The need of simplification of viral hepatitis care to be delivered in LMIC

World Health Organization

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New data on Hepatitis B and C burden, incidence and mortality by WHO region (2021 WHO Global progress report)

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Global Burden

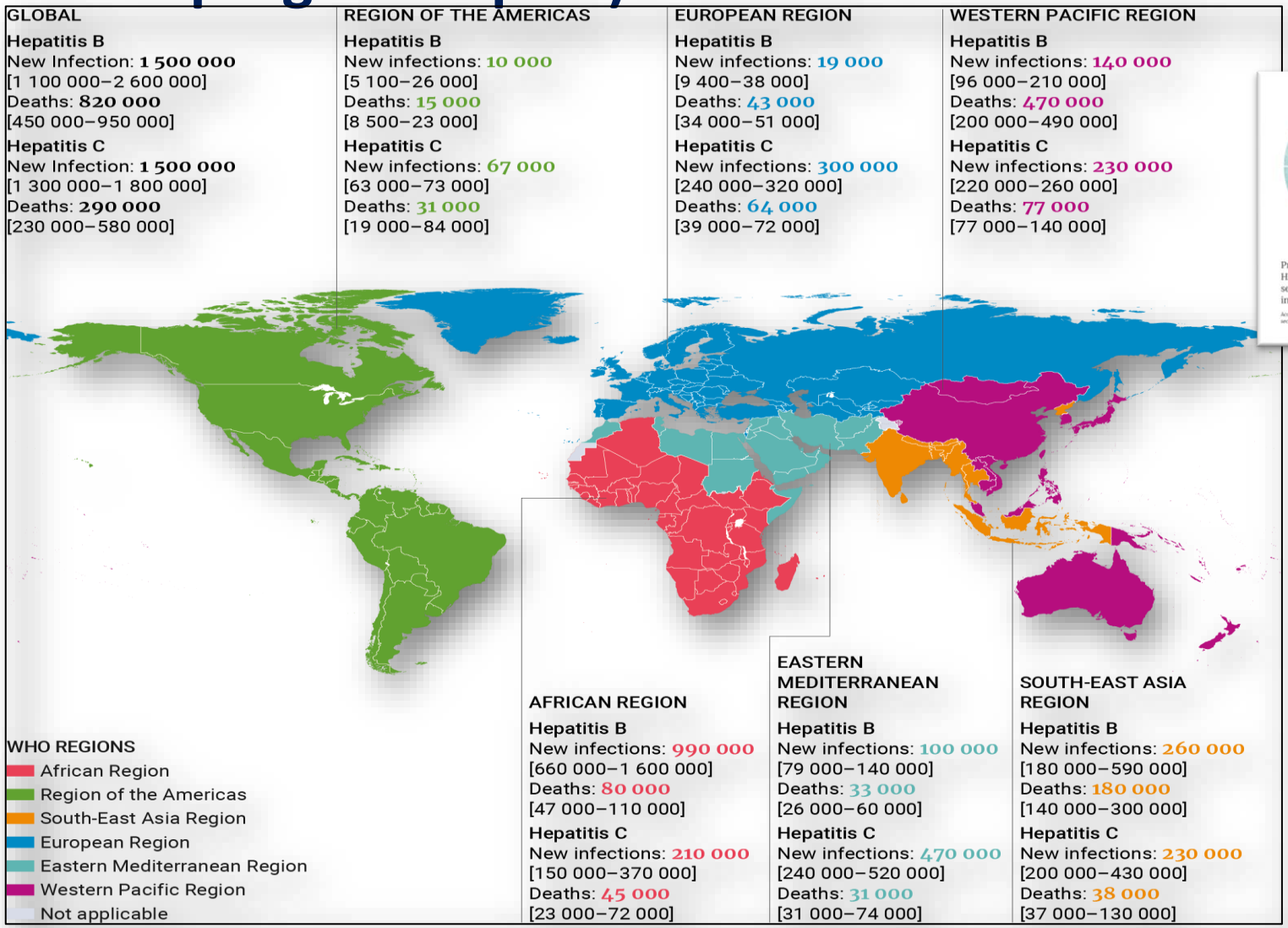
Hepatitis B - 296 m

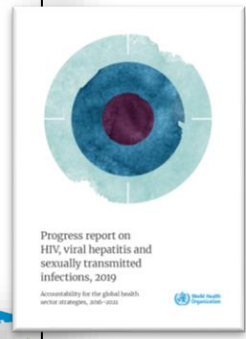
Hepatitis C - 58 m

Viral Hepatitis

New data on incidence, prevalence

- 3.0 million new HCV & HBV infections
- 1.1 million HCV & HBV deaths with initial signs of HCV declines (290,000 deaths)
- Achieved <5 yr HepB prevalence SDG 2020 targets and GHSS goals





