Optimizing Treatment for People Living with HIV Using New-Generation Regimens

The Challenge

New and improved drug regimens have opened the door to enhanced treatment efficacy, adherence, tolerability, safety, and convenience for people living with HIV. For example, TLD—a once-daily, single-tablet, three-drug antiretroviral (ARV) regimen containing tenofovir, lamivudine, and dolutegravir (DTG)—rapidly reduces viral load and has a high genetic barrier to resistance. This means that even with suboptimal adherence, patients are less likely to develop resistance than with nonnucleoside reverse transcriptase inhibitors (NNRTI) such as nevirapine (NVP) or efavirenz, which are widely used for HIV treatment. The anticipated approval of DTG for infants four weeks of age and older will create an unprecedented opportunity to harmonize and simplify ARV regimens for patients of all ages. Recent advances in anti-tuberculosis (TB) treatment, including availability of shortened-duration regimens for TB preventive treatment, are expected to improve adherence and substantially reduce HIV/TB co-infection rates and global TB incidence.

Countries face enormous planning and operational challenges as they seek to transition people living with HIV to optimized treatment regimens. Complexity of existing regimens, skepticism or lack of information about evidence from international drug trials, concerns about supply chain disruptions, weak pharmacovigilance systems, and change fatigue among frontline health workers can impede or delay adoption of the best-available treatment regimens. To harness the full potential of treatment optimization, in-country stakeholders require a clear understanding of the latest global evidence and its implications for the national HIV response, as well as targeted technical assistance and capacity building for key clinical and supply chain interventions.
Technical Approach

To drastically shorten the time it takes for optimized drugs and treatment regimens to reach patients in low- and middle-income countries, ICAP provides ministries of health and other partners with customized technical assistance for data-driven planning, management, and monitoring of new product introduction and rollout, with a focus on the following domains (see Figure 1):

**Policy, advocacy, and finance**
Country stakeholders are supported to carefully assess national implications of global ARV recommendations and develop rational plans to harmonize and simplify regimens across populations. National treatment guidelines are revised to maximize public health benefit, including through development of specialized guidance on transitioning children. Culturally sensitive demand generation messages are adapted for patients, their family members, and the wider community.

**Planning processes and tools**
ICAP provides tailored technical support for comprehensive national transition planning, including definition of timebound clinical and supply chain targets at the national, regional, district, and health facility levels. Operational guidance is developed to support health workers in coordinating the rollout of new products such that they are distributed in appropriate quantities and wastage of legacy drugs is minimized.

**Implementation capacity**
Through a combination of training, mentorship, and remote technical assistance for decision-making, ICAP builds provider capacity to assess patient eligibility, transition eligible patients to optimized regimens, monitor viral load suppression, report adverse events, and assess progress to treatment targets.

**Transition monitoring and visibility**
Development or adaptation of custom data systems and tools supports routine collection and analysis of data at national and sub-national levels to enable assessment of clinical outcomes, strengthening of pharmacovigilance, and monitoring of transition progress.
By 2015, Kenya faced a complex antiretroviral therapy (ART) prescribing landscape characterized by use of multiple suboptimal first-line regimens. Rates of viral suppression were low among children, adolescents, and men, with increasing rates of pre-treatment NNRTI resistance. TLD presented an opportunity to switch adults and adolescents to a single, highly effective regimen and catalyze progress toward viral suppression for at least 95 percent of patients on ART.

Motivated by the public health potential of TLD, Kenya moved to introduce DTG 50mg single tablets in 2016, before TLD was available as a once-daily, single-tablet regimen (STR). Being an early adopter presented Kenya’s National AIDS and STI Control Programme (NASCOP) with a national planning challenge: how to utilize the existing national supply of DTG 50mg effectively while preparing for a nationwide transition to the TLD STR once it came to market.

Engineering a national transition to TLD required collaborative action across several domains:

**National planning and guidelines**
ICAP supported NASCOP and the relevant national technical working group to develop a plan for incremental phase-in of DTG 50mg, starting with patients who stood to benefit the most: those on an NVP-containing regimen consisting of two or more pills per day. Once the TLD STR was available, ICAP assisted in the revision and rollout of the 2018 National ARV Guidelines, which include TLD as a preferred treatment option.

**Training and implementation support**
Following the release of updated national guidelines, NASCOP launched the Rapid Response Initiative, a 100-day effort to rapidly transition 400,000 patients to TLD. ICAP bolstered this effort by developing ARV optimization training materials and participating in the facilitation of provider training sessions via the online ECHO platform. Communications materials on TLD were developed and disseminated to patients and providers, and select high-volume facilities received on-site mentorship on TLD prescribing and pharmacovigilance.

**Outcome**
In total, 2,476 providers across all 47 counties in Kenya completed training on ARV optimization, pharmacovigilance, and routine commodity reporting. The number of people living with HIV receiving optimized treatment has grown steadily; as of mid-2019, 381,943 people living with HIV were on DTG-based regimens, including more than 120,000 who were taking the once-daily TLD STR. ICAP’s support also catalyzed a shift from passive to active toxicity monitoring in Kenya. Health providers now monitor ART patients for drug toxicity at every consultation and monitoring extends to all patient medications (not just ARVs). As a result, the quantity and quality of ADR data have improved.
Considerations for Implementation

Country-level actions are essential to ensuring that people living with HIV receive the best available treatment in the most efficient and cost-effective manner possible. Following are several considerations for implementing successful transitions to new-generation regimens:

- Focused planning and preparation that bridge clinical, community, and supply chain considerations are essential to the smooth rollout of new treatment regimens. ICAP has developed a suite of tools to assist ministries of health and other stakeholders (see next section).

- Because treatment optimization occurs against the backdrop of other changes to service delivery approaches, it is important to integrate messages about optimized regimens into training curricula for all relevant change initiatives (e.g., Test and Start, differentiated service delivery).

- Community-based demand creation activities should be timed strategically to complement the introduction and rollout of new regimens at nearby health facilities.

- Providers require clear guidance on how and when to transition patients to new regimens as well as training and job aids that reinforce the importance of routine screening for pregnancy intention, toxicity monitoring, and viral load monitoring before and after a regimen change.

- Accurate reporting and vigilant monitoring of new regimen uptake are required to match supply to consumption rates and ensure procurement of appropriate quantities. Enhanced monitoring of adverse events and clinical outcomes is essential to detect issues and allow for timely course correction.
ICAP Publications and Resources

Antiretroviral Treatment Optimization


Available at: https://optimize.icap.columbia.edu/resource/hcw-training-on-the-introduction-of-dtg-for-the-treatment-of-hiv/


Available at: https://icap.columbia.edu/ptb-dtg-pbfw


Available at: https://icap.columbia.edu/ptb-dtg-toxicity

Checklist to Guide Optimal ARV Introduction.

Available at: https://optimize.icap.columbia.edu/resource/checklist-to-guide-optimal-ary-introduction/


