and pooled POC HIV RNA be used?
3. Various user patterns with more PrEP products
    a. Can more frequent CAB-LA visits and switching between oral and LA products and missed injections be handled?

Challenges and enablers to be considered for long-acting PrEP implementation

1. Convenience and comfortability
    a. Simplification and differentiation: Moving CAB-LA from public hospital/clinic to community-led or key population-led clinic, home
    b. Differentiate the who, where, what and when for CAB-LA initiation, continuation, discontinuation, re-initiation and switch between oral and injectable products
    c. Differentiate HIV testing algorithm according to PrEP status to understand the use of 3rd/4th-generation rapid test versus 3rd/4th-generation HIV self-test
    d. Simplify through integration with family planning, gender affirming and STI/HCV test and treat services
    e. Adherence support for a clinic visit (which now equals product administration)

2. Competence in product administration
    a. De-medicalization: Task shifting from doctor, nurse to lay provider, oneself
    b. Lack of clinical research data on self-injection, reduced volume, reduced visits, alternative injection sites (thigh muscle, subcutaneous injection) and difficulties in planning for implementation research

c. Capacity building and quality assurance for injection by lay providers and self-injection
d. Professional institution regulations/rules and mindset

Implementation considerations of long-acting PrEP products: