

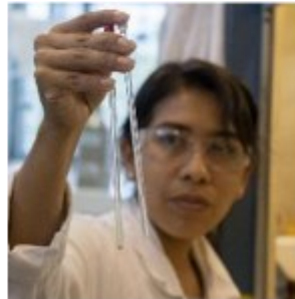


hepatitisC PACT  
Hepatitis C Partnership for Control and Treatment

# Hepatitis C Initiative Globally & Simplification

HACC 88th NGOs & Community Membership Meeting

23 June 2023



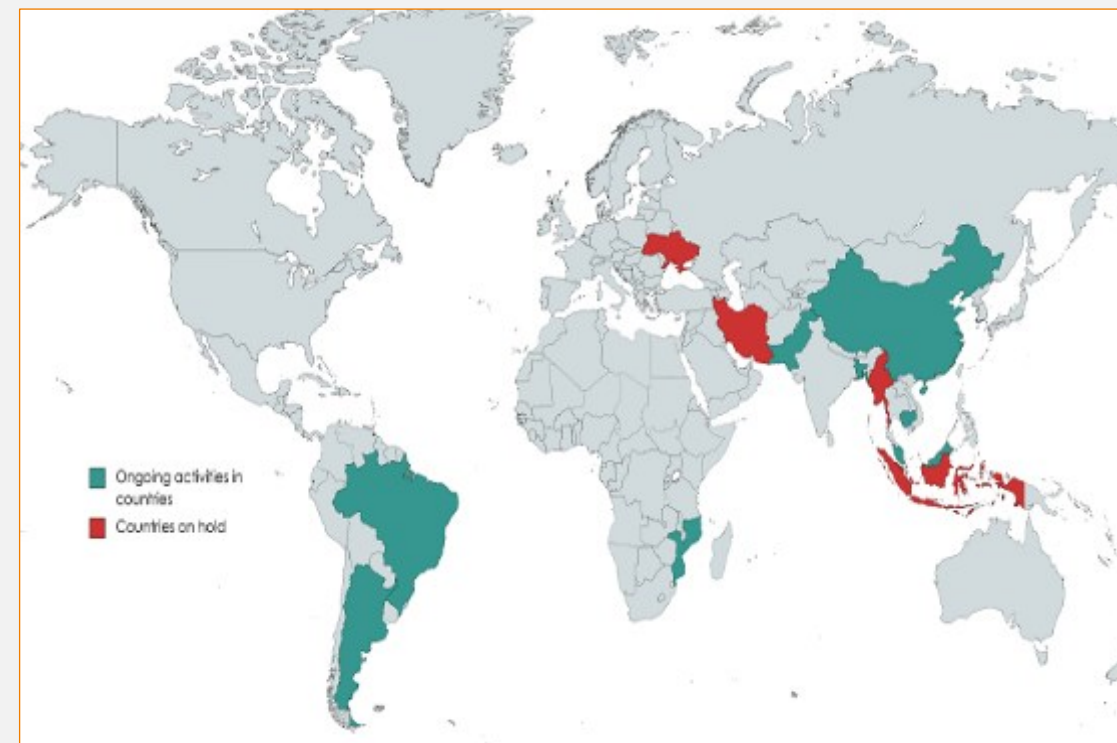
Chung Han Yang  
Access & Advocacy Manager

**DNDi** 20 years  
Best Science for the Most Neglected

## To help foster an enabling environment for improved availability of HCV diagnostics and treatments in LMICs

- Developing **awareness among decision-makers** of HCV and the opportunity for elimination
- Designing **sustainable financing** mechanisms for HCV scale-up in LMICs
- Supporting **simplified HCV diagnostic** tools and strategies
- Supporting improved **access to all simple and affordable DAA** treatments in high-burden LMICs

## HEP C PACT, PRIORITY COUNTRIES:







# Hepatitis C in Cambodia

# The burden of hepatitis C is especially high in Cambodia

*Hepatitis C is highly prevalent in Cambodia, resulting in a heavy health burden and high mortality*

## Cambodia overview



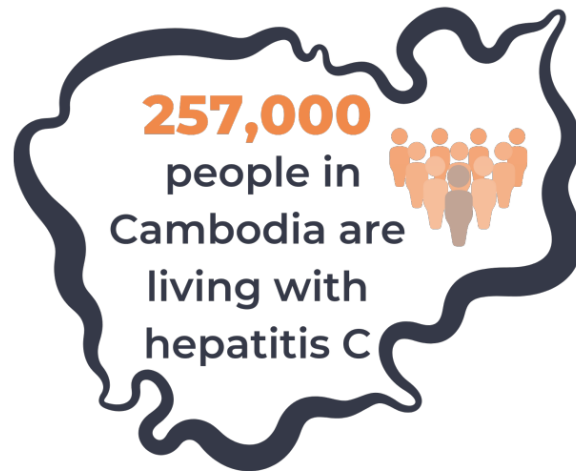
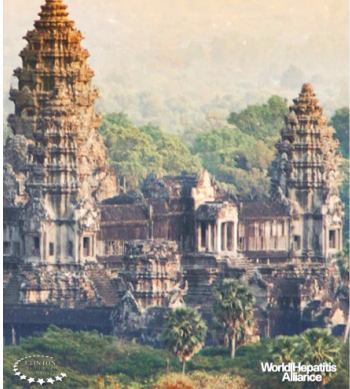
## HCV is one of the main causes of cancer in Cambodia



Liver cancer is the most frequently reported cancer in Cambodia

- 1<sup>st</sup> common cancer among men and 3<sup>rd</sup> most frequent cancer among women in Cambodia
- HCV is the main risk factor in 43% of the cases of liver cancer/HCC

### CAMBODIA EXPERIENCE DEVELOPING A HEPATITIS C FINANCING STRATEGY





# HCV in Cambodia: Risk factors creating huge burden

Patient characteristics	All subjects (n = 3,133)
<b>Risk factors for infection, n (%)</b>	
Invasive medical procedures	2,021/3,124 (64.7%)
Blood transfusion	307/3,107 (9.9%)
Partner with HCV	461/2,367 (19.5%)
Healthcare worker	220/3,119 (7.1%)
Imprisonment	40/3,108 (1.3%)
FEW, MSM, or TG	27/3,119 (0.9%)
History of drug use	18/3,120 (0.6%)

The prevalence of HCV ranges between **2.8%** and **14.7%** in rural areas depending on study sites and between 5.5% and 10.4% among people with HIV in hospital-based programs in Phnom Penh

OPEN Molecular epidemiology of hepatitis C virus in Cambodia during 2016–2017

Received: 13 February 2019  
Accepted: 1 May 2019  
Published online: 15 May 2019

Janin Nounin<sup>1</sup>, Momoko Iwamoto<sup>1,2</sup>, Sophearot Prak<sup>1</sup>, Jean-Philippe Dousse<sup>1</sup>, Kerya Phon<sup>1</sup>, Seïha Heng<sup>1</sup>, Alexandra Kerleguer<sup>1</sup>, Mickaël Le Palh<sup>1</sup>, Philippe Dussart<sup>1</sup>, David Maman<sup>1</sup> & François Rouet<sup>1</sup>

In Cambodia, little epidemiological data of hepatitis C virus (HCV) is available. All previous studies were limited to only small or specific populations. In the present study, we performed a characterization of HCV genetic diversity based on demography, clinical data, and phylogenetic analysis of HCV non-structural 5B (NS5B) sequences belonging to a large cohort of patients (n = 3,133) coming from majority part of Cambodia between September 2016 and December 2017. The phylogenetic analysis revealed that HCV genotype 1 and 6 were the most predominant and sharing equal proportions (46%). The

---

## HCV is one of the leading infectious disease threats in Cambodia

---

Disease	Prevalence	Annual deaths
HCV	~2%	2,976
HBV	3%	2,446
HIV/AIDS	0.5%	1,296
TB	0.82%	3,240
Malaria	1.29%	345

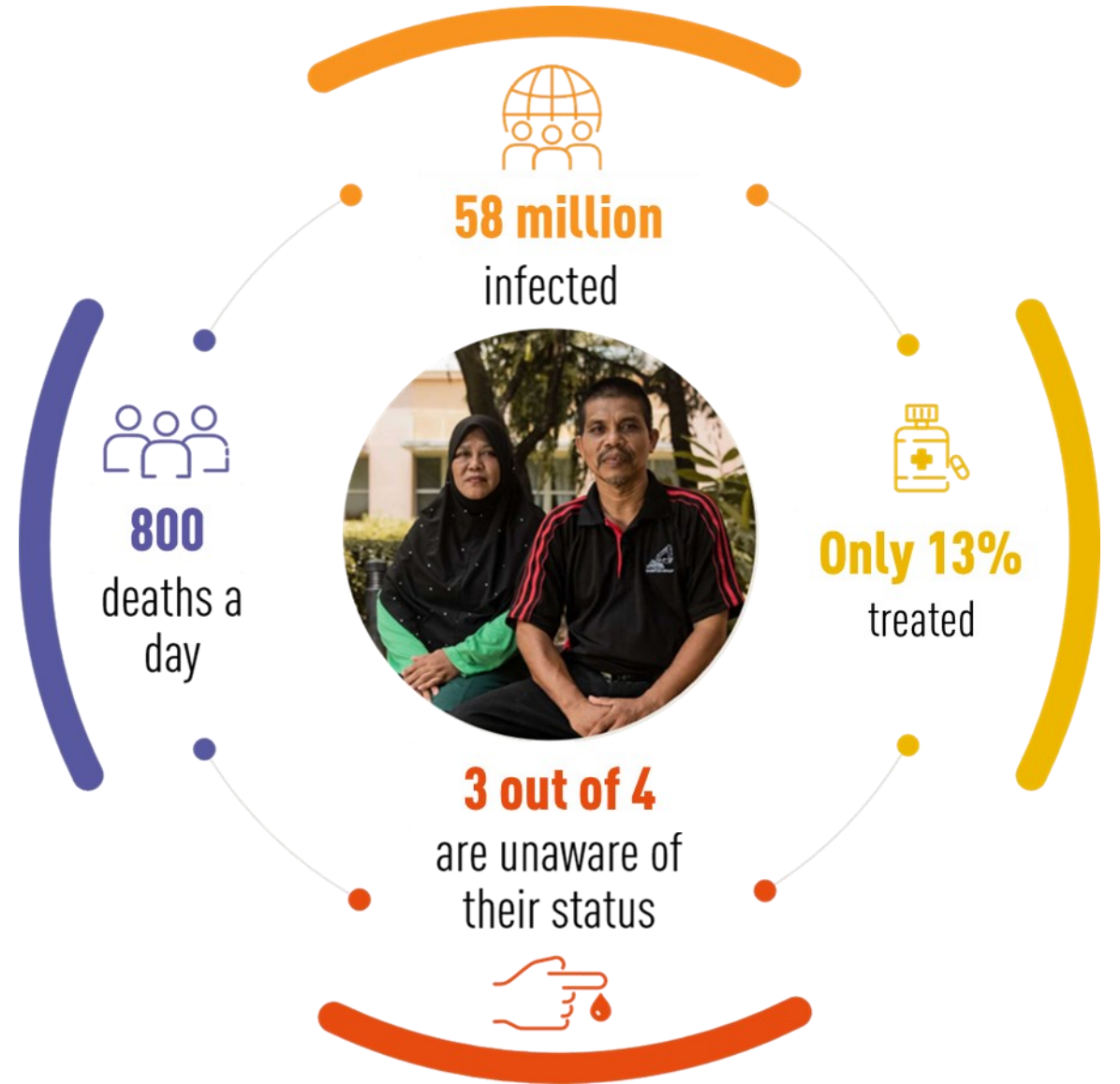
---



# Hepatitis B & C Situation Globally



# HEPATITIS C is a Silent Epidemic

