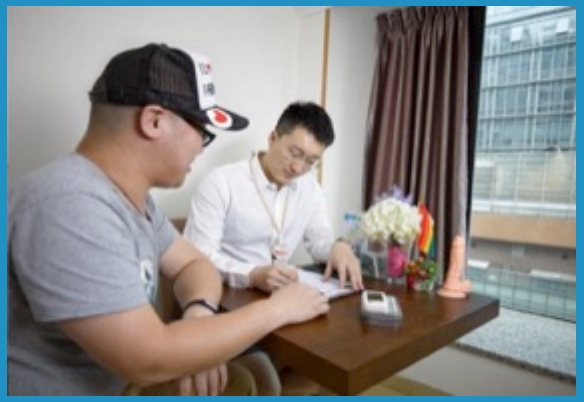
World Health Organization

From data collection to recommendation

Philippa Easterbrook
Global Hepatitis Programme
HIV Department



globalhepatitis programme

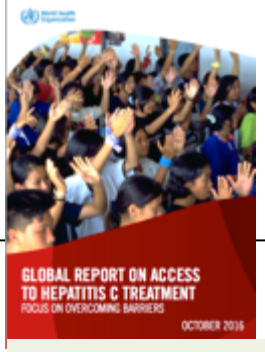
HEPATITIS-C COMMUNITY SUMMIT
Amsterdam 18/19 April 2017

Outline

- The Global Hepatitis Strategy towards elimination
- WHO guidelines and recommendations
  - Hepatitis B, C and testing
  - Higher risk populations
  - How do they differ from other guidelines?
- Next steps and priorities for implementation and scale-up
- The critical role of civil society

What has WHO been doing in viral hepatitis?

- ✓ First ever **global health sector strategy** and regional action plans adopted
- ✓ **Normative and policy work**: Hep B and C treatm and Hepatitis testing guidelines, safe injection policy; surveillance guidelines
- ✓ **Country support** for policy uptake and implementation
- ✓ Supporting **access to affordable medicines** (B an C) – price reporting, pre-qualification; patent landscape; access approaches for countries (Hep Access Report)
- ✓ **Strategic info:** global reports, surveillance guidance
- ✓ G**lobal convener -** World Hepatitis Summit; Regional conferences



Champion HCV countries: Over 1 million people treated with DAAs

Towards elimination of hepatitis

Australia, France and Portugal: universal access to HCV Rx; prisoners +PWID priority in Australia

Georgia: HCV elimination programme (20 000 treated per year)

