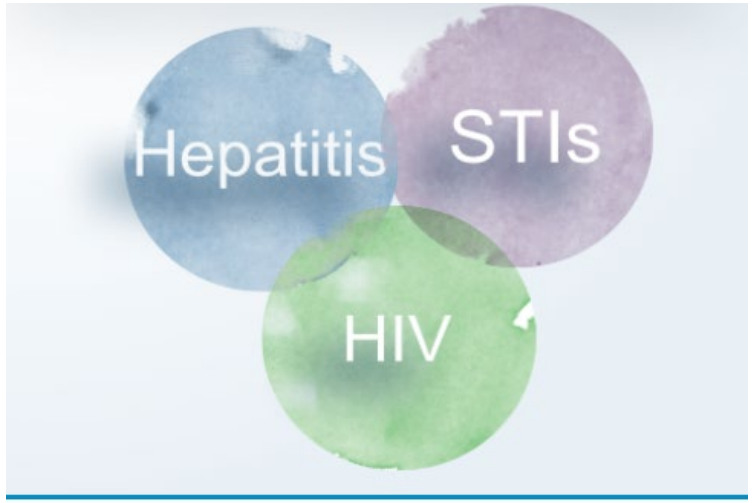
HIV/STI/Hepatitis diagnostic and treatment guidelines: current guidelines and upcoming updates



Marco Vitoria
WHO/HHS/TAC
Geneva, 09 March 2022

HHS Flagship Priorities 2022

unicef | UNFPA | World Health Organization

Initiatives

Global Health Sector Strategies

- HIV, Hep and STIs remain as priorities
- From WHA adoption to regional frameworks to action via country National Strategic Plans (NSPs)
- 2025 and 2030 global targets

COVID-19 & HIV, Hepatitis and STIs interactions, adaptations & learning

- Maximize understanding COVID impact on EHS and recovery (data and guidance)
- Vaccination and PLHIV and/or Hepatitis, Cervical Ca

The Elimination agenda

- Hepatitis B & C elimination - (goal for at least 1 country certified in 2022)
- Triple Elimination of HIV, HepB and Syphilis MTCT / vertical transmission (goal for XX countries to be certified in 2022)
- Ending childhood HIV Initiative

New areas

HIV - innovations

- The Cure and HIV vaccine agenda (new priority)
- Long-acting prevention and treatment (LA-CAB PrEP guidelines) and implementation science learning for scale up
- Reducing HIV related deaths - AHD, Crypto, NCDs, engagement of men and SD innovations (virtual etc) to improve VLS & quality of life

Hepatitis - towards greater integration and simplification

- Consolidated Hepatitis B & C guidelines - focus on simplification and country implementation
- Hepatitis M&E framework and strengthening country data collection & reporting
- Financing & sustainability through UHC & PHC

STIs - reinforcing and growing new interventions

- Consolidated guidelines - updating for better treatment, diagnostics, vaccines
- Invest in reducing STI-DR – EGASP surveillance, developing POCT, link to AMR
- STI M&E framework for improved data collection & reporting
- Scale up STI interventions via UHC & PHC packages and programmes

X-cutting

Key and focus populations

- Implementation of KP guidance for HIV, hepatitis and STIs in counties
- Increase community engagement
- Address stigma and discrimination in the health sector

Pathway to PHC – collaborations within WHO and with partners

- 3 level implementation of UHC and PHC packages for impact
- Strengthen primary prevention across all 3 diseases

Person-centred data systems and use

- 2022 Consolidated Guidelines on Strategic Information for HIV, Hepatitis and STIs
- Use of person-centered drug and diagnostics access data
- Surveillance of epidemics and monitoring of policy implementation

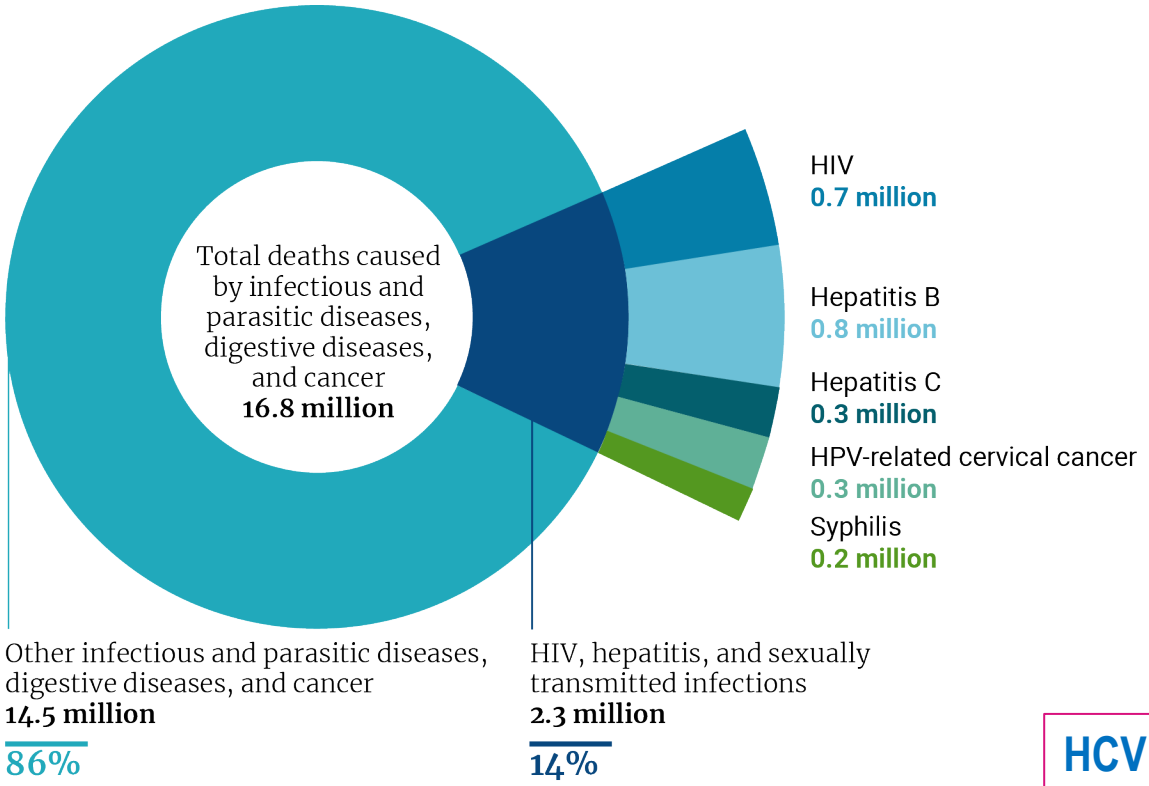





Scaling HIV, Hepatitis and STI global responses has the potential to save 2 million lives per year by 2030



2.3m deaths per year



Disease	New cases
Hepatocellular carcinoma caused by hepatitis B and C	500 000
Cervical cancer caused by HPV	570 000
Other types of cancer caused by viral hepatitis and HPV	140 000
Total	**1 210 000**

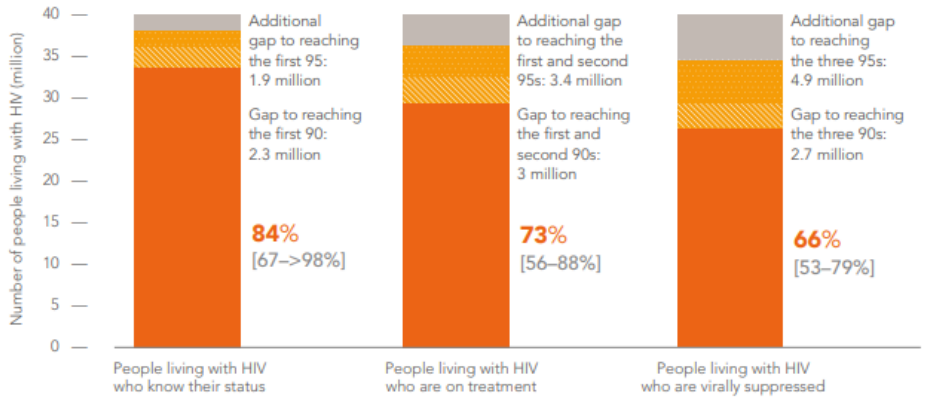
1m
new STI infections each day

1.2m
new cancer cases each year

HCV Prevalence – 57.8 m (46.2 m – 75.9 m)
HBV Prevalence – 295.9 m (228.2 m – 422.6m)
HBV Prevalence under 5 years – 6.4 m (4.4 m – 10.8 m)

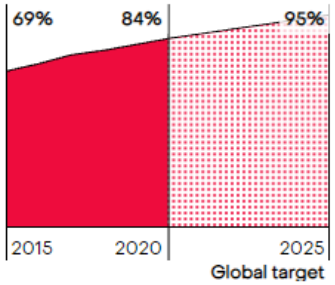
The challenges towards the “last mile” to end AIDS

FIGURE 0.3 | **HIV TESTING AND TREATMENT CASCADE, GLOBAL, 2020**

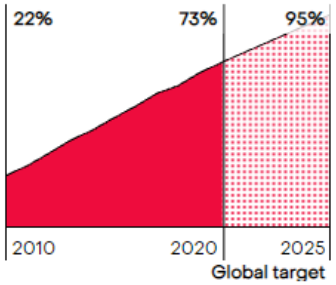


Source: UNAIDS special analysis, 2021.

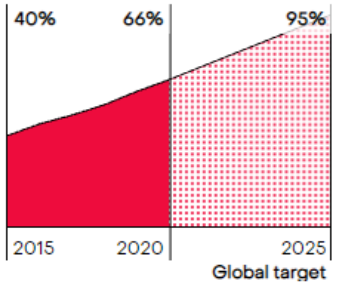
People living with HIV who know their status



ARV coverage

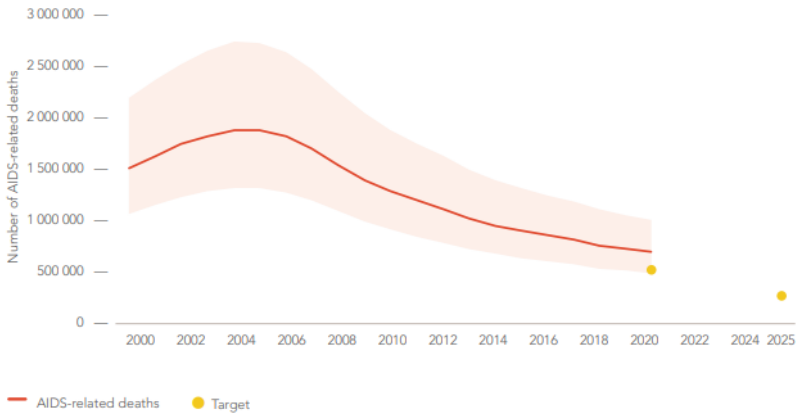


People living with HIV with suppressed viral load



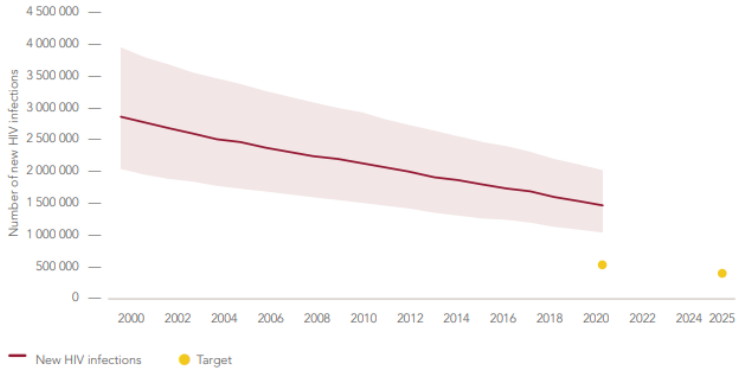
Progress graphs are based on latest published data from UNAIDS, 2021 release.

FIGURE 0.4 | **AIDS-RELATED DEATHS, GLOBAL, 2000–2020, AND 2020 AND 2025 TARGETS**



Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).

FIGURE 0.5 | **NEW HIV INFECTIONS, GLOBAL, 2000–2020, AND 2020 AND 2025 TARGETS**

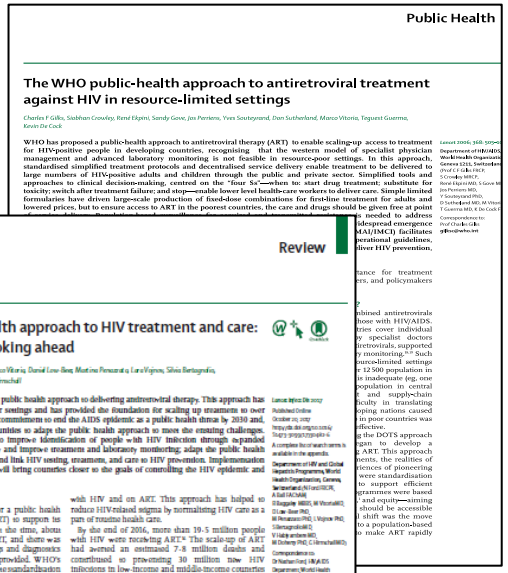


Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).
Note: Please see the Annex on Methods for a description of how these estimates are calculated.



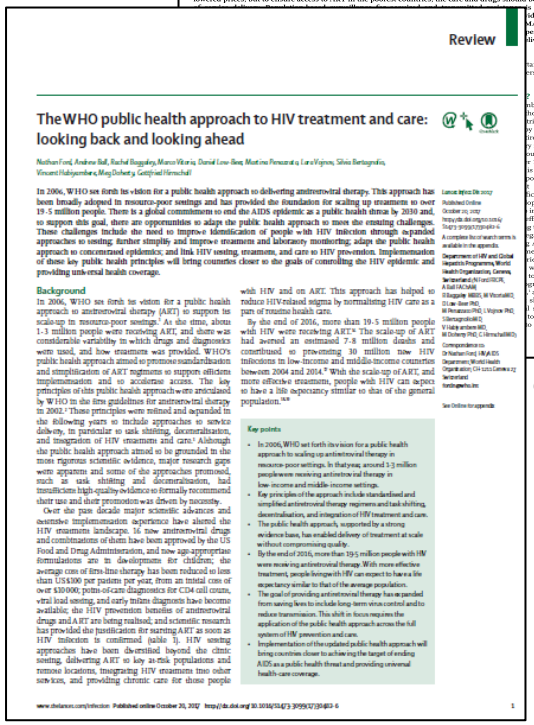
The public health approach to HIV treatment

Policy	PAST	PRESENT	Basis for policy change
When to start	"Treat the sickest" Low CD4 cell count or WHO clinical stage 3 or 4	"Treat all" Rapid ART start	Reduced mortality, morbidity and transmission
What to start	6 possible regimens	Single preferred regimen	Superior efficacy and safety; better adherence using fixed-dose, once daily ART
How to monitor	Clinical or CD4 cell count monitoring (every 6 months)	Viral load monitoring (annual)	Better ascertainment of adherence & treatment failure
Where to provide treatment	Health district	All health facilities; community; DSD	Comparable clinical outcomes & improved retention
Who can provide treatment	Clinical team of doctors, clinical officers, nurses	Doctors, nurses, midwives; trained lay providers refill	Comparable clinical outcomes


Public Health

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

Gilks et al, *Lancet* 2006


Review

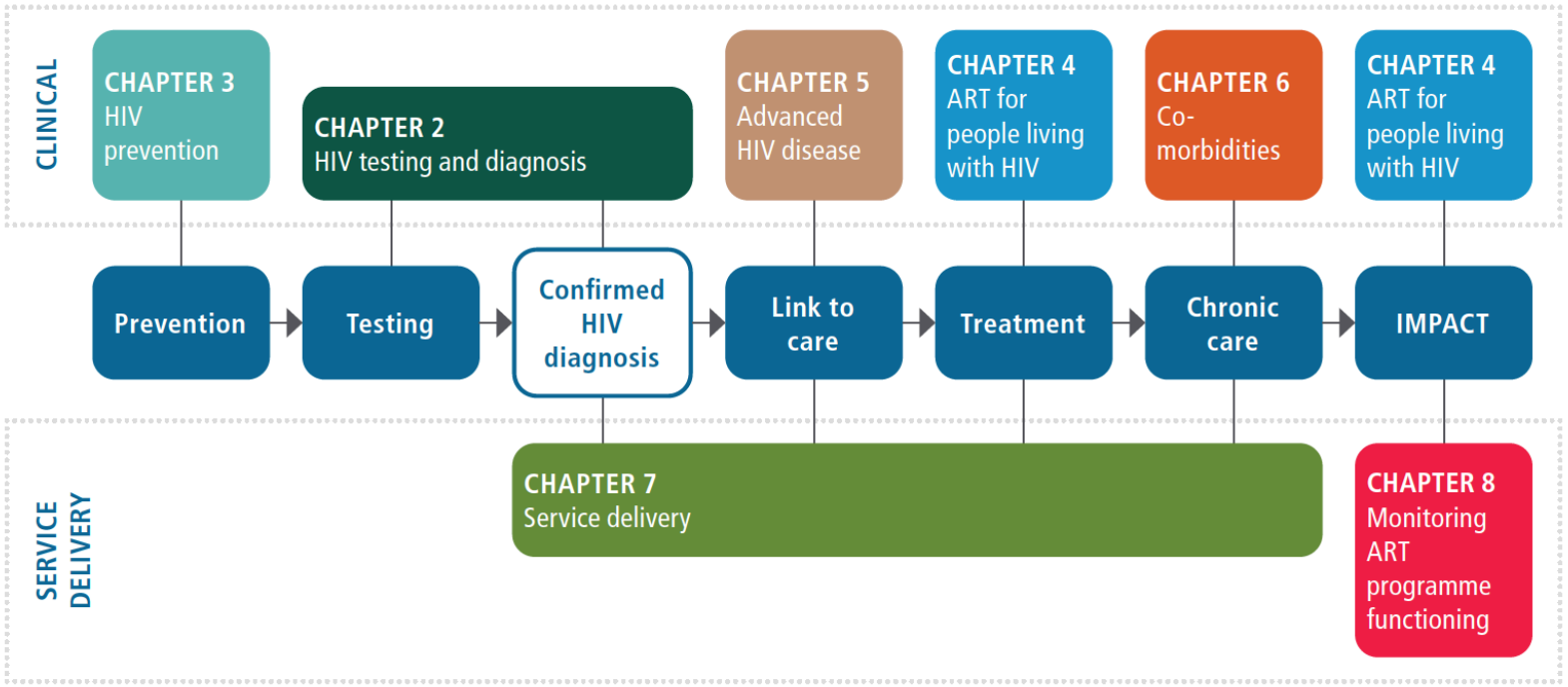
The WHO public health approach to HIV treatment and care: looking back and looking ahead

Ford et al, *The Lancet Infectious diseases* 18 3 (2017): e76-e86

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The new 2021 Consolidated Guidelines on HIV

Continuum of care and relevant sections of the guideline



- Incorporation of WHO new and updated recommendations published **between 2016 – 2021**
- Target-focused revision of chapters for maximum **impact**
- **A new chapter on advanced HIV disease**
- Brings together over **200 recommendations and good practice statements**



What's new in the HIV treatment and care chapter?



WHO continues to recommend the use of **dolutegravir-based ART** with 2 NRTIs as preferred first and second-line regimens for adults, adolescents and children



Enhanced guidance on the **timing of ART initiation** in those with HIV-associated infections/comorbidities to support rapid ART initiation in all populations



Key guidance on the use of **point-of-care tests** for treatment monitoring, management of toxicities related to ARVs and monitoring of drug resistance has also been updated.



The revised and updated **treatment monitoring algorithm** has also been incorporated.






2021 WHO HIV clinical recommendations at a glance

Point-of-care viral load test may be used to monitor ARV treatment	Conditional
Point-of-care NAT should be used to diagnose HIV among infants and young children	Strong
ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count	Strong

Point-of-care viral load recommendation

- **Improves turnaround time of results to patients (HR 17.7)**
- Improves turnaround time of results to clinician (HR 11.7)
- Increases probability of same-day results to patients
- **Reduces time to clinical action for elevated VL (HR 10.9)**
- Increases probability of and reduces time to differentiated care (RR 2.2 and HR 3.5, respectively)
- Increases retention in care and viral suppression at 18 months (RR 1.2)

Box 4.5. Priorities for point-of-care viral load testing

The following populations should be given priority for point-of-care viral load testing:

- Pregnant and breastfeeding women
- Infants, children and adolescents
- People requiring a repeat viral load after a first elevated viral load
- People for whom treatment failure is suspected
- People presenting sick, living with advanced HIV disease or having a known opportunistic infection (TB, cryptococcal infection, etc.)
- First scheduled viral load test for people re-entering care

Point-of-care infant diagnosis recommendation

Infants 8 times more likely to start treatment within 60 days with POC testing compared to SOC testing

- OR 7.9 (95% CI 5.4-11.5, p<.001)
- 92.8% start within 60 days with POC, 50.5% with SOC
- Time to ART initiation: *0 days (95% CI 0-1 days) for POC vs 39.5 days (95% CI 34-43 days) for SOC*
- Same day treatment initiation 51% with POC, 0% with SOC