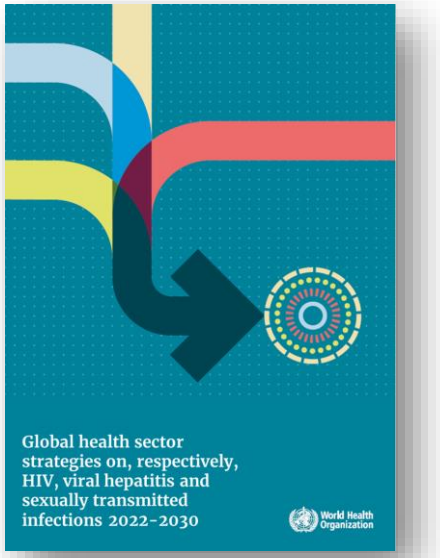
Link to GHSS: 9789240053779-eng.pdf

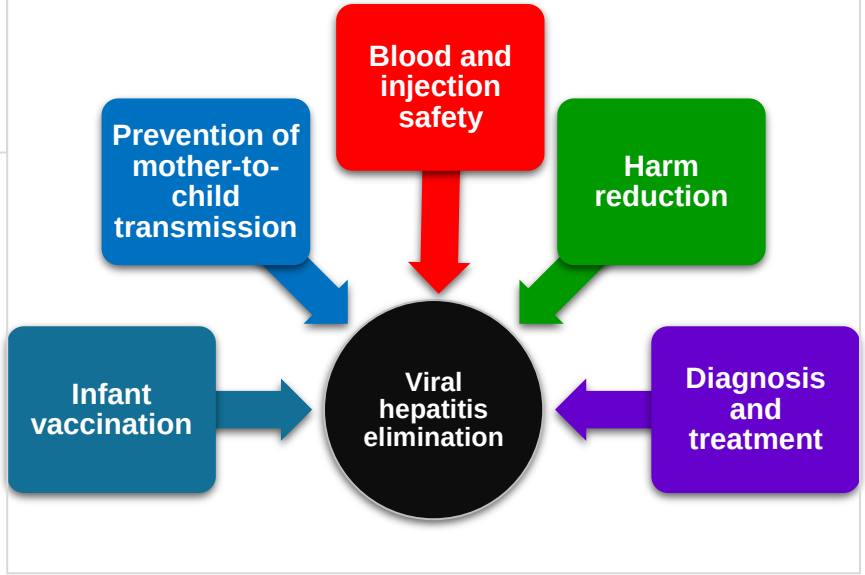
New Global Health Sector Strategy for HIV, VH and STIs

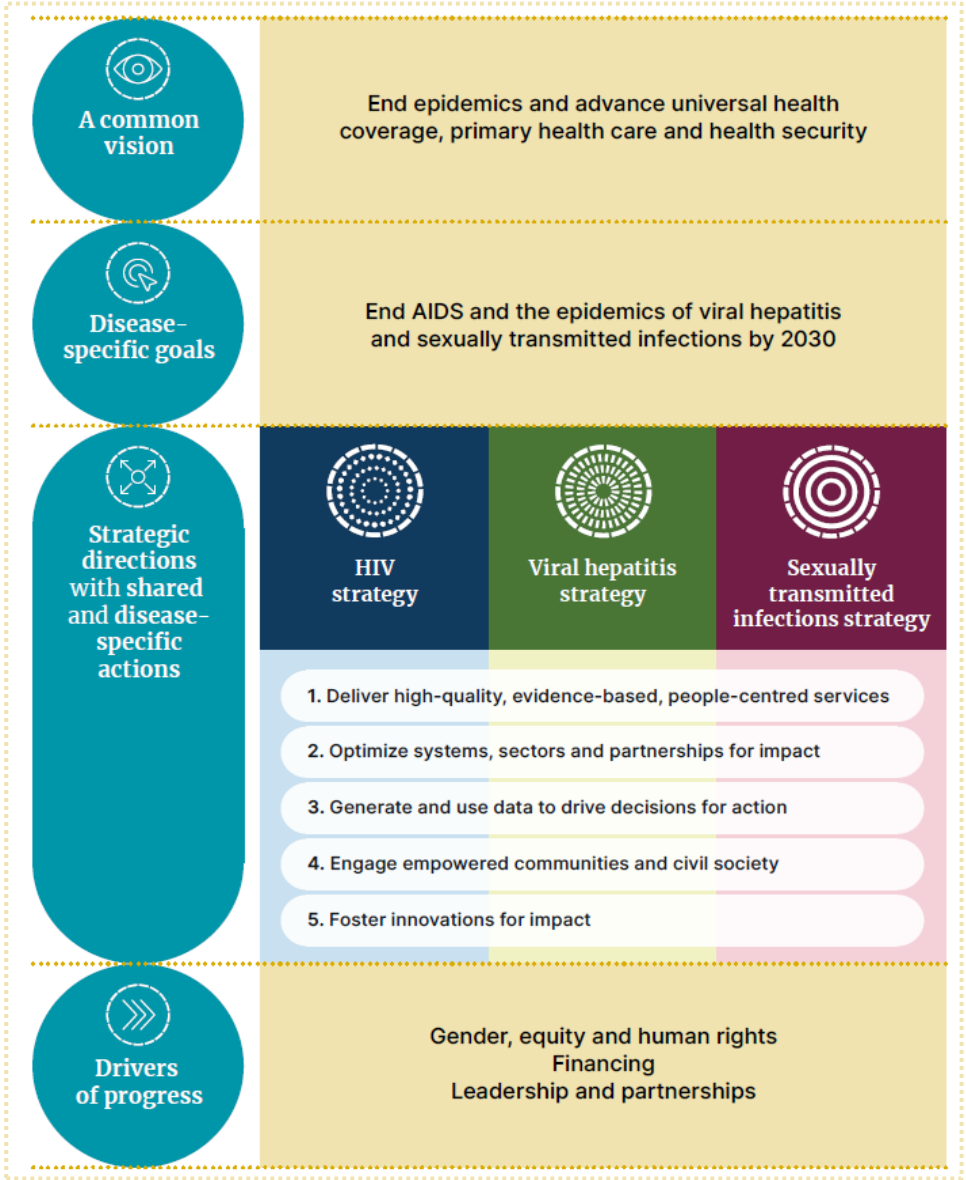
World Health Organization

National planning efforts are guided by the global shifts of GHSS 2022-2030:

- **Putting people at the centre**
- **Taking a shared approach towards strengthening health and community systems**
- **Eliminating stigma, discrimination and other structural barriers**







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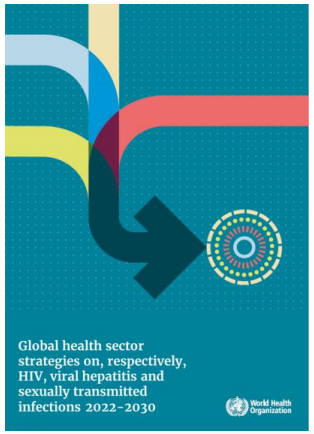
Hepatitis B and C Impact & Coverage Targets to reach 2030