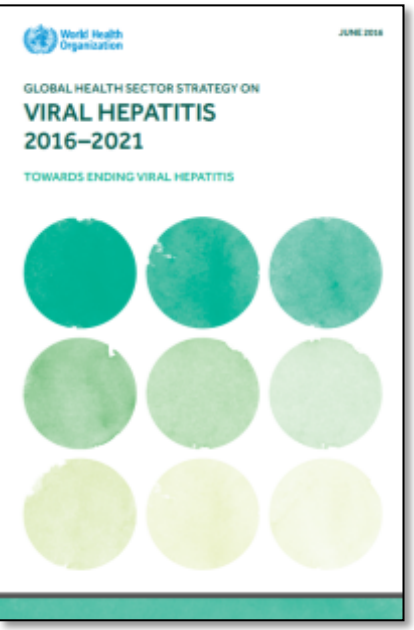
Morocco: goal of HCV free in 2030

WHO "HCV Barriers Report" October 2016

The first Global Hepatitis Strategy and elimination Targets

Towards elimination of hepatitis B and C by 2030

First global strategy on viral hepatitis: 2016-2021

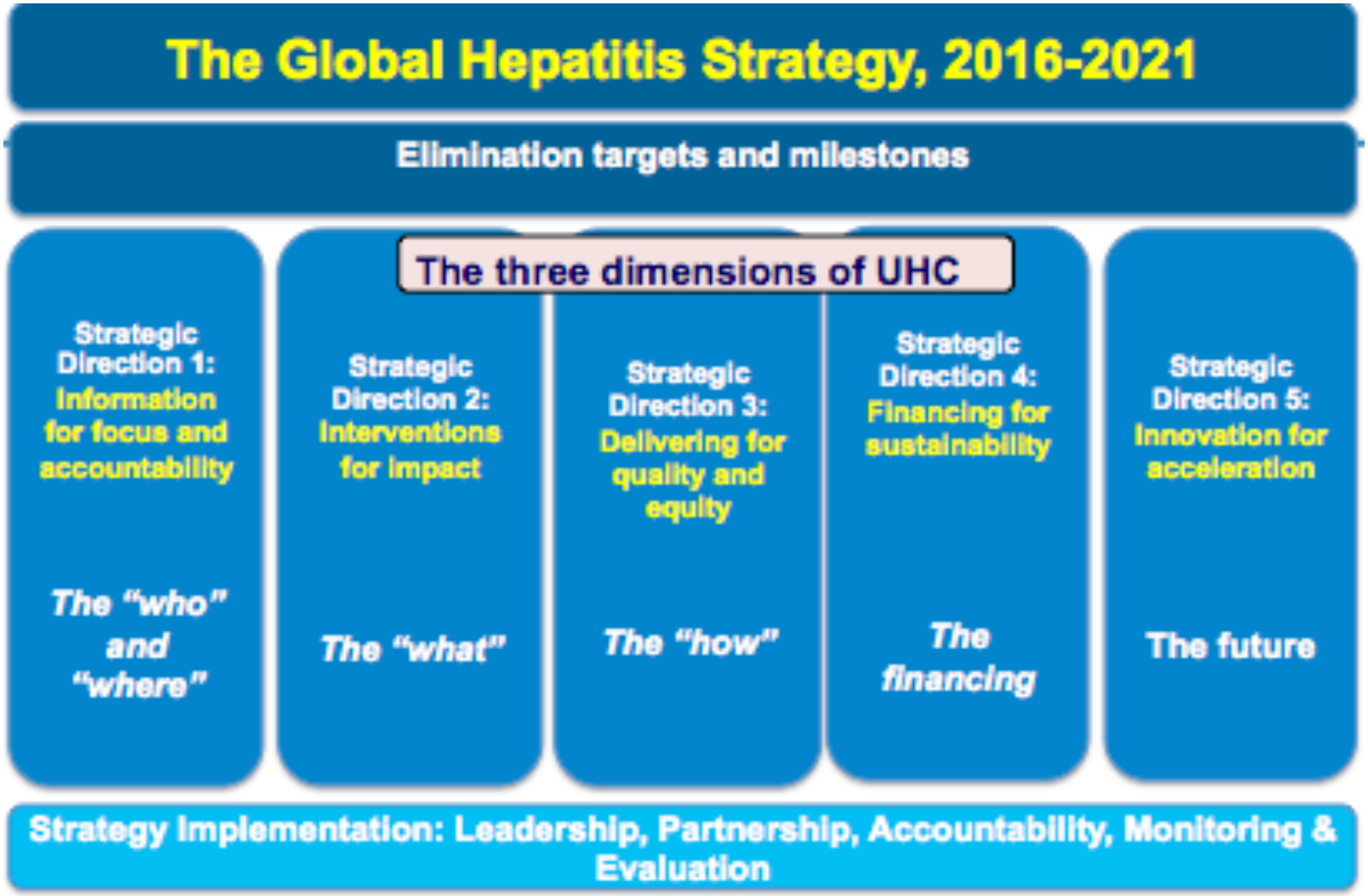


Vision ***"A world where viral hepatitis transmission is stopped and everyone has access to safe, affordable and effective treatment and care"***

Goal*: Eliminate viral hepatitis as a major public health threat by 2030*

- I**dentifies priorities** and **sets global targets** for a coordinated global response
- **Hepatitis in context of new SDGs**
  - Health in all policies, Integration
- **Setting Targets towards "Elimination"** – Responding to SDG Target 3.3.
- **Common framework** with other disease strategies
  - Universal Health Coverage, Sustainable Financing, Public Health Approach

5 Strategic Directions to guide country responses



Why are a strategy and targets important?

- ✓ A powerful tool for mobilizing resources and action
- ✓ Promote development of regional and national action plans
- ✓ To set common targets for countries – towards joint accountability

Setting Targets for elimination…
Balancing Feasibility with Ambition

- **Technically feasible** by scaling up six key interventions to high coverage

- **Impact targets** for HBV and HCV– incidence and mortality by 2030

- Supported by **Coverage targets for key interventions**
  - HBV vaccination (including birthdose)
  - Safe injection practices + safe blood
  - Harm reduction IDUs
  - Safer sex (condom promotion)
  - Hepatitis B treatment
  - Hepatitis C cure

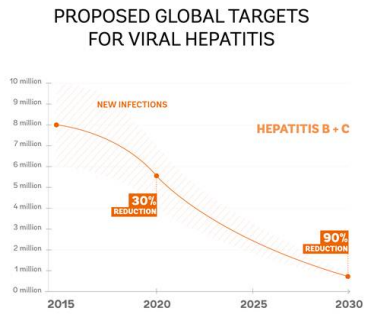
Set agenda to 2030 with milestones for 2020

Set of Impact and Coverage targets for elimination

First ever global hepatitis targets

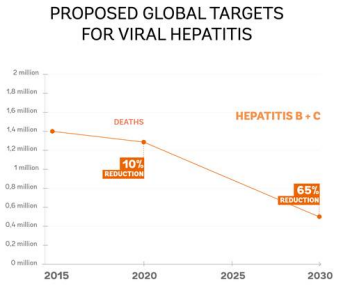
6-10 million chronic HBV and HCV infections (in 2015) to 900,000 (by 2030)

90% reduction



1.4 million deaths (in 2015) to under 500,000 (by 2030)

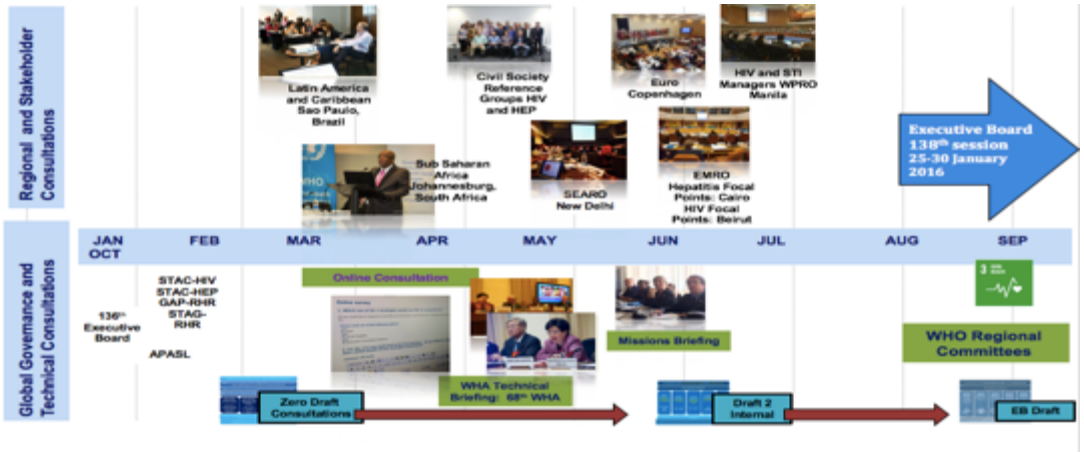
65% reduction



Technically feasible by scaling up six key interventions to high coverage

Intervention	2030	2020	Baseline 2015
1. HBV vaccination	90%	90%	81%
2. HBV MTCT; birthdose	90%	50%	38%
3. Safe injection	90%	50% coverage	5%
4. Harm reduction	300 (75% coverage)	200 (50% coverage)	20
5. HBV Treatment	80%	8 million treated (5m HBV, 3m HCV)	<1%
6. HCV Treatment	80%		<1%

What did we hear from consultation? Broad support with some concerns

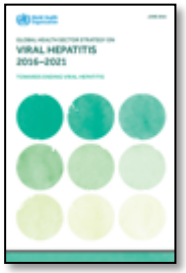


- Balance ambition with feasibility
- Health systems vs vertical programmes; Prominence to integration
- Centralization vs decentralization
- Sensitivities: *key populations, harm reduction, sexual and reproductive rights*
- Comprehensive prevention not just biomedical solutions

- Who will pay? - Guidance on health system financing – transition to domestic funding and role of private sector
- Middle income countries require specific focus
- Differentiation needed between global, regional and country level strategies
- Need for focus on how strategies will be implemented/operationalized
- Prioritize data strengthening, and other work around "Know Your Epidemic" agenda

Key WHO hepatitis publications

- Strategies and Action Plans



- Progress Reports

- Evidence-based Guidelines

- Technical Updates and Briefs

- Implementation Tools

Distinctive Features of WHO Guidelines

Feature	WHO Guidelines	Other Guidelines
Settings	• Low- and middle-income countries • Generalised/concentrated epidemic settings	• High-income countries
Target audience	• National Program Managers	• Treating clinicians
Approach	• The "public health approach" • Simplified and standardized approaches • Preferred regimens	• Individualized treatment • Multiple treatment options
Formulating recommendations: Evidence-based approach	GRADE - Feasibility, equity, end-user acceptability, resource use considered	• Variable use of evidence-based framework
Guidelines Committee representation	• 50% LMICs, programme managers, civil society	• Clinicians and researchers HICs

The "Public health approach" and health equity
Lessons learnt from ARV scale-up:

The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings

Charles F Gilks, Siobhan Crowley, René Ekpini, Sandy Gove, Jos Perriens, Yves Souteyrand, Don Sutherland, Marco Vitoria, Teguest Guerma, Kevin De Cock

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. Simplified formularies have driven large-scale production of fixed-dose combinations for first-line treatment for adults and lowered prices, but to ensure access to ART in the poorest countries, the care and drugs should be given free at point of service delivery. Population-based surveillance for acquired and transmitted resistance is needed to address concerns that switching regimens on the basis of clinical criteria for failure alone could lead to widespread emergence of drug-resistant virus strains. The integrated management of adult or childhood illness (IMAI/IMCI) facilitates decentralised implementation that is integrated within existing health systems. Simplified operational guidelines, tools, and training materials enable clinical teams in primary-care and second-level facilities to deliver HIV prevention, HIV care, and ART, and to use a standardised patient-tracking system.

Lancet 2006; 368: 505–10

Department of HIV/AIDS, World Health Organization, Geneva 1211, Switzerland

Prof C F Gilks FRCP, S Crowley MRCP, René Ekpini MD, S Gove MD, Jos Perriens MD, Y Souteyrand PhD, D Sutherland MD, M Vitoria MD, T Guerma MD, K De Cock FRCP

Correspondence to: Prof Charles Gilks gilkscr@who.int

The "public health approach" seeks to:

- **Simplified** and **standardized** approaches to ensure the **widest possible access** to high-quality services at the population level
- Strike a balance between implementing the **best-proven standard of care** and what is **feasible** on a large scale in resource-limited settings

Promotion of "health equity and human rights" so that:

- Expanded access is **fair** and **equitable**
- **Priority** for treatment given to those **most in need**
- In environment **free of stigma and discrimination**

WHO Guidelines Development process

1. Constitute Guideline Development Group
2. Formulate questions (PICO format)
3. Conduct systematic reviews of data
4. Evaluate quality of evidence (GRADE)
5. Formulate recommendations
6. Disseminate, Adapt, Evaluate

Grading of Recommendation Assessment, Development and Evaluation

Quality of Evidence	**By outcome:** • High quality • Moderate • Low • Very low
Strength of Recommendation	**Strong or Conditional depends on:** • Quality of evidence • Balance of benefits and harms • Values and preferences • Resource use • Feasibility

Key domains to consider in formulating recommendations

12 Systematic reviews

HOW TO TEST? (DIAGNOSTIC PERFORMANCE)

- RDTs vs. EIAs
- 1 vs 2 assays
- NAT (quant/qual) HCVcAg
- Dried Blood Spots

HOW TO OPTIMISE UPTAKE OF TESTING AND LINKAGE TO CARE?

Evidence (GRADE)

Costs and Cost-Effectiveness

WHO TO SCREEN?

CE studies and Modelling

Diagnostic costs

Acceptability (Values and Preferences)

Feasibility

Surveys of country and implementing partners experience

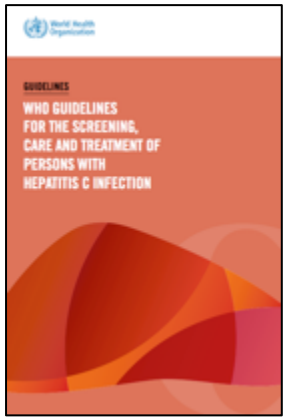
Target Product Profiles for diagnostics

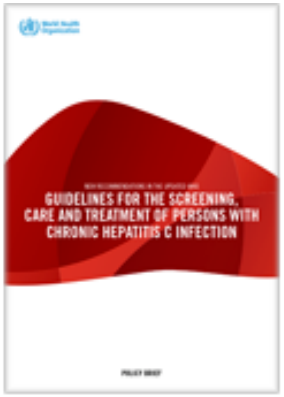
Community and Health worker Values and Preferences

- #HepTestContest Innovation Contest
- 64 contributions from 27 countries

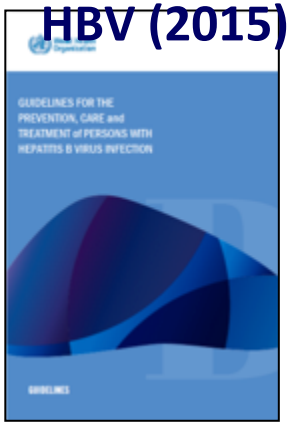
The GHP Trilogy of Normative Guidance

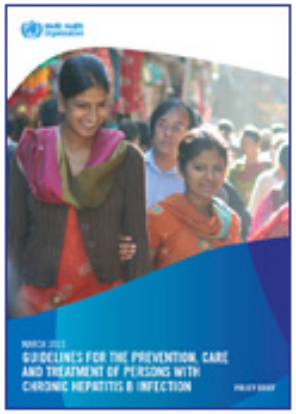
HCV (2014 +2016)



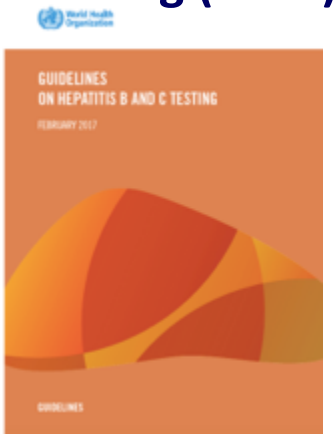


HBV (2015)





Testing (2017)



HCV Guide

2017 guidelines UPDATE:

- Pan-genotypic regimens: (SOF-VEL in 2017 SOF-RAV 2018)
- "Treat All" – prioritisation criteria
- Second-line/salvage therapy
- Special situations – renal impairment: (GLE/ PIB)
- Paeds treatment (priority regimens and formulations for development)
- MTCT - Use of DAAs in pregnant women

Topic	
Staging	ent of liver
Treatment	HCV,
Considerations for prioritisation:	festations, nsmission.

PATIENTS WITHOUT CIRRHOSIS

	Daclatasvir / sofosbuvir	Ledipasvir / sofosbuvir	Sofosbuvir / ribavirin
Genotype 1	12 weeks	12 weeks[a]	
Genotype 2			12 weeks
Genotype 3	12 weeks		24 weeks
Genotype 4	12 weeks	12 weeks	
Genotype 5		12 weeks	
Genotype 6		12 weeks	

PATIENTS WITH CIRRHOSIS

	Daclatasvir / sofosbuvir	Daclatasvir / sofosbuvir / ribavirin	Ledipasvir / sofosbuvir	Ledipasvir / sofosbuvir / ribavirin	Sofosbuvir / ribavirin
Genotype 1	24 weeks	12 weeks	24 weeks	12 weeks[b]	
Genotype 2					16 weeks
Genotype 3		24 weeks			
Genotype 4	24 weeks	12 weeks	24 weeks	12 weeks[b]	
Genotype 5			24 weeks	12 weeks[b]	
Genotype 6			24 weeks	12 weeks[b]	

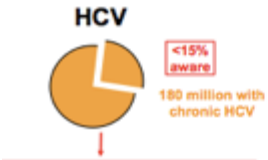
HBV/HCV Prevention Guidance + Activities in higher risk populations

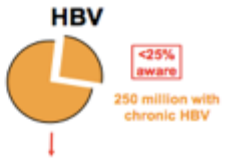
Confirms need for scaling up harm reduction, and includes new recommendations:

1. Recommendations on **HBV** catch-up vaccination of priority adult populations including **MSM, SW, Transgender people, people in prisons and PWID**
   - Consider rapid HBV vaccination regimens for PWID with incentives
   - Combined HAV/HBV vaccination in HAV low ender
2. Minimize **HCV transmission** through intensifi **reduction**, incl. in closed settings
   - OST for opioid dependent individuals,
   - NSPs, including low dead- space syringes
   - Prevention of sexual transmission in stimulant use
3. Prevention of **sexual transmission** in (young) **HIV/HCV**. Ensure access to condoms and lubricants

- **Advocacy at key events**
  - UN partners, UNODC
  - GF - funding treatment of HCV in PWID
  - Sessions at harm reduction conferences
  - UNGASS 2016