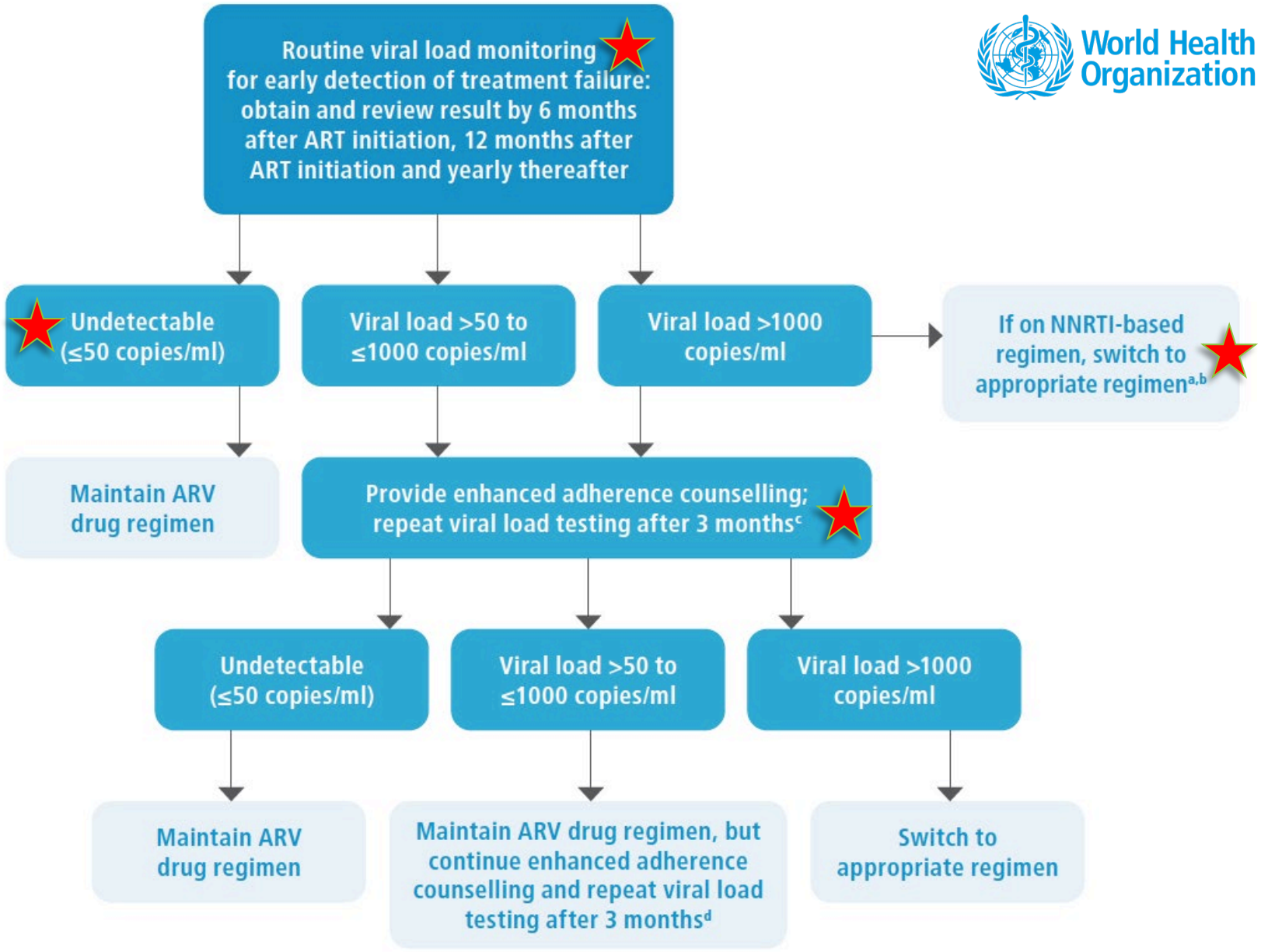



2021 updated treatment monitoring algorithm

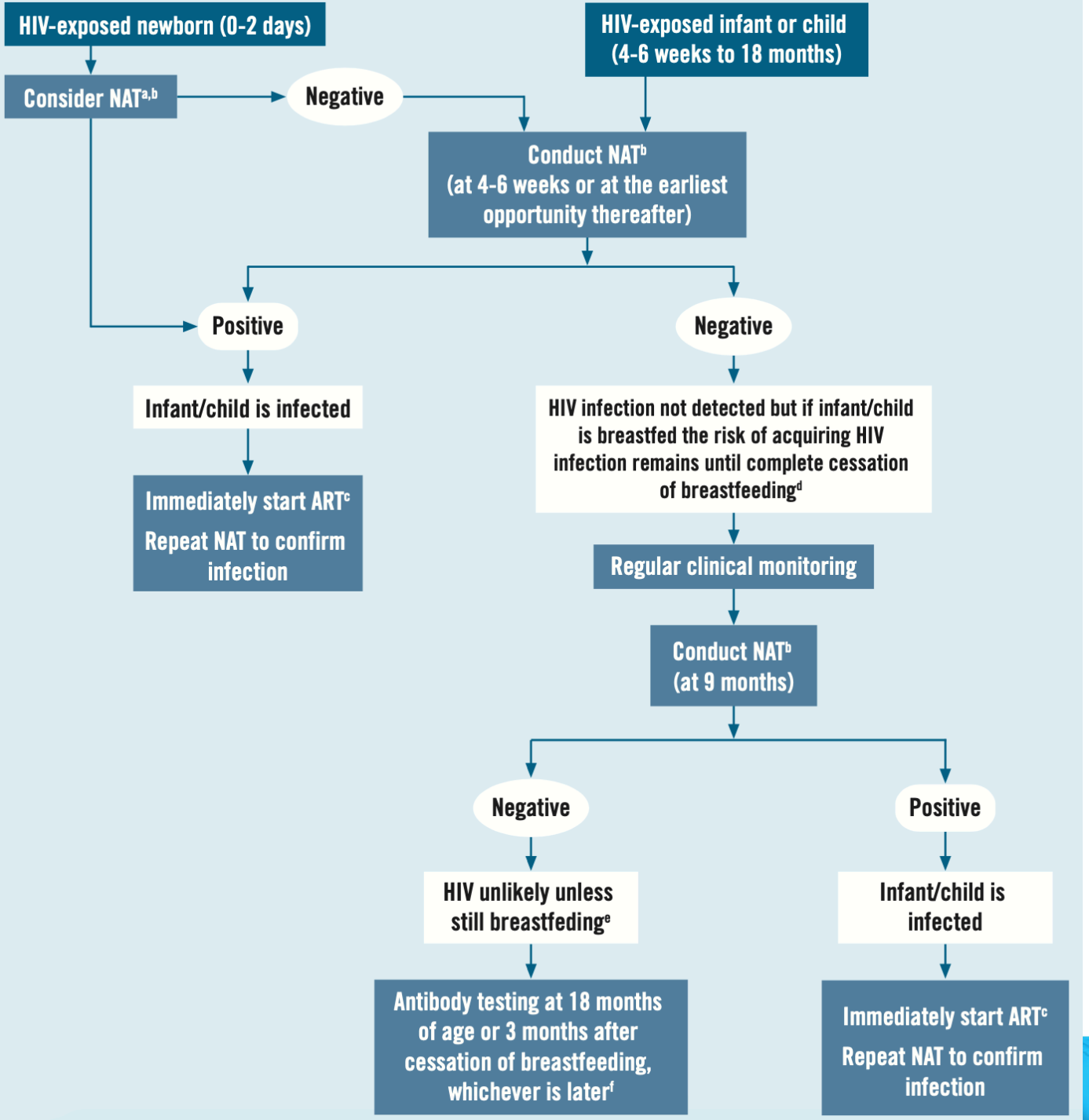
Four key questions considered for thee revision:

1) Timing of first viral load
2) Timing of repeat viral load after elevated viral load
3) Immediate (single viral load) switch to second-line ART in patients on EFV-based ART
4) Treatment failure threshold (and consideration for a suppression/undetectable threshold)

Implementation considerations also include treatment monitoring for **pregnant and breastfeeding women** for their own health and with the goal of reducing vertical transmission



Adherence counselling should be provided at all visits to ensure that viral suppression is maintained or given priority throughout care



unicef | UNFPA | World Health Organization

Infant testing algorithm: it's a process!

Moving to a multi-HIV NAT algorithm

- Birth (where of value)
- 6 weeks
- 9 months
- Any time HIV exposed infants present sick

Strongly recommend POC at all time points

Ensuring **confirmatory** testing of a positive NAT result is undertaken

Diagnosis is not completed without "final diagnosis" at the end of the period of risk for transmission





2021 WHO HIV Service Delivery Recommendations at a glance

ART initiation may be offered outside the health facility	Conditional
Clinical visits every 3-6 months, preferably 6 months if feasible*	Strong
ART dispensing every 3-6 months, preferably 6 months if feasible*	Strong
Tracing and support for people who have disengaged	Strong
SRH services, including contraception, may be integrated with HIV services	Conditional
Diabetes and hypertension care may be integrated with HIV services	Conditional
Psychosocial interventions should be provided to all adolescents and young adults living with HIV	Strong
Task sharing of specimen collection and point-of care testing with non-lab personnel when professional capacity is limited	Strong

***People who are established on ART: new definition given**





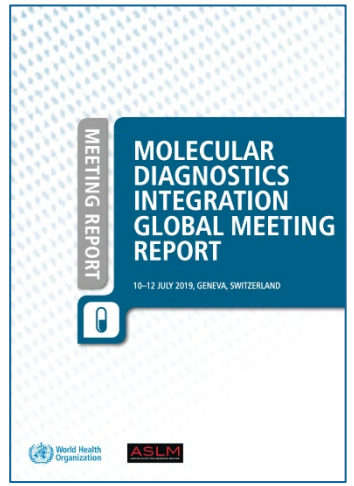

Diagnostic integration across programmes

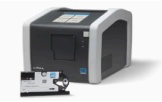
Offering TB, EID and targeted VL through integrated testing increased device utilization, without exceeding capacity or impacting TB services

- Integrated testing is operationally feasible with appropriate site selection to balance the expected demand

Near-POC testing can enable faster and increased rates of clinical action for HIV+ infants and PLHIV on ART experiencing viremia

- Same-day result delivery was possible for EID with near-POC device
- Faster clinical action was achieved for both EID and VL improving outcome
- Integrated testing does not impact the potential impact of near-POC testing and is viable option to scale-up near-POC testing which has been shown to be impactful

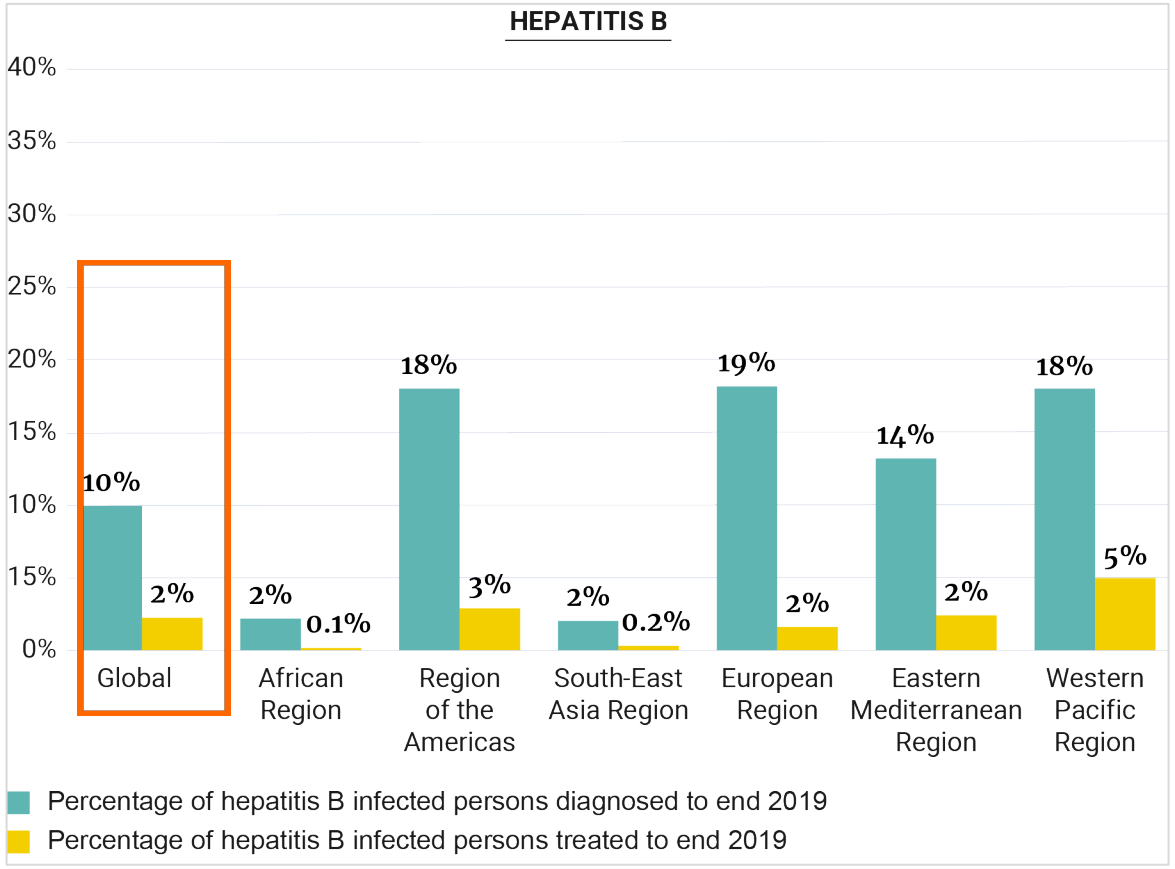


		Abbott m2000sp	Abbott m-PIMA	Cepheid GeneXpert GX-4, 16, 48, 80	Hologic Panther	Roche CAP/CTM 96	Roche 4800/ 6800/8800
							
