BHIVA Hepatology Highlights for the Healthcare Specialist

in collaboration with the British Viral Hepatitis Group

15 November 2017 • QEII Centre, London

Meeting sponsors

[AbbVie, Gilead, MSD logos]

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Dr Nathan Ford
World Health Organization, Geneva, Switzerland

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<th>Speaker Name</th>
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<td>Dr Nathan Ford</td>
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Date: November 2017

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15 November 2017 • QEI Centre, London
What can hepatitis learn from HIV as we look to elimination?

Nathan Ford
Dept HIV & Global Hepatitis Programme
Hepatitis-related mortality is increasing

Global Hepatitis Report, WHO 2017
Elimination of viral hepatitis as a public health threat by 2030

Global Hepatitis Report, WHO 2017
The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings

The WHO has proposed a public-health approach to antiretroviral therapy (ART) to enable scaling-up access to treatment for HIV-positive people in developing countries, recognising that the western model of specialist physician management and advanced laboratory monitoring is not feasible in resource-poor settings. In this approach, standardised simplified treatment protocols and decentralised service delivery enable treatment to be delivered to large numbers of HIV-positive adults and children through the public and private sector. Simplified tools and approaches to clinical decision-making, centred on the “four Ss”—when to: start drug treatment; substitute for toxicity, switch after treatment failure; and stop—enable lower level health-care workers to deliver care. Simple treatment regimens, supported by education and monitoring of outcomes of treatment, are developed. The integrated management of adult, adolescent, and childhood illness (IMAI/IMCI) has been developed to provide a framework for ART delivery. Other publications support the public-health approach to ART delivery.

Why a public-health approach?

Despite these achievements, there remains considerable uncertainty about what should constitute a public-health approach to ART. We summarise here the WHO’s approach, and clarify its importance for treatment providers, HIV programme managers, and policymakers in developing countries.

Why a public-health approach?

Intensive evidence shows that combined antiretrovirals can substantially extend the life of those with HIV/AIDS. Guidelines for industrialised countries cover individual patient management delivered by specialist doctors prescribing from the full range of antiretrovirals, supported by highly complex drug monitoring. This approach is feasible in well-resourced settings with sufficient healthcare delivery. However, an approach that is not feasible in resource-limited settings where doctors are scarce (eg, one per 12 500 population in Uganda), laboratory infrastructure is inadequate (eg, one working microscope per 100,000 population in central Malawi), and the procurement and supply-chain management is fragile. This difficulty in translating guidelines from developed to developing nations caused concern over whether ART scale-up in poor countries was feasible, let alone affordable or cost-effective.

Drawing on experience from using the DOTS approach for tuberculosis, the WHO began to develop a public-health approach to providing ART. This approach took into account country requirements, the realities of weak health systems, and the experiences of pioneering countries which have set standards for treatment that should be accessible to all in need. The key conceptual shift was the move from an individual-based approach to a population-based approach, and clarify its importance for treatment providers, HIV programme managers, and policymakers in developing countries.

Background

About 40 million people worldwide are thought to be infected with HIV. Many of these people live in developing countries. Since 2001, the WHO has been promoting a public-health approach to antiretroviral therapy (ART) to improve access in resource-poor settings. Existing guidelines for ART,\(^1\) and the prevention of mother-to-child transmission,\(^2\) were revised earlier this year, and separate guidelines for treating children were developed.\(^3\) Other publications support the public-health approach to ART delivery.\(^7\)

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Simplification of treatment

240 different initial treatments were prescribed in Switzerland in 10 years (Wandeler et al, PLoS 2011)

19 different first line regimens in US guidelines

WHO 2002
8 different first line regimens recommended

WHO 2013
1 single preferred first line recommended
Individual vs public health response

Despite more frequent regimens (4 vs 36) and monitoring.

Keiser et al, Plos Medicine, 2008
Evolution in “when to start”

Eholie et al, AIDS Res Ther 2016
Starting earlier reduces mortality and morbidity.
Viral suppression reduces incidence
Task shifting to address health worker shortage

“ART initiation and prescribing by nurses can be done safely, and improve health outcomes and quality of care”

Sanne, 2012; Fairall 2012
Time to ART initiation decreased from nearly 100 days in 2003 to less than 3 weeks in 2009.

Bemelmans et al, Trop Med Int Health 2010
Service delivery: differentiated care

Decroo et al BMJ Open 2017
Tracking progress: the cascade of care

- People living with HIV: 36.7 million
- People living with HIV who know their status: 25.5 million
- People living with HIV who are receiving ART: 19.5 million
- People living with HIV and viral suppression: 16.0 million

Ford et al. Lancet ID 2017
Expanded access to testing

1. Health provider testing

2. Lay testing

   Already policy in 64% of African countries

3. Community testing

   Home, partner, workplace…

4. Self-testing

   Dalal et al, AIDS 2017
RESEARCH ARTICLE
Initiating Antiretroviral Therapy for HIV at a Patient’s First Clinic Visit: The RapIT Randomized Controlled Trial
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Abstract
Background
High rates of patient attrition from care between HIV testing and antiretroviral therapy (ART) initiation have been documented in sub-Saharan Africa, contributing to persistently low CD4 cell counts at treatment initiation. One reason for this is that starting ART in many countries is a lengthy and burdensome process, imposing long waits and multiple clinic visits on patients. We estimated the effect on uptake of ART and viral suppression of an accelerated initiation algorithm that allowed treatment-eligible patients to be dispensed their first supply of antiretroviral medications on the day of their first HIV-related clinic visit.