Large burden of undiagnosed and untreated hepatitis B and C





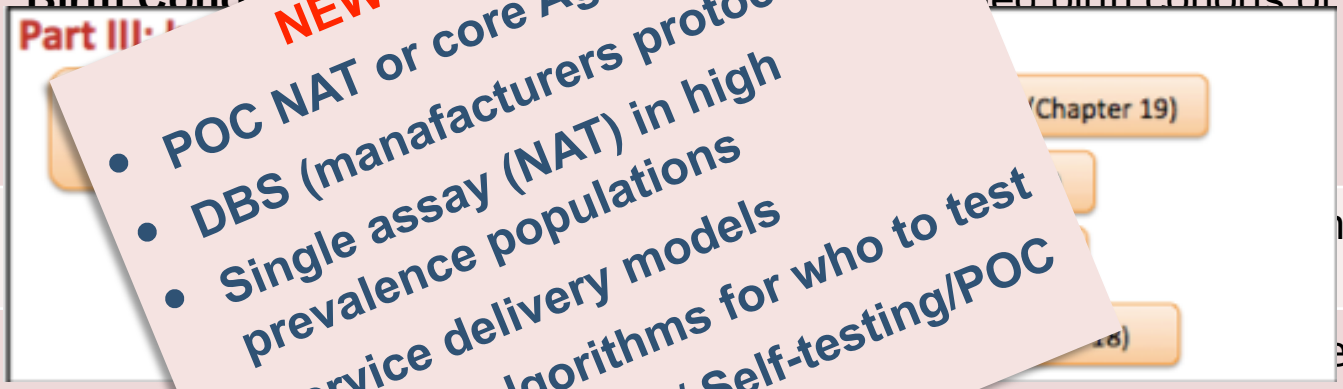
Barriers to testing, linkage and treatment

- Screening
- Diagnosis
- Case selection
- Treatment
- Monitoring
- Assess SVR

	Patient	Healthworker
Lack of awareness, knowledge, understanding	✔	✔
Stigmatisation and discrimination	✔	✔
Lack of testing and treatment services	✔	✔
Rapid diagnostic tests (varying quality, lack of quality approved choice)	✔	✔
Nucleic acid tests (Expensive, complex, limited availability)	✔	✔
Financial (Expensive tests/ treatments)	✔	

Hepatitis testing guideline recommendations (2

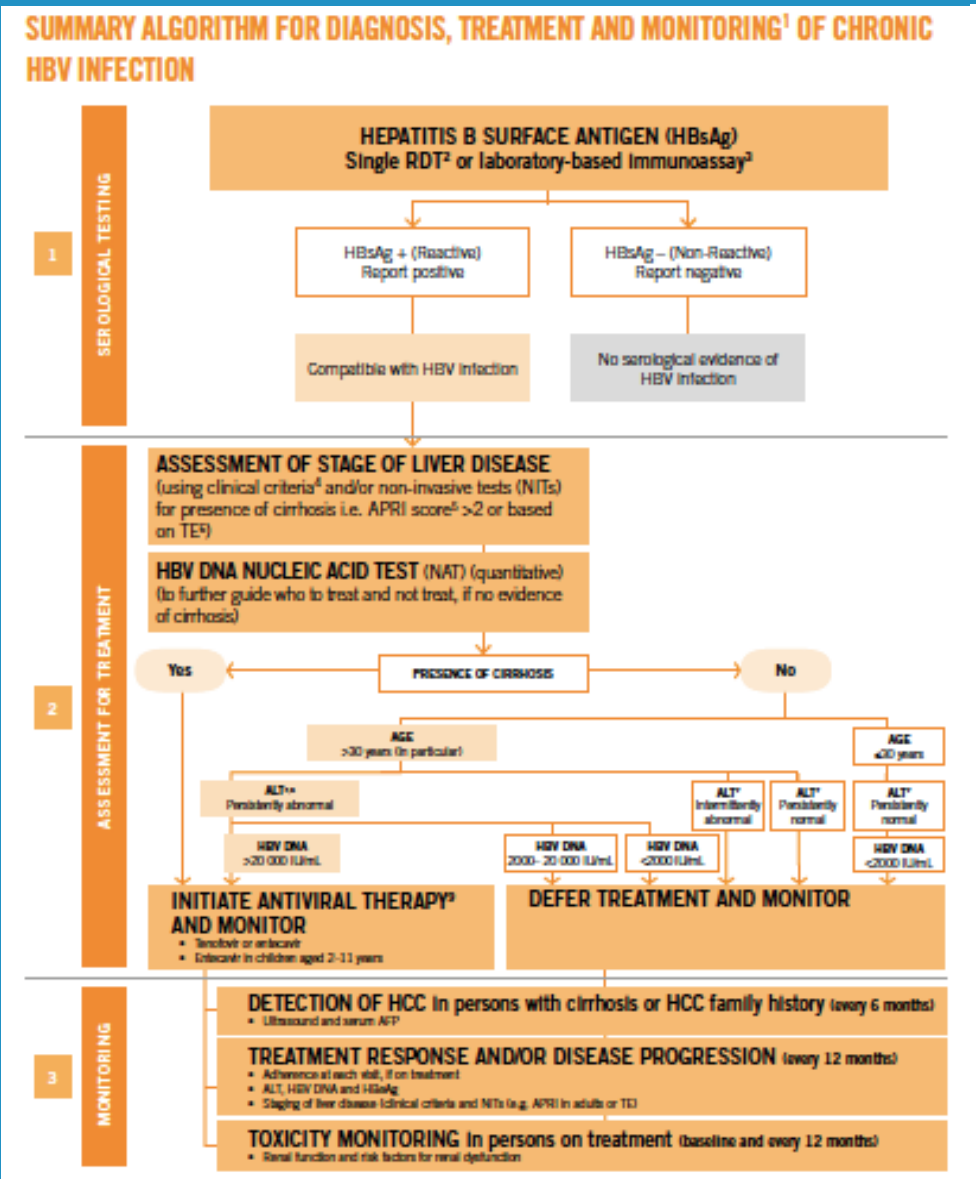
Topic	Recommendation
Who to test?	▪ **Focused testing** for most affected populations, those with a clinical suspicion of chronic viral hepatitis, family members/children, and sexual partners (HBV), healthcare worker.
	PWID, people in prisons, MSM, sex workers, HIV-infected, some migrant populations from high/ intermediate endemic countries, some indigenous populations, children of mothers with HBV/HCV
	▪ **General population testing:** ≥2% or ≥5% (intermediate/ high) HBsAg or HCV Ab ▪ **Birth Cohor** ied birth cohorts of older ▪
How to test?	▪ ance
Confirmation of viraemia	▪ e HCV antigen ivity
Promoting uptake and linkage	▪ Use of DB ± serology ▪ On-site or i esting with same day results ▪ Trained peer ay health workers ▪ Clinician reminders + Testing as part of integrated services at single facility