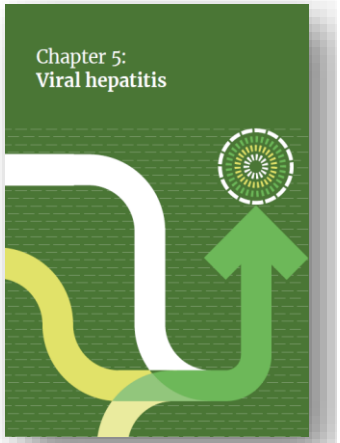


Table 5.1. **Impact and coverage indicators, targets and milestones for viral hepatitis by 2030**

	Indicator	Baseline – 2020[a]	Targets – 2025	Targets - 2030
Impact	Hepatitis B surface antigen (HBsAg) prevalence among children younger than 5 years old[b]	0.94%	0.5%	0.1%
	Number of new hepatitis B infections per year	1.5 million new cases 20 per 100 000	850 000 new cases 11 per 100 000	170 000 new cases 2 per 100 000
	Number of new hepatitis C infections per year	1.575 million new cases 20 per 100 000	1 million new cases 13 per 100 000	350 000 new cases 5 per 100 000
	Number of new hepatitis C infections per year among people who inject drugs per year	8 per 100	3 per 100	2 per 100
	Number of people dying from hepatitis B per year	820 000 deaths 10 per 100 000	530 000 deaths 7 per 100 000	310 000 deaths 4 per 100 000
	Number of people dying from hepatitis C per year	290 000 deaths 5 per 100 000	240 000 deaths 3 per 100 000	140 000 deaths 2 per 100 000
Coverage	Hepatitis B – percentage of people living with hepatitis B diagnosed / and treated	30%/30%	60%/50%	90%/80%
	Hepatitis C – percentage of people living with hepatitis C diagnosed / and cured	30%/30%	60%/50%	90%/80%
Coverage	Percentage of newborns who have benefitted from a timely birth dose of hepatitis vaccine and from other interventions to prevent the vertical (mother-to-child) transmission of hepatitis B virus[c]	50%	70%	90%
	Hepatitis B vaccine coverage among children (third dose)	90%	90%	90%
	Number of needles and syringes distributed per person who injects drugs[d]	200	200	300
	Blood safety - proportion of blood units screened for bloodborne diseases	95%	100%	100%
	Safe injections - proportion of safe health-care injections	95%	100%	100%

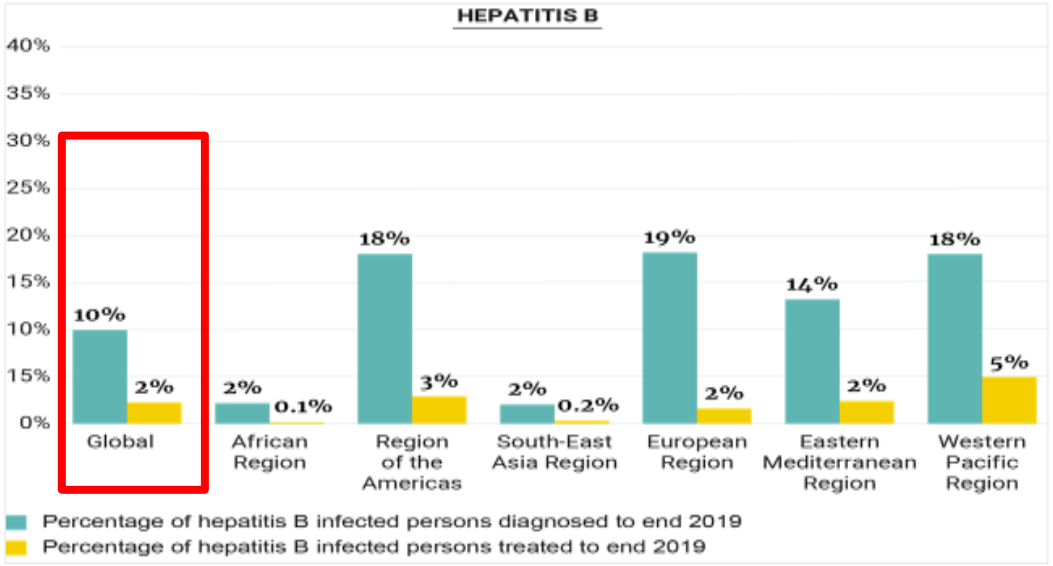
[a] Latest data for end 2020. Some targets use data from 2019 because of COVID-19 related service disruptions in the data reported for 2020. COVID-19 is not currently expected to affect the targets for 2025. All data will be disaggregated by age, sex and when relevant the focus populations specific to the disease.

[b] Please note that the targets in this table are global targets and should be adapted to set targets for countries in relation to the national context. For example, in some countries a target for hepatitis B surface antigen prevalence among children younger than five years may be less than 0.1% or 0.2%, although the overall global target should be 0.1%.

Link to GHSS: [9789240053779-eng.pdf]