Max daily throughput (incl. controls)		96 (8hrs) 288 (24hrs)	8 (8 hrs)	GX4: 16 (8hrs) GX16: 64 (8hrs)	320 (8hrs) 1,220 (24hrs)	168 (8hrs) 312 (24hrs)	384/960 (8hrs) 1,344/3,072 (24hrs)
Test menu	HCV VL	✔[a]	✘	✔[a]	✔	✔	✔[c]
	HBV VL	✔	✘	✔	✔	✔	✔
	HIV EID	✔[a]	✔[a]	✔[a]	✔	✔[a]	✔[c]
	HIV VL	✔[a]	✔[a]	✔[a]	✔[a]	✔[a]	✔[c]
	MTB	✔	✘	✔[b]	✘	✔	✔
	HPV	✔[a]	✘	✔[a]	✔	✔[c]	✔[c]

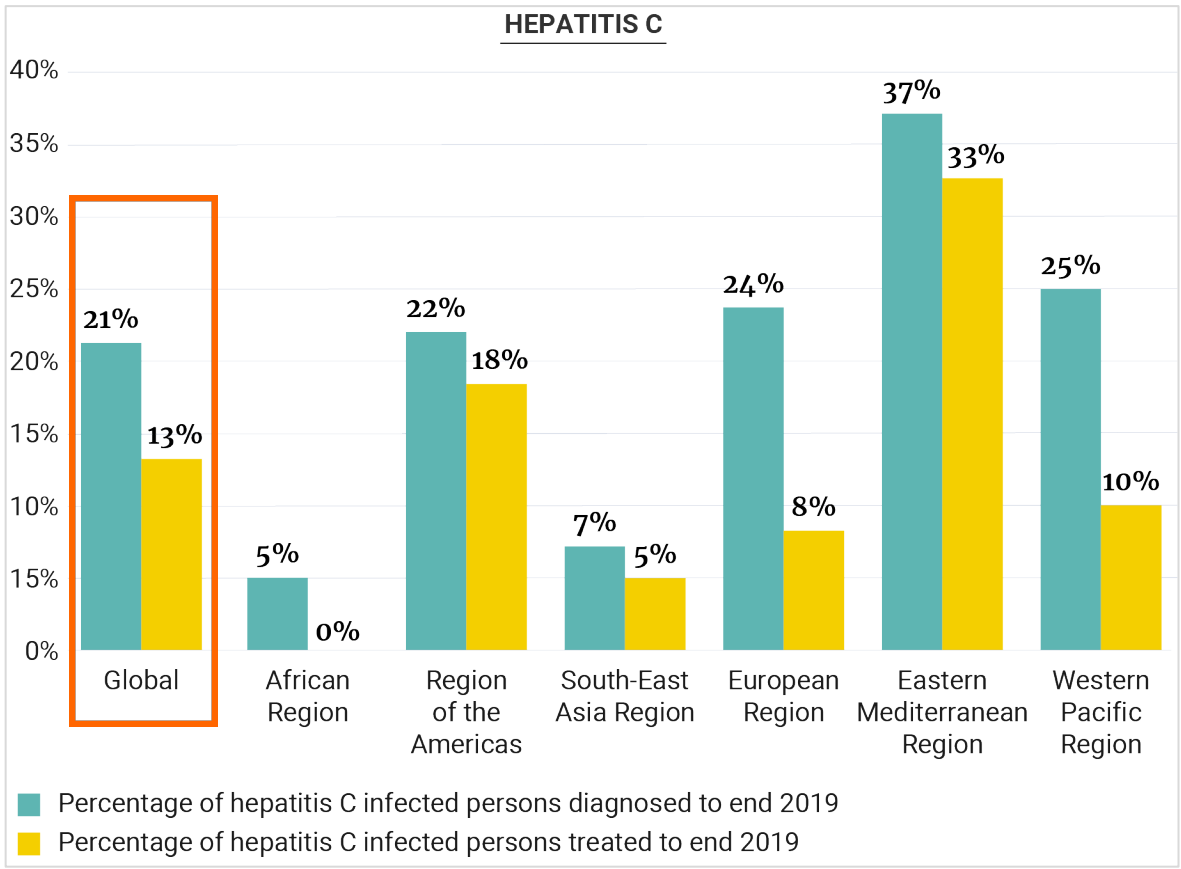
[a] Technologies with WHO prequalification listing
[b] Technologies endorsed by WHO (Global Tuberculosis Program)
[c] Technologies currently undergoing WHO prequalification review
Information included as of December 20, 2019. Pictures are not to comparable scale.

Improved data shows major gaps in path towards public health elimination of Hepatitis B & C

- **10% of estimated 296 million people with chronic HBV were diagnosed in 2019 and 2% treated**
- **6.6 million people receiving HBV treatment in 2019**



- **21% of estimated 58 million people with chronic HCV were diagnosed in 2019 and 13% treated**
- **9.4 million people had been treated 2015-2019**



WHO Guidelines for viral hepatitis is available to support hepatitis elimination

2015

- ✓ Elimination strategy
- ✓ HBV Guidelines

2016

- ✓ Revised HCV Guidelines (inclusion DAAs)
- ✓ National plan development manual

2017

- ✓ Baseline estimates: Global Hepatitis Report
- ✓ HBV/HCV testing Guidelines
- ✓ Injection safety campaign

2018

- ✓ Global hepatitis reporting system piloted
- ✓ HCV treatment Guidelines: Treat All
- ✓ Cost effectiveness calculators (HBV/HCV)

2019

- ✓ Consolidated strategic information guidelines (Feb 2019)