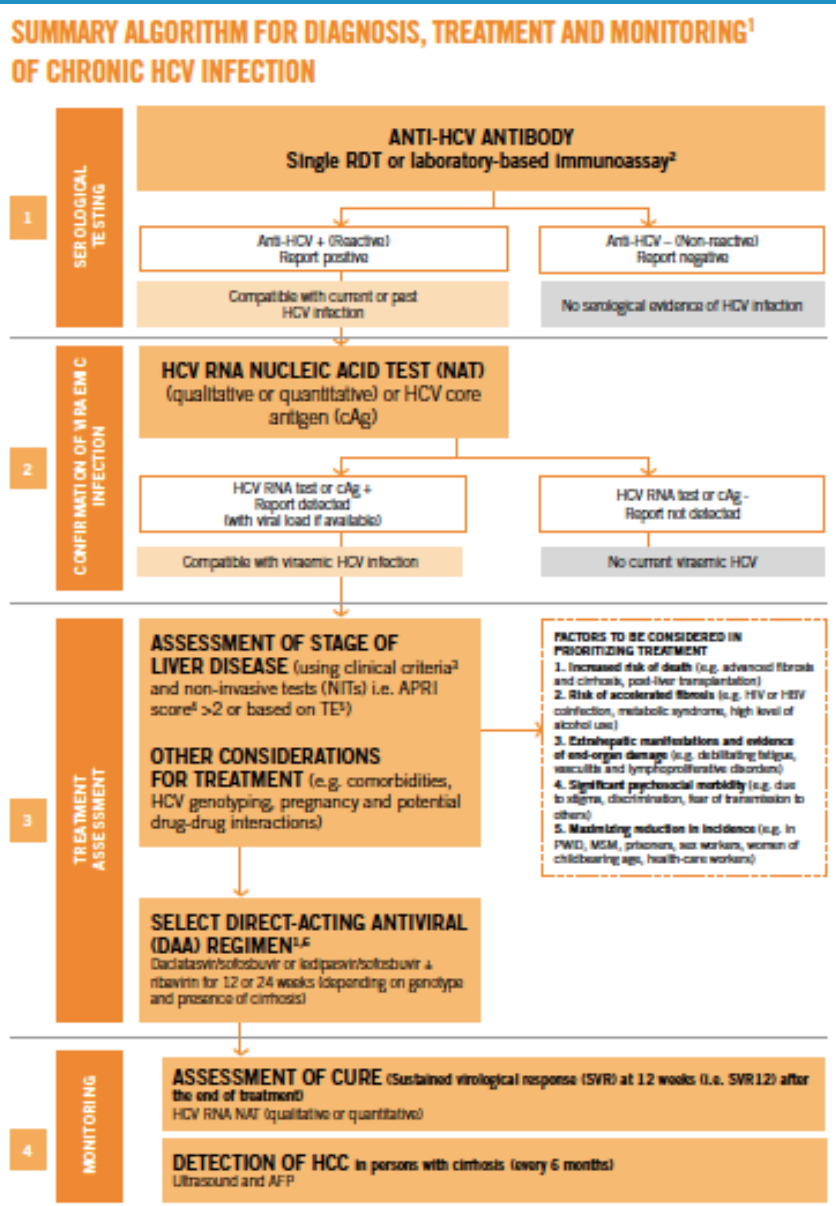


NEW DIRECTIONS:

- POC NAT or core Ag
- DBS (manafacturers protocols)
- Single assay (NAT) in high prevalence populations
- Service delivery models
- Country algorithms for who to test
- Multiplex testing/ Self-testing/POC
- APRI