Cascade of care - major gaps in path towards public health elimination

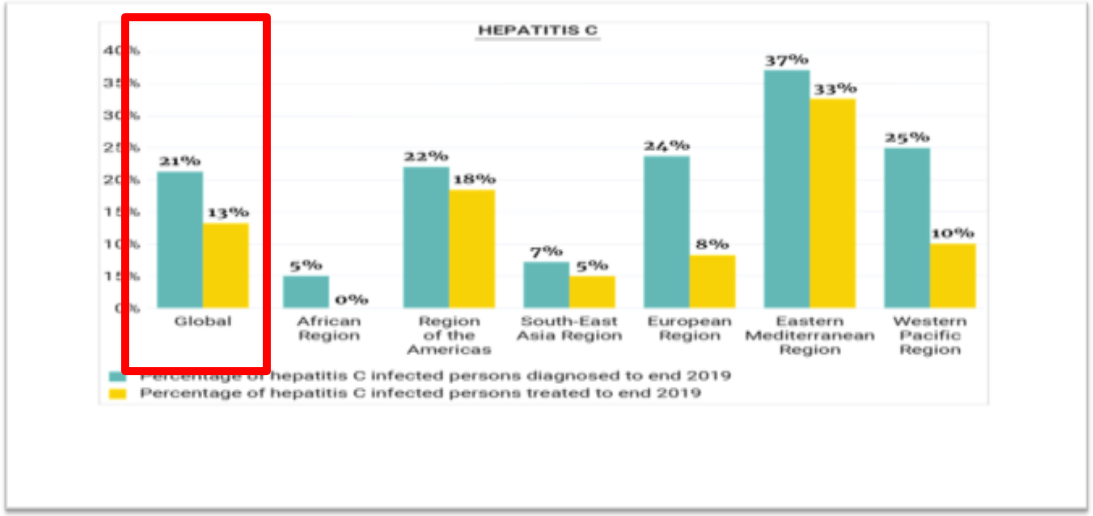
10% of estimated 296 million people with chronic HBV infection were diagnosed in 2019 with variation by regions



Data shows major gaps in path towards universal health access and public health elimination

Progress report on HIV, viral hepatitis and sexually transmitted infections 2021: accountability for the global health sector strategies, 2016–2021: actions for impact. Geneva: World Health Organization; 2021

21% of estimated 58 million people with chronic HCV infection were diagnosed in 2019 with variation by regions



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Link to GHSS: [9789240053779-eng.pdf]

WHO Guidelines and simplification

Distinctive Features of WHO Guidelines

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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

Evolution of WHO HCV Guidelines

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Topic	2014	2016	2018	2022
Who to treat?			Treat All	Treat All
Genotyping	Yes	Yes	No	No
Regimens	PEG-IFN+RBV	DAAs preferred	Pan-genotypic DAAs	Pan-genotypic DAAs
	8 options - PEGIFN+RBV - SOF+RBV - SIMP or TELAP or BOCEP /PEGIFN+RBV	6 options DAAs preferred by GT or cirrhosis	3 options SOF/DAC SOF/VEL G/P PEGIFN phase out	3 options SOF/DAC SOF/VEL G/P
Age group	Adults ≥18yrs	Adults≥ 18yrs	Adults ≥18yrs and adolescents ≥12 yrs	Adults, adolescents and children≥3 yrs
Service Delivery			8 Good Practice Principles for Simplified Service	Decentralization Integration Task-shifting

SIMPLER TREATMENTS

TREATMENT OF CHILDREN AND ADOLESCENTS

SIMPLIFIED SERVICE DELIVERY

CHAPTER 6. SIMPLIFIED SERVICE DELIVERY FOR A PUBLIC HEALTH APPROACH TO TESTING, CARE AND TREATMENT FOR HCV INFECTION

Box 6.1. Good practice principles for health service delivery

1. **Comprehensive national planning for the elimination of HCV infection** based on local epidemiological context, existing health-care infrastructure, current coverage of testing, treatment and prevention, and available financial or human resources
2. **Simple and standardized algorithms** across the continuum of care from testing, linkage to care and treatment
3. **Strategies to strengthen linkage from testing to care,** treatment and prevention
4. **Integration of hepatitis testing, care and treatment with other services** (e.g. HIV services) to increase the efficiency and reach of hepatitis services
5. **Decentralized** testing and treatment services at primary health facilities or harm reduction sites to promote access to care. This is facilitated by two approaches:
   - **5a. task-sharing,** supported by training and mentoring of health-care workers and peer workers;
   - **5b. a differentiated care** strategy to assess level-of-care needs, with specialist referral as appropriate for those with complex problems.
6. **Community engagement and peer support** to promote access to services and linkage to the continuum of care, which includes addressing stigma and discrimination
7. **Strategies for more efficient procurement and supply management** of quality-assured, affordable medicines and diagnostics
8. **Data systems to monitor the quality of individual care and coverage** at key steps along the continuum or cascade of care at the population level.

TABLE 5.4 Monitoring framework before and during DAA treatment

Time	DAA alone	DAA + ribavirin[a]
	Full blood count, renal, liver function	Full blood count, renal, liver function
Baseline	X[b]	X
Week 4		X
Week 12 after end of treatment	X	X

[a] Recommended treatment for adolescents with genotypes 2 and 3 HCV infection
[b] If Hb >10 g/dL then no need to check again at week 4

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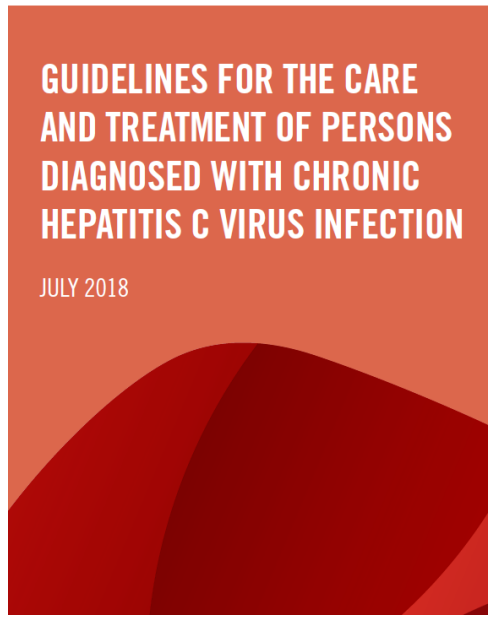


TABLE 5.1 Low and high cut-off values for the detection of significant fibrosis and cirrhosis

	APRI (low cut-off)	APRI (high cut-off)	FIB-4 (low cut-off)	FIB-4 (high cut-off)
Significant fibrosis (METAVIR ≥F2)	0.5	1.5	1.45	3.25
Cirrhosis (METAVIR F4)	1.0	2.0	–	–

Service delivery

RECOMMENDATIONS

Decentralization, Integration and Task-shifting

Moving treatment and care out of speciality clinics

Decentralization:
We recommend delivery of HCV **testing** and **treatment** at peripheral health or community-based facilities, and ideally at the same site, to increase access to diagnosis, care and treatment.
These **facilities** may include primary care, harm reduction sites, prisons and HIV/ART clinics as well as community-based organizations and outreach services.