Methods and Findings
RapIT (Rapid Initiation of Treatment) was an unblinded randomized controlled trial of single-visit ART initiation in two public sector clinics in South Africa, a primary health clinic (PHC) and a hospital-based HIV clinic. Adult (≥18 y old), non-pregnant patients receiving a positive HIV test or first treatment-eligible CD4 count were randomized to standard or rapid initiation. Patients in the rapid-initiation arm of the study (“rapid arm”) received a point-of-care (POC) CD4 count if needed; those who were ART-eligible received a POC tuberculosis (TB) test if symptomatic, POC blood tests, physical exam, education, counseling, and antiretroviral (ARV) dispensing. Patients in the standard-initiation arm of the study (“standard arm”) followed standard clinic procedures (three to five additional clinic visits over 2–4 wk prior to ARV dispensing). Follow up was by record review only. The primary outcome was viral suppression, defined as initiated, retained in care, and suppressed (<400 copies/ml) within 10 mo of study enrollment. Secondary outcomes included initiation of ART at 90 d of study enrollment, patient-level predictors of primary outcomes, and cost-effectiveness of the rapid-initiation arm versus the standard-initiation arm.

Results
Of 665 patients randomized (330 rapid, 335 standard), 657 (99%) were included in the analyses. In the rapid arm, 50% (95% CI, 45%–56%) of patients were started on ART at <7 d, and 43% (95% CI, 38%–48%) of patients were virally suppressed within 10 mo of enrollment. In the standard arm, 16% (95% CI, 12%–21%) of patients were started on ART at <7 d, and 15% (95% CI, 11%–20%) of patients were virally suppressed within 10 mo of enrollment. No significant differences were observed between the two arms in baseline characteristics or outcomes for CD4 ≥350 mm3. The rapid arm was estimated to cost US$149 (95% CI, US$135–US$163) per patient started on ART, compared with US$209 (95% CI, US$189–US$230) in the standard arm.

Conclusions
RapIT was effective at increasing ART initiation and viral suppression compared with standard clinic procedures. Accelerated ART initiation algorithms such as RapIT are feasible in busy public sector settings and may improve ART initiation in sub-Saharan Africa.

Rosen et al, Plos Med 2016
Simplified HCV service delivery in a public health approach

- Simplified and standardized algorithms
- Strategies to strengthen linkage to care
- Differentiated care
- Integrated testing, care and treatment
- Decentralisation of care to promote access
- Community engagement and peer support

- Persons who inject drugs
- People in prisons and other closed settings
- MSM and sex workers
- Adolescents and Children
- Pregnant women
- Migrant/indigenous populations
Simplified HCV testing, treatment and monitoring algorithm

1. Single quality assured RDT
2. Prompt or reflex HCV RNA or core Ag
3. Assess and triage: Stage liver disease using NITs (APRI, FIB4, TE)
4. Treat All with Pan-genotypic regimens
5. One-step monitoring One test of cure SVR12
Strategies to consider for increasing uptake and improving linkage

Trained Peer and lay health workers in community settings (and for treatment and adherence)

Clinician reminders to prompt provider initiated, facility-based testing

Testing (and treatment) as part of integrated services at a single facility, especially within mental health/drug treatment services

On-site or immediate RDT testing with same day results

Zhou et al, Lancet ID 2017
<table>
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<th>Who?</th>
<th>What?</th>
<th>Where?</th>
<th>By Whom?</th>
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<tr>
<td>Persons clinically well and stable</td>
<td>Standard care package: Counselling, adherence support, treatment initiation and monitoring</td>
<td>Facility-based including primary care or community-based settings, including mobile/outreach</td>
<td>Physician or nurse</td>
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<td>Advanced liver disease or serious co-morbidities, HCC, previous treatment failure</td>
<td>Requiring more intensive clinical support and follow-up: Management of liver related complications (e.g. variceal bleed, ascites, encephalopathy, HCC treatment, genotyping)</td>
<td>Facility-based - hospital</td>
<td>Physician</td>
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<td>Mental health issues, active injecting drug users, alcohol misuse, adolescents</td>
<td>Requiring more intensive psychosocial/mental health support</td>
<td>Can be Facility-based or Community-based, Harm reduction site</td>
<td>Physician and counsellor/peer support</td>
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Integration

- Integration with other testing settings or opportunities eg. HIV, antenatal or TB
- Integrated combo serology (HIV/HCV RDTs), including self-testing
  Use of integrated multi-disease platforms for HCV RNA (centralised or decentralised)
- HCV care at harm reduction sites
- HCV care at HIV, STI, TB clinics
- HCV care in prisons

Integrated information systems
Task shifting & decentralization

Models
- Hub and spoke
- Mobile outreach
- Other...

ENABLERS

Community & peer support

HCW Training and mentorship
Training courses and curriculum
Distance support

Simpler treatment & labs

Integrated information systems
(enhanced sample referral system, connectivity, SMS results)
Elimination of viral hepatitis as a public health threat by 2030

Global Hepatitis Report, WHO 2017
We have a long way to go.

Global Hepatitis Report, WHO 2017