Algorithms of diagnosis, treatment and monitoring



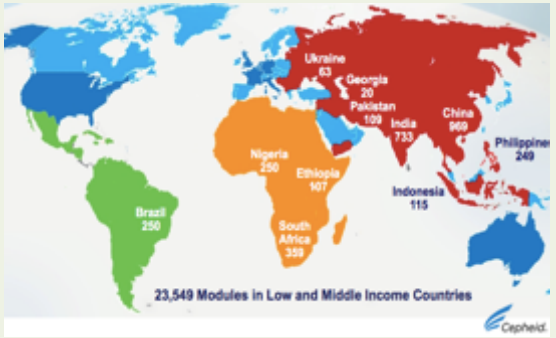


Key Messages - Service Delivery

Use health facility or community- based testing services and opportunities

TESTING SITES	*TESTING APPROACHES*	
	Routinely offered	Focused (Risk-based)
HEALTHCARE FACILITY TESTING		
Primary care settings	X	
Antenatal clinics	X	
HIV clinics	X	
TB clinics	X	
STI clinics	X	
Drug treatment and harm reduction services	X	
Inpatient and outpatient hospital settings	X	
Paediatric and adolescent clinics	X	
COMMUNITY-BASED		
Mobile/outreach testing for priority populations		X
Mobile/outreach for the general population (for example young people)		X
National testing campaigns/camps	X	X
Testing of family members		X
Partner testing (for all partners of people with viral hepatitis)		X
Mass media and social media	X	X
Home-based/ door-to-door testing	X	X
Workplace testing		X
School/educational institution testing		X

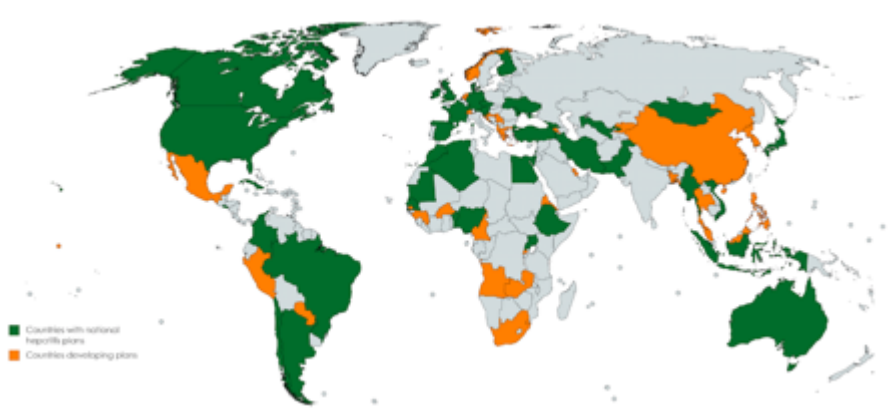
- **Build on substantial existing lab and diagnostics capacity, esp HIV/TB**



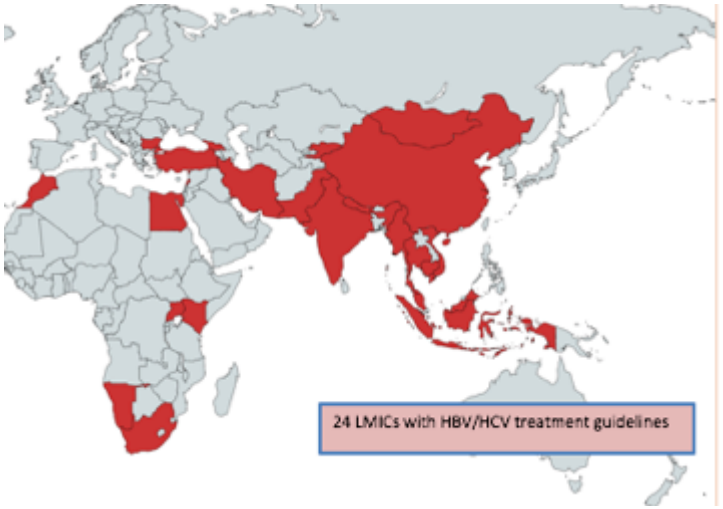
- **Make use of existing opportunities for testing eg. HIV**
- **Strategic use of focused testing in health facilities**
- **Moving testing into community**

Assessing the response and guidelines uptake (2016)

44 with National Viral Hepatitis Plans



24 with HBV ± HCV treatment guidelines



13 with hepatitis testing guidelines

Region (total number of countries)	Number of countries with testing guidelines (n=13)	Number of countries with self-reported government policy related to testing (n=51)
AFRO (47)	1	1
EURO (53)	5	21
PAHO (47)	3	8
EMRO (23)	3	9
SEARO (11)	0	3
WPRO (27)	1	9

Demonstration projects

Generating evidence for scale-up

ACCESS CAMPAIGN — MEDICINS SANS FRONTIERES

FIND

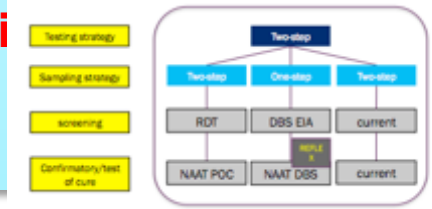
World Health Organization

MSF UNITAID funded

- HCV treatment of 1300 persons over 5 years
- Use of new DAAs
- **Service delivery models**

FIND-WHO UNITAID funded

- **7 countries:** Myanmar, India, Georgia, Vietnam, Cameroon, Malaysia/ Indonesia
- **2017 PROGRAMME EVALUATION AND LESSONS LEARNT**
  - **HCV:** Egypt, Georgia, Mongolia, Pakistan, India
  - **HBV:** Uganda, China
- **…ment**
- **…erate evidence for WHO guidelines**
- **Guide mini… assurance**