Integration:
We recommend integration of HCV **testing** and **treatment** with existing care services at peripheral health facilities.
These **services** may include primary care, harm reduction (needle and syringe programme (NSP)/opioid agonist maintenance therapy (OAMT) sites), prison and HIV/ART services.

Strong recommendation/ moderate certainty of evidence (PWID/prisoner) low (general population, PLHIV)

Task-sharing: We recommend delivery of HCV **testing, care and treatment** by trained non-specialist doctors and nurses to expand access to diagnosis, care and treatment.

Strong recommendation/ moderate certainty of evidence

https://www.who.int/publications/i/item/9789240052697

RATIONALE for Recommendations on Decentralization, Integration and Task-sharing

Evidence review

- 142 studies from 33 countries (14%) LMICs) compared full decentralization/integration vs. partial decentralization or none, and task-sharing to non-specialists.
- Increased uptake of HCV viral load testing, linkage to care and treatment among people who inject drugs and prisoners for full decentralization/integration.
- Comparable SVR12 cure rates between specialists and non-specialists across all populations and in all settings

https://www.who.int/publications/i/item/9789240052697

Decentralisation, integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis

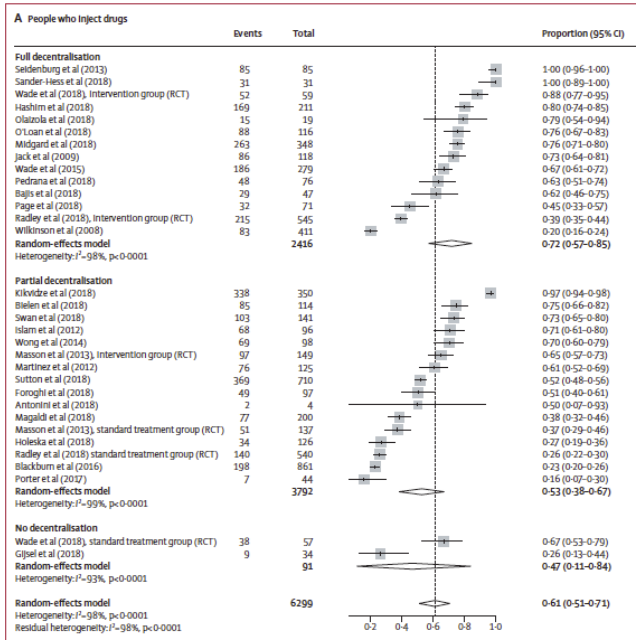
Eno Oru, Adam Trickey, Rohan Shiroti, Steve Kanters, Philippa Easterbrook

Summary

Background Increasing access to hepatitis C virus (HCV) care and treatment will require simplified service delivery models. We aimed to evaluate the effects of decentralisation and integration of testing, care, and treatment with harm-reduction and other services, and task-shifting to non-specialists on outcomes across the HCV care continuum.

Methods For this systematic review and meta-analysis, we searched PubMed, Embase, WHO Global Index Medicus, and conference abstracts for studies published between Jan 1, 2008, and Feb 28, 2018, that evaluated uptake of HCV testing, linkage to care, treatment, cure assessment, and sustained virological response at 12 weeks (SVR12) in people who inject drugs, people in prisons, people living with HIV, and the general population. Randomised controlled trials, non-randomised studies, and observational studies were eligible for inclusion. Studies with a sample size of ten or less for the largest denominator were excluded. Studies were categorised according to the level of decentralisation: full (testing and treatment at same site), partial (testing at decentralised site and referral elsewhere for treatment), or none. Task-shifting was categorised as treatment by specialists or non-specialists. Data on outcomes across the HCV care continuum (linkage to care, treatment uptake, and SVR12) were pooled using random-effects meta-analysis.

Findings Our search identified 8050 reports, of which 132 met the eligibility criteria, and an additional ten reports were identified from reference citations and grey literature. Therefore, the final synthesis included 142 studies from 34 countries (20 [14%] studies from low-income and middle-income countries) and a total of 489 996 patients (239 446 [49%] from low-income and middle-income countries). Rates of linkage to care were higher with full decentralisation compared with partial or no decentralisation among people who inject drugs (full 72% [95% CI 57–85] *vs* partial 53% [38–67] *vs* none 47% [31–64]) and among people in prisons (full 94% [79–100] *vs* partial 50% [29–71], although the CIs overlap for people who inject drugs. Similarly, treatment uptake was higher with full decentralisation compared with partial or no decentralisation (people who inject drugs: full 73% [65–80] *vs* partial 66% [55–77] *vs* none 35% [23–48]; people in prisons: full 72% [48–91] *vs* partial 39% [17–63]), although CIs overlap for full versus partial decentralisation. The results in the general population studies were more heterogeneous. SVR12 rates were high (≥90%) across different levels of decentralisation in all populations. Task-shifting of care and treatment to a non-specialist was associated with similar SVR12 rates to treatment delivered by specialists. There was a severe or critical risk of bias for 46% of studies, and heterogeneity across studies tended to be very high (I^2>90%).