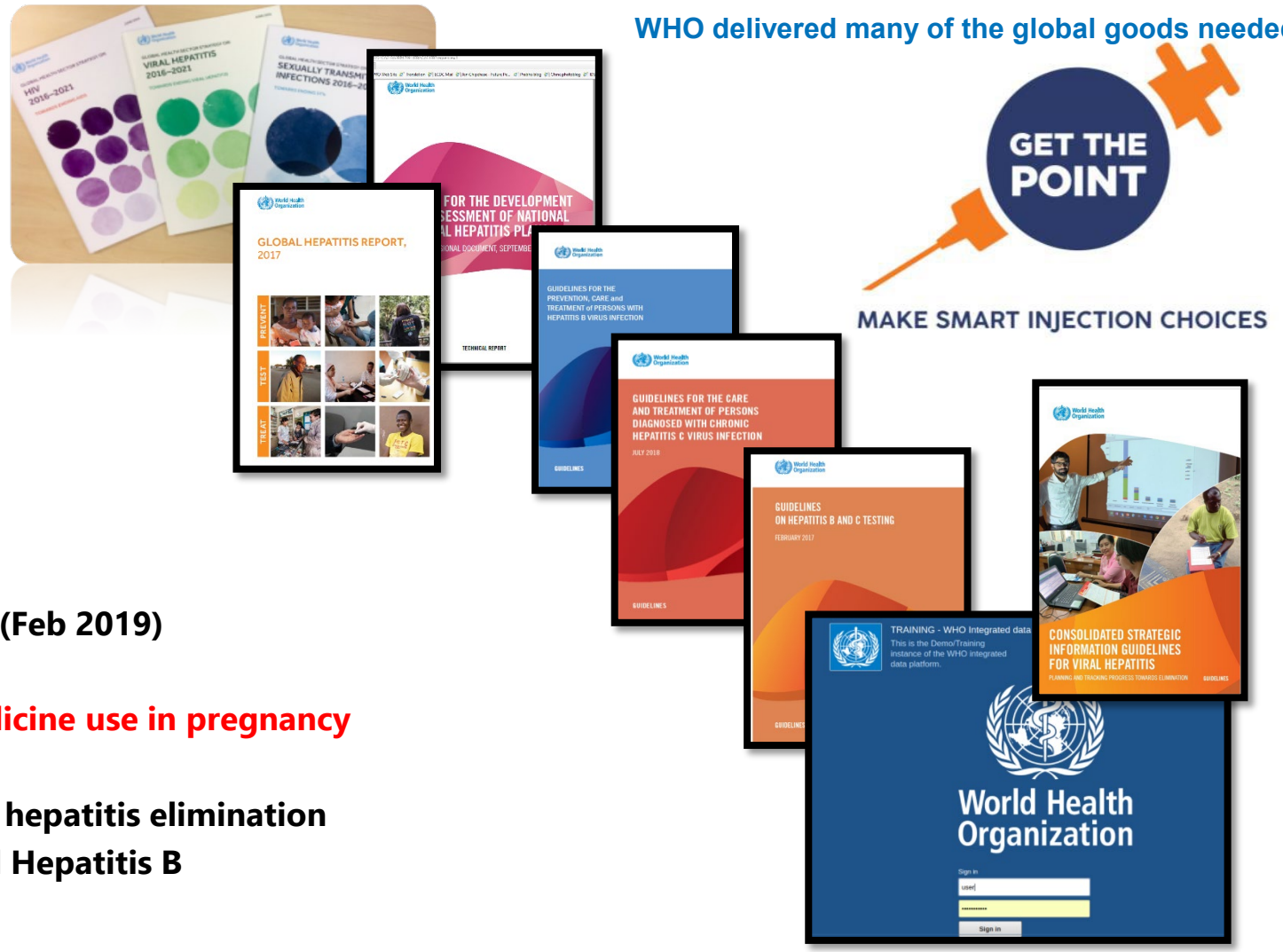
2020

- ✓HBV PMTCT recommendations on antiviral medicine use in pregnancy

2021

- ✓Interim Guidance for country validation of viral hepatitis elimination
- ✓Global Validation of EMTCT of HIV, Syphilis and Hepatitis B
- ✓HCV self -testing guidelines

WHO delivered many of the global goods needed



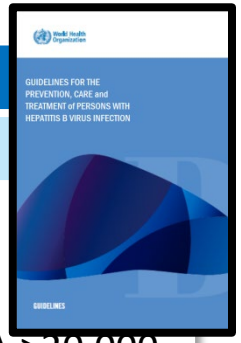








HBV Guideline Recommendations (2015)

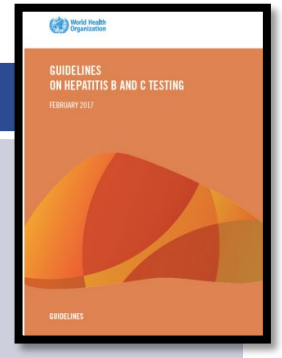


TOPIC	RECOMMENDATION
Staging/ non-invasive test (NIT)	▪ APRI preferred NIT to assess for the presence of cirrhosis
Who to treat	▪ Decompensated cirrhosis or cirrhosis (clinical criteria or APRI score >2), regardless of ALT levels, HBeAg, or HBV DNA. ▪ No cirrhosis but persistently abnormal ALT levels +/- ongoing HBV replication, (HBV DNA >20,000 IU/mL *or* HBeAg +ve).
First line treatment	▪ Drugs with a high barrier to resistance (TDF or ETV). ▪ ETV in children aged 2-11 years.
Treatment failure	▪ Switch to TDF if evidence of resistance to 3TC, ETV, ADF, TBV.
Treatment discontinuation	▪ Never discontinue in persons with cirrhosis. ▪ If no cirrhosis, discontinuation on case-by-case basis (persistent HBeAg and/or HBsAg loss or undetectable HBV DNA)
Monitoring (treatment response/toxicity)	▪ *On or pre-treatment:* ALT + HBV DNA (HBsAg, HBeAg + APRI pre-treatment) annually. More frequent monitoring with cirrhosis. ▪ Assessment of baseline renal function prior to treatment initiation.
Monitoring for HCC	▪ Ultrasound + AFP every 6 months in persons with cirrhosis and/or family history of HCC.
PMTCT antiviral prophylaxis (2020)	▪ TDF prophylaxis in those with HBV DNA >200,000 IU/mL from 3rd trimester or HBeAg positive (if HBV DNA not available)






Hepatitis B&C testing guideline recommendations 2017



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 workers. ▪ **General population testing:** In settings with ≥2% or ≥5% (intermediate/high) HBsAg or HCV Ab prevalence. ▪ **Birth cohort testing (HCV):** where specific identified birth cohorts of older persons at higher risk of HCV infection ▪ **Routine antenatal clinic testing (HBV)**
How to test?	▪ A **single** serological assay (**EIA or RDT**) that meets minimum performance standards with prompt NAT testing + linkage to care
Confirmation of HCV viraemia	▪ **Nucleic acid testing (NAT) (quantitative or qualitative RNA)** or core HCV antigen assay, with comparable clinical sensitivity
Promoting uptake and linkage	▪ Use of DBS specimens for virology ± serology ▪ On-site or immediate RDT testing with same day results ▪ Trained peer and lay health workers ▪ Clinician reminders to prompt provider initiated, facility-based testing ▪ Testing as part of integrated services at a single facility






DAA regimens across adults and adolescents

WHO Hepatitis C Guidelines (2018)



>18 years

Without cirrhosis

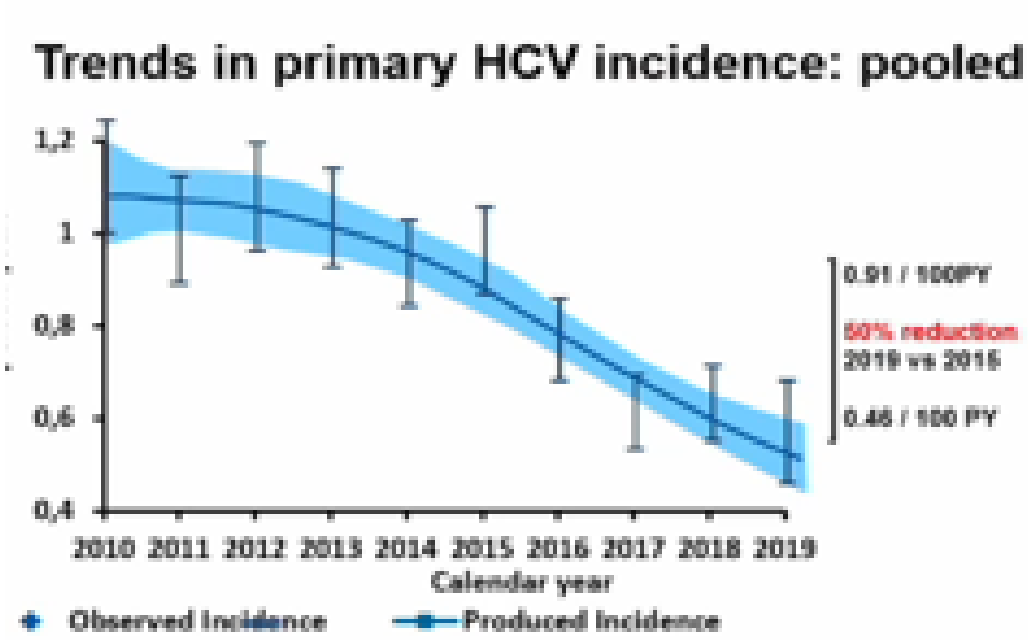
Sofosbuvir / Velpatasvir for 12 weeks or
Sofosbuvir /Daclatasvir for 12 weeks or
Glecaprevir /Pibrentasvir for 8 weeks

In adolescents 12-17 years/≥ 35kg

Sofosbuvir/Ledipasvir for 12 weeks
Sofosbuvir/Ribavirin for 12 weeks in GT 2
Sofosbuvir/Ribavirin for 24 weeks in GT 3

In children <12 years

Deferring treatment until age 12 years
Avoiding interferon-based regimens





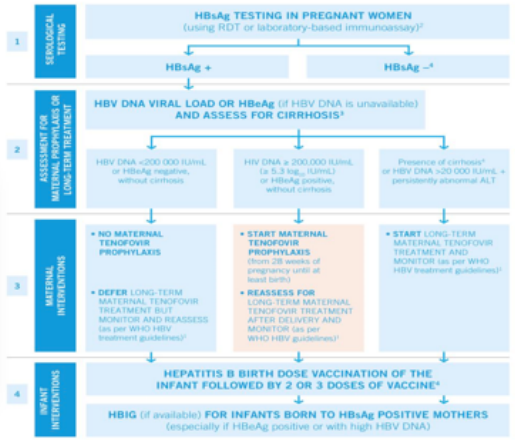



WHO Hep B&C testing strategies (2020/2021)

PMTCT: Antenatal testing and use of HBV: antiviral prophylaxis in pregnancy WHO guidelines (2020)

evidence-based guidance on the use of peripartum antiviral prophylaxis in HBsAg-positive pregnant women for the prevention of mother-to-child transmission of HBV and infant vaccination at birth