CHAI- DFID funded

- **Potential countries:** Myanmar, Indonesia, …eria, Rwanda, …pia
- **…r drug and …ostic prices**
- **…rt countries to … HCV programs**

1. Strategic Planning
2. Lab System Strengthening
3. Patient Service Delivery
4. Training
5. Supply Chain

Simplified Service Delivery Models

- Community engagement and peer led services
- Task-sharing
- Integrated services
- Differentiated care
- Effective linkage to care
- Support for adherence/retention in care (HBV)

- Persons who inject drugs
- Prisoners
- Sex workers
- Adolescents and children
- Pregnant women

- "Hub and spoke"
- Training curriculum
- Apps and ECHO support

2017 PRIORITIES

- **Technical report/paper on models of service delivery (testing and treatment** (Co-location, task-shifting/ decentralisation)

How to share best practice in viral hepatitis testing and treatment?

- Integrated patient care team at WHO has established some excellent websites that have standardised an approach to collating models of good practice.
- Some sites are led and maintained by collaborating centres and partners, and others by WHO HQ.
- Could serve as a model for development of a hepatitis good practice site
- http://www.integratedcare4people.org/practi
- http://www.integratedcare4people.org/communities/integrated-people-centred-palliative-care/

The Way Ahead: WHO Priorities

- **Data to increase awareness, inform strategic choices and priority setting:**
  - **Strengthening surveillance** – disease burden analysis
  - **Monitoring and evaluation** of HCV/HBV treatment scale-up and outcomes

- **Birth dose vaccination:** Advocacy and support to countries in region on introduction/expansion of birth dose of Hepatitis B

- **National plans and guidelines**: Development of tailored national (integrated and costed) plans and guidelines

- **Promoting affordability:** Support countries in affordable access to hepatitis medicines and diagnostics; shared costs with other strategies eg. Harm reduction and HIV)

- **Optimize Service Delivery for reach and quality:** A public health approach (simplification, integration, affordability, equitable access)

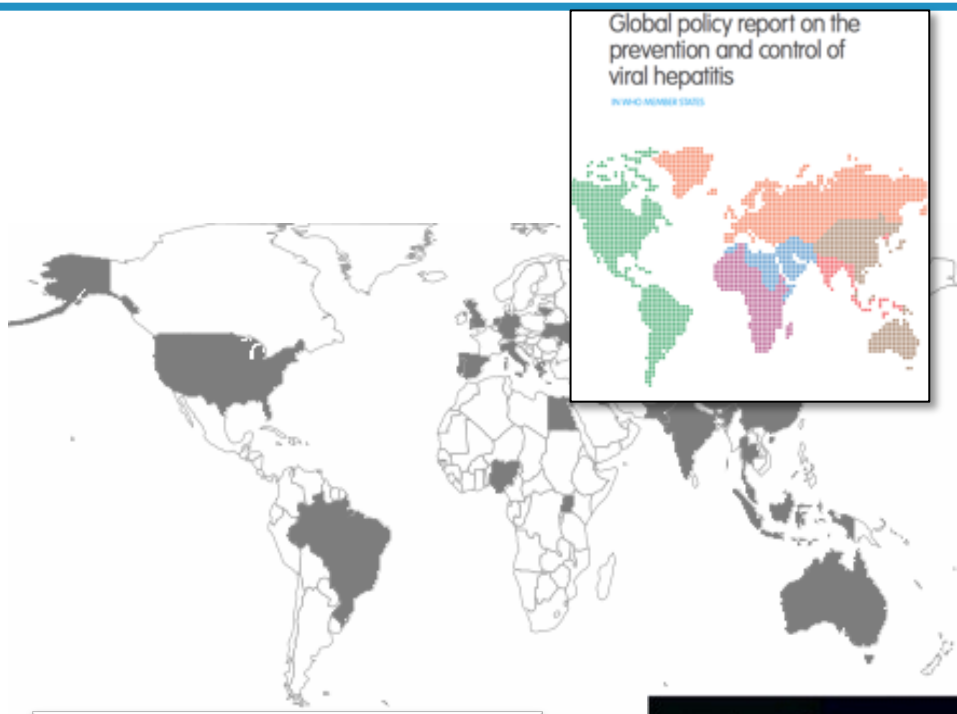
Hepatitis focus countries

	AFR	AMR	EMR	EUR	SEAR	WPR
1st tier	Nigeria Uganda	Brazil	Egypt Pakistan	--	India Indonesia Myanmar	China Mongolia Vietnam
2nd tier	Cameroon Ethiopia Sierra Leone South Africa Tanzania Zimbabwe	Colombia Mexico Peru	Morocco	Georgia Kyrgyzstan Ukraine Uzbekistan	DPR Korea Nepal Thailand	Cambodia Philippines

World Health Organization

Civil Society-WHO partnership activities

- **Guidelines development**
- **Demonstration projects** (FIND-WHO UNITAID)
- **Social Media Innovation Contest** #HepTest
  - To solicit descriptions of different HBV/HCV testing models to inform WHO Testing Guidelines
  - 64 contributions from 27 countries
- **Advocacy events**
  - Promotion of World Hepatitis Day
  - Global Hepatitis Policy Report
  - Global Partners' Meeting on Hepatitis
  - Civil Society Reference Group
  - World Hepatitis Summit



A global hepatitis movement building up…

from Glasgow…. ….to Sao Paulo