RECOMMENDATIONS

2022 Recommendations on HCV diagnostics

World Health Organization

HCV point-of-care (POC) viral load RNA testing:

- Point-of-care (POC) HCV RNA viral load assay can be an alternative approach to laboratory-based HCV RNA NAT assays to **diagnose HCV viraemic infection**.
- Point-of-care (POC) HCV RNA assays with comparable limit of detection to laboratory-based assays can be used as an alternative approach as **test of cure**.

https://www.who.int/publications/i/item/9789240052697

WHO recommendation on HCV self-testing (2021)

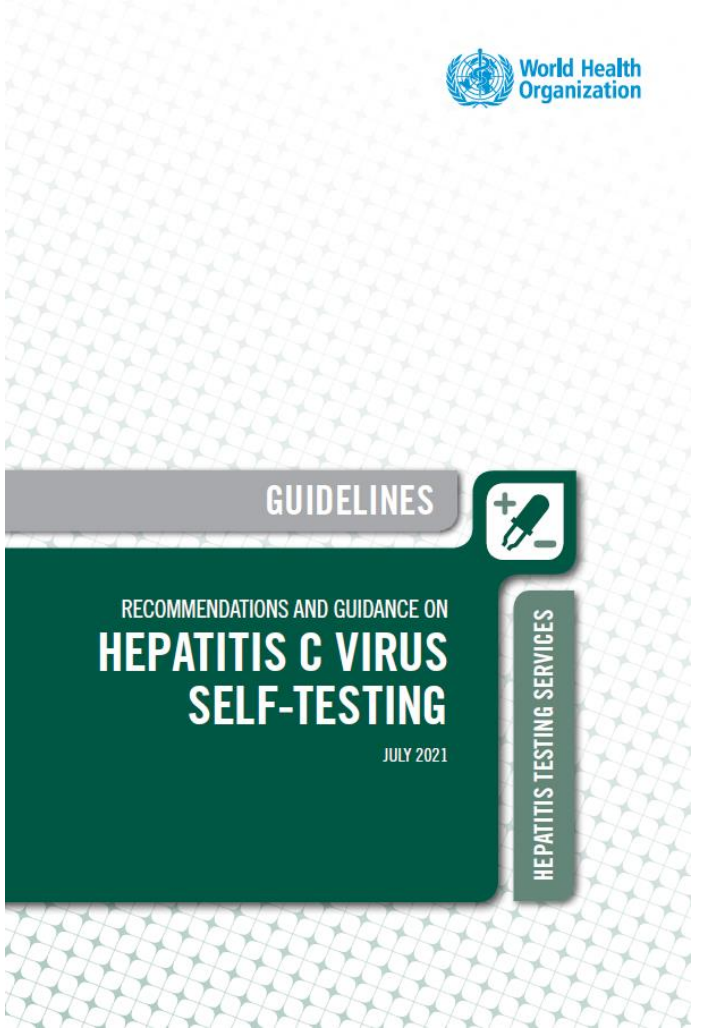
NEW

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

(strong recommendation, moderate-certainty evidence)

Remarks:

- *HCV self-testing needs to be followed by **linkage to appropriate post-test services**, including confirmation of viraemic infection, treatment, care and referral services, according to national standards.*
- *It is desirable to **adapt HCV self-testing service delivery and support options** to the national and local context, which includes community preferences.*
- ***Communities, including networks of key and vulnerable populations and peer-led organizations, need to be meaningfully and effectively engaged** in developing, adapting, implementing and monitoring HCV self-testing programmes.*



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Case example India

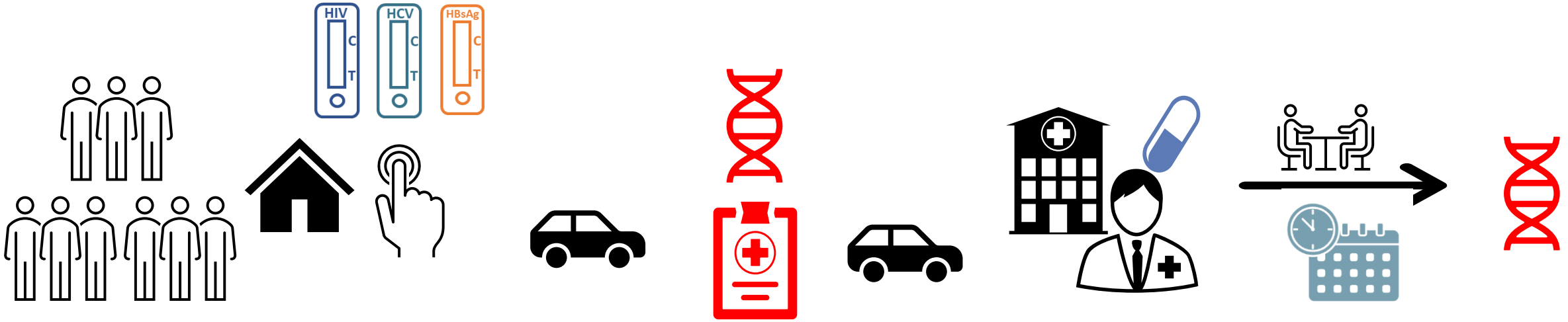
CoNE is a network of 11 CBOs of people who use drugs in Manipur

Realized that the uptake of testing, diagnosis and treatment within the national program was very limited

- Thus initiated a replicable model of same day HCV screening, diagnosis and treatment initiative among PWID

- Providing free diagnosis and treatment through philanthropic and local support
- Developing different models of HCV treatment, including for prison inmates
- Developing policy materials and state specific standard operating procedure on HCV
- Uninterrupted HCV services during COVID-19 restrictions
- Advocating for quality HCV services both at state and national level