Triple elimination strategy (HIV, Syphilis and HBV)

WHO recommendation on HCV self-testing (2021)

Hepatitis C virus (HCV) self-testing should be offered as an additional approach to HCV testing services

(strong recommendation, moderate-certainty evidence)



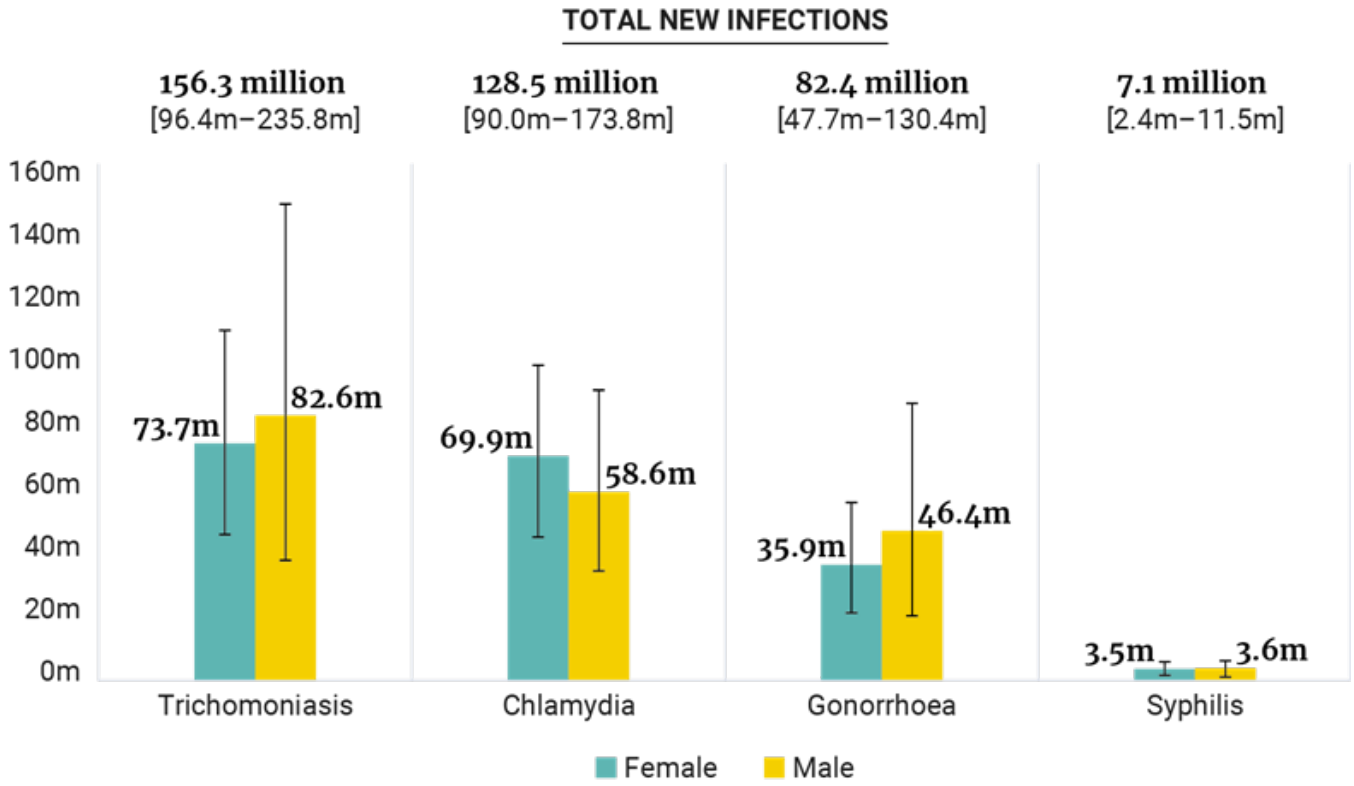
Remarks

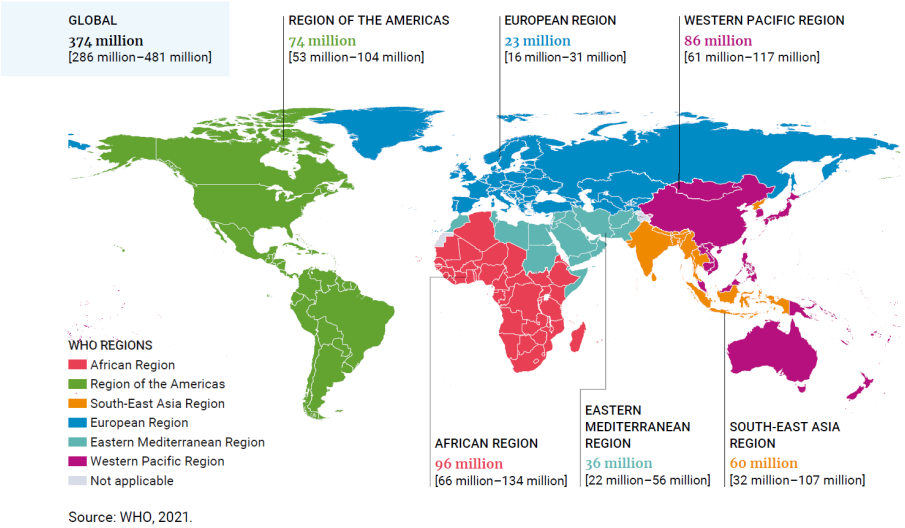
- **linkage to appropriate post-test services** (confirmation, treatment, care and referral services)
- **adapt HCV self-testing service delivery and support options** according local context, and community preferences.
- **Communities, including networks of key and vulnerable populations and peer-led organizations, need to be meaningfully and effectively engaged.**






Incident cases of four curable STIs among adults (15–49 years old), by WHO region, 2020





Source: WHO, 2021.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.



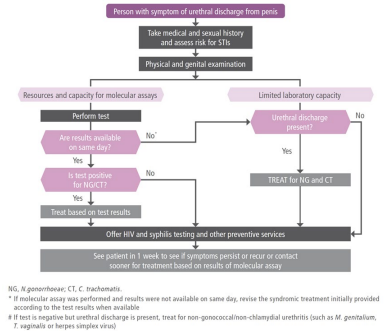


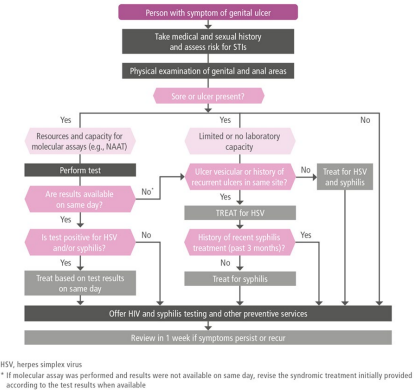

WHO Guidelines for the Management of Symptomatic Sexually Transmitted Infections

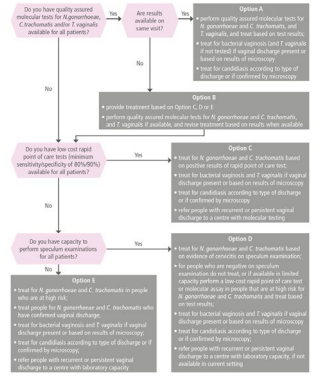
https://www.who.int/publications/i/item/9789240024168

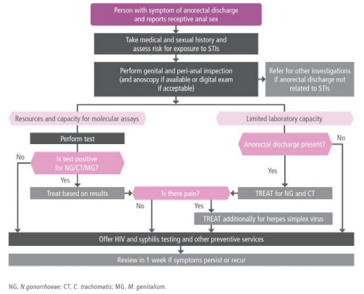


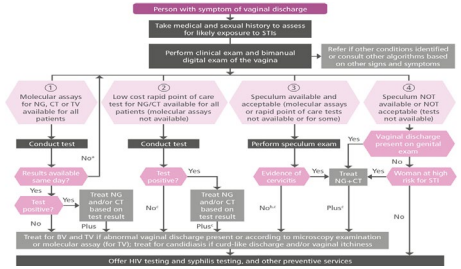
- Last update in mid-2021
- Evidence based recommendations
- “Upgrade” to case management options (more accuracy and minimize overtreatment)
- Treatment based on lab diagnosis (molecular assays, PoC, rapid diagnostic tests) and modified syndromic management
- Management of urethral discharge, vaginal discharge, anorectal infection, genital ulcer and low abdominal (standardized flowcharts)
- Gonococcal antimicrobial resistance (GASP /GLASS)