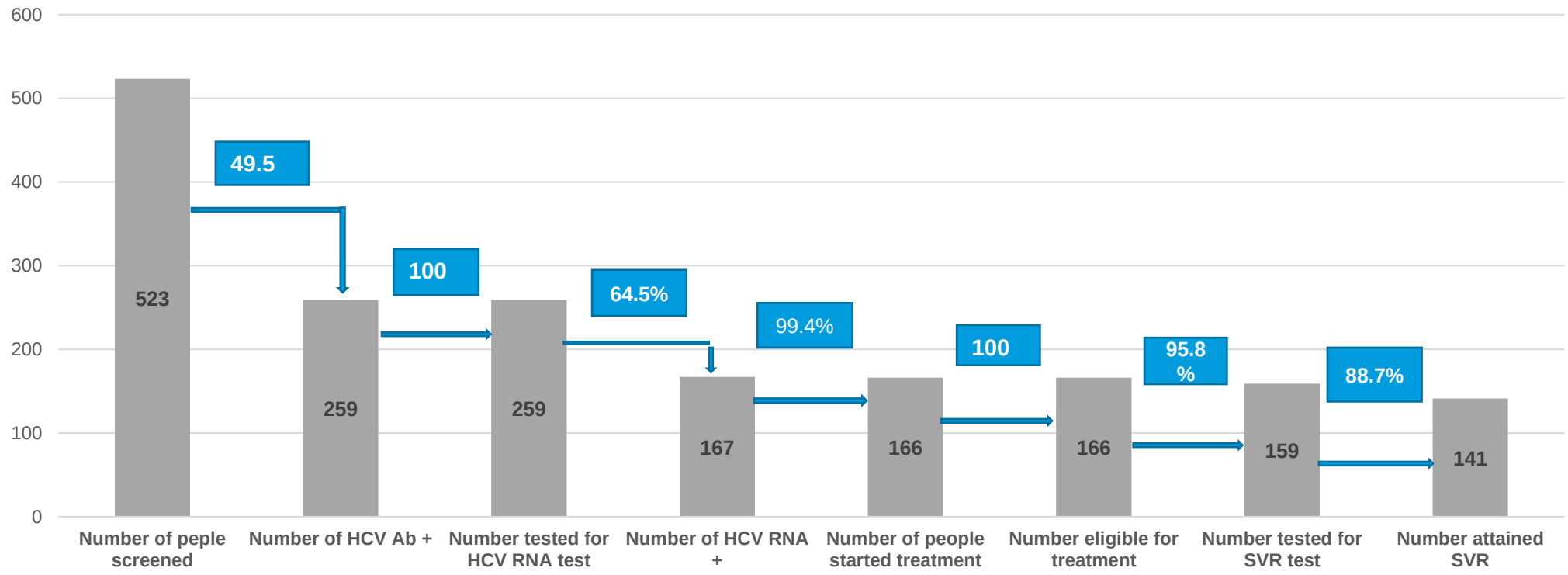
Method



Turn Around Time

Time between RDT and treatment initiation	
n	164
median	6 hours 49 min
min - max	4 hours 36 min - 12 hours 18 min
IQR 1 – IOR 3	5 hours 48 min - 8 hours 35 mins

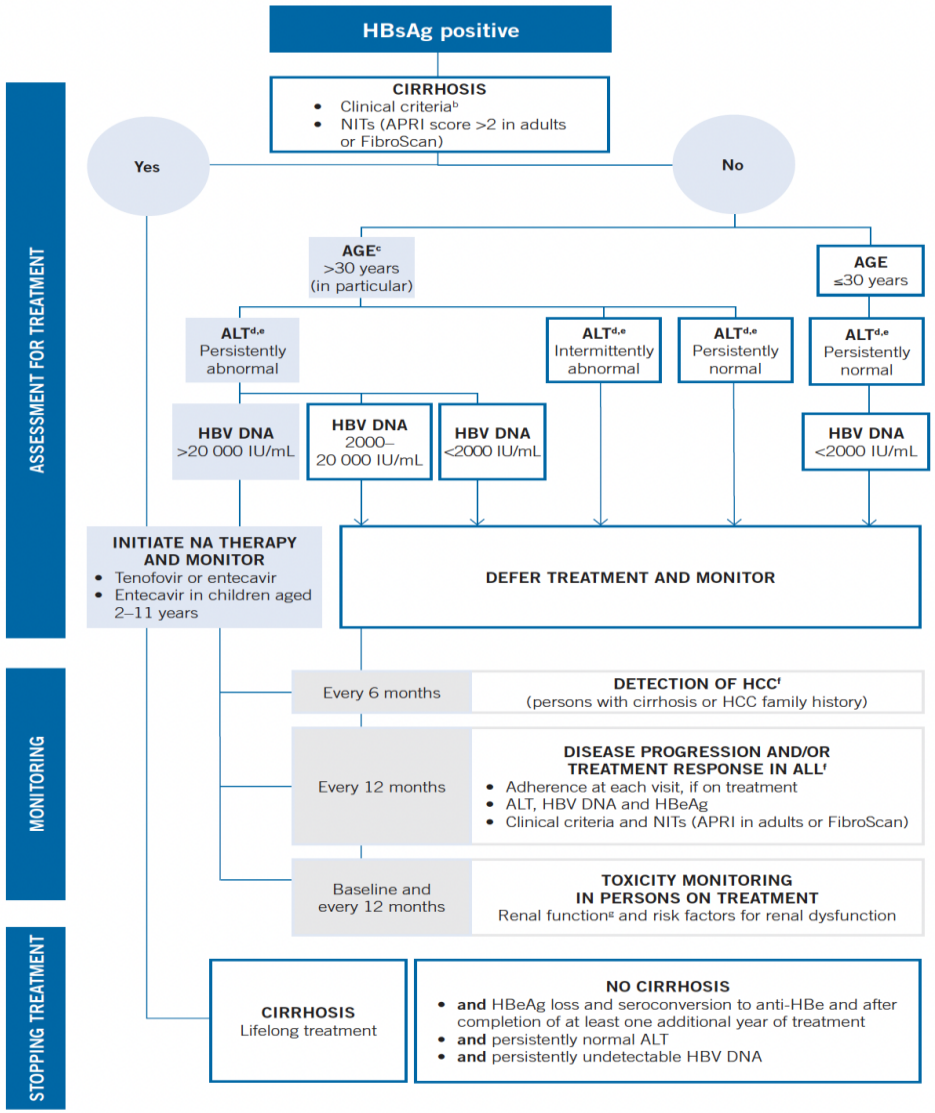
HCV Care Cascade (Results)

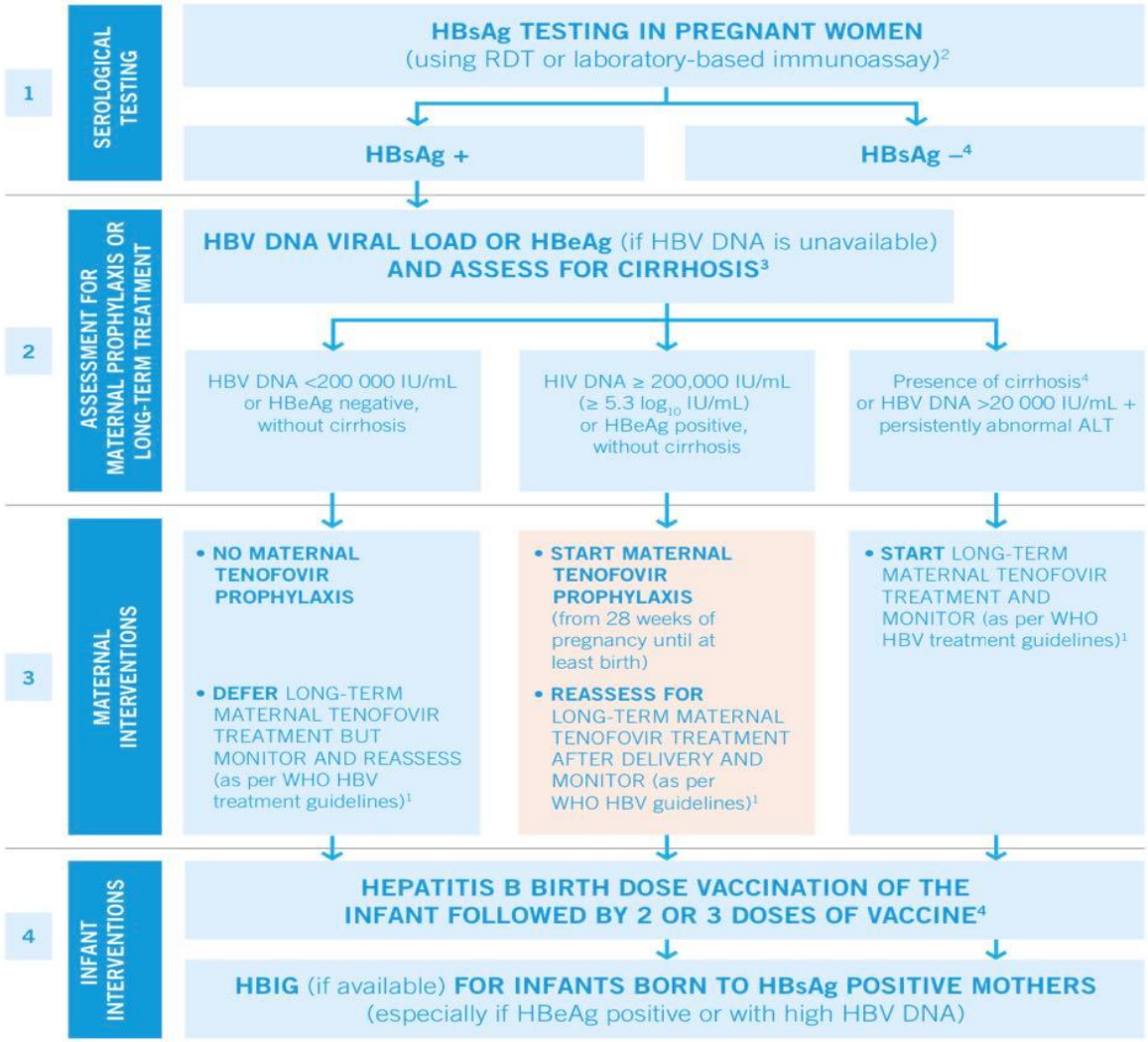


*** 1 participant not initiated on treatment is also living with hepatitis B and will be initiated on treatment as per India's National Viral Hepatitis Control Program guidelines**
*** 2 expired due to drug overdose**
*** 5 out of station**
*** 18 SVR not achieved**

HBV Guideline Recommendations (2015) and PMTCT update (2020)

ALGORITHM OF WHO RECOMMENDATIONS ON THE MANAGEMENT OF PERSONS WITH CHRONIC HEPATITIS B INFECTION[a]





New Directions – Updating WHO hepatitis B guidelines 2023

Who to treat?

- Expanding criteria for treatment (lower APRI score >0.5 and HBV DNA threshold >2000 IU/ml)

PMTCT

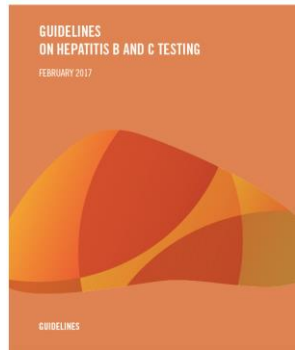
- Expanding criteria for use of antiviral prophylaxis to all HBsAg positive pregnant women

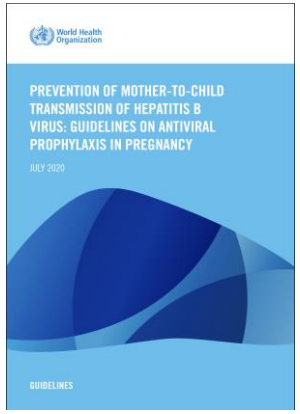
Simplifying diagnosis

- Use of PoC HBV DNA viral load and reflex viral load testing
- Delta virus testing – Who to test and how to test and reflex testing

Simplifying service delivery

- Decentralisation, integration and task-sharing





Summary

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Simplification has diverse “faces” :

- **Simplified clinical algorithms**
- **Simplified service delivery – including PHC**

- **It is crucial to make care person-centred and to reach elimination**

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Thank You!

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