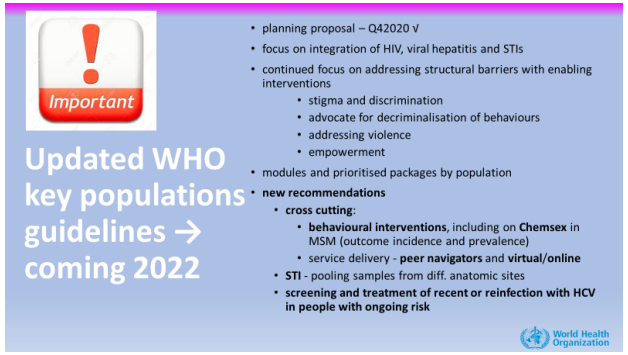


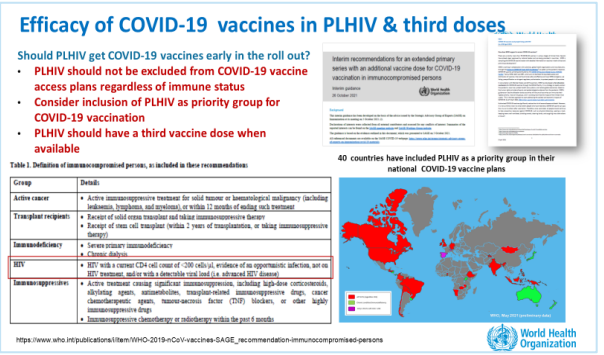
“Strengthening STI case management that ensures access to high-quality services, based on simplified and standardized interventions and services that can be taken to scale, especially in resource-limited settings is a priority

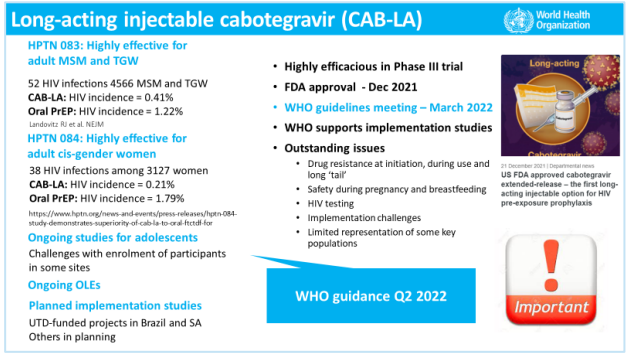
New WHO HHS Guidelines under development –2022/2023

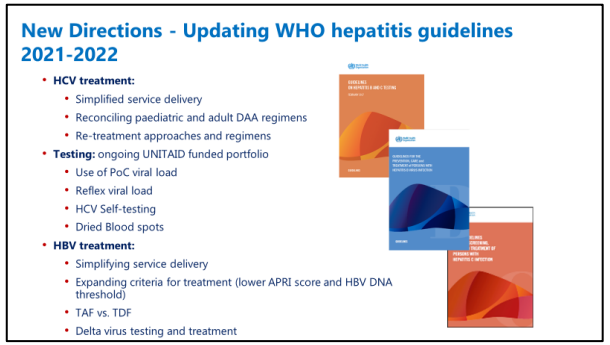
Fully developed and being finalized:

- **Updated Consolidated Key Populations guidelines** – July 2022
- **Long-acting agents for PrEP** –July 2022
- **Updated treatment for Cryptoccocal infection** - July 2022
- **Updated Person-centered Strategic Information Guidelines** – July 2022
- **With SAGE – Updated recommendations for COVID-19 vaccines among PLHIV** – March 2022
- **Hepatitis C peadiatric treatment and service delivery guidelines** – June 2022



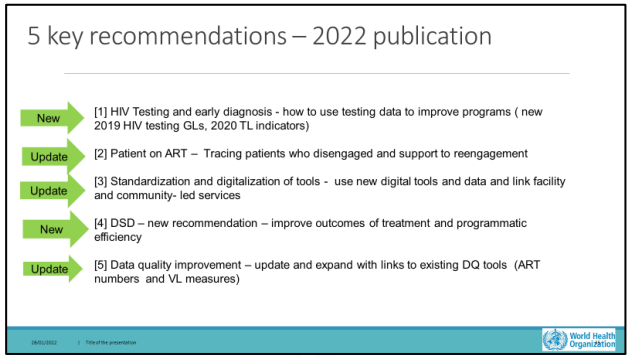


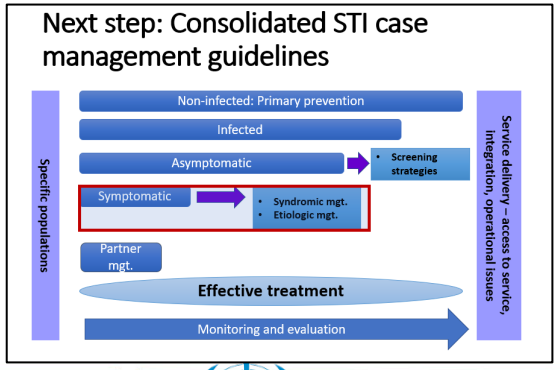




Under development:

- **Updated Hepatitis B Guidelines** – end 2022/23
- **Updated Consolidated STI treatment guidelines** – end 2022/23
- **Transgender guidelines** - 2023

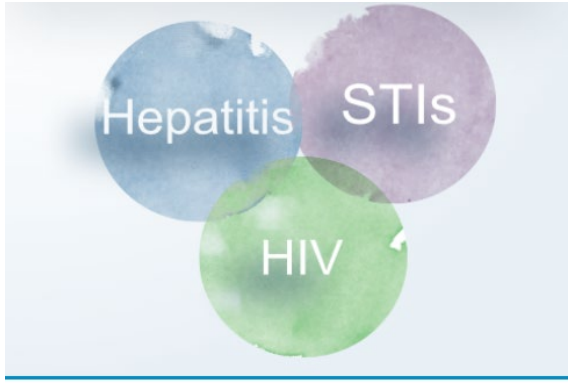




CONCLUSIONS: WHAT ARE THE COMMON ELEMENTS IN HHS DIAGNOSTIC AND TREATMENT GUIDELINES?

- SIMPLIFICATION
- INNOVATION
- INTEGRATION
- IMPACT

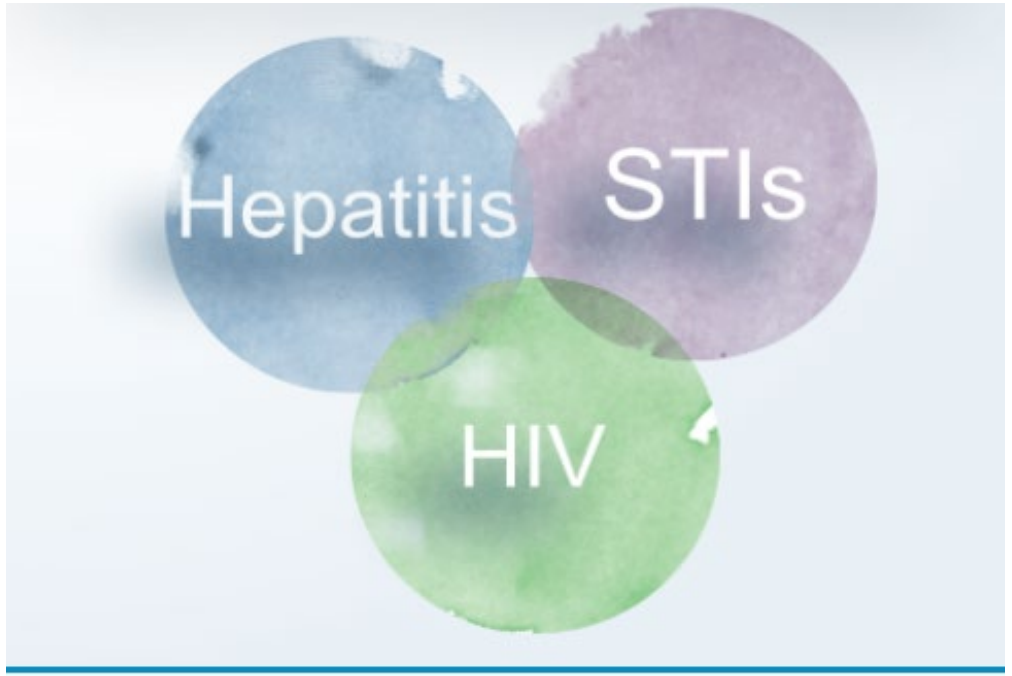
- Use of **evidence based and patient centred** approach
- Moving towards **consolidation and harmonization** across populations and programmes
- **Early diagnosis and treatment** to impact on incidence and mortality
- **Inclusion of molecular assays, PoC technologies, rapid diagnostic tests**, balanced integration of diagnostic services and simplification of management algorithms will enhance the diagnosis and treatment
- **Optimization of treatment regimens and service delivery strategies** to improve uptake and adherence
- **Strengthening integration** with at primary health care services and community engagement





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THANK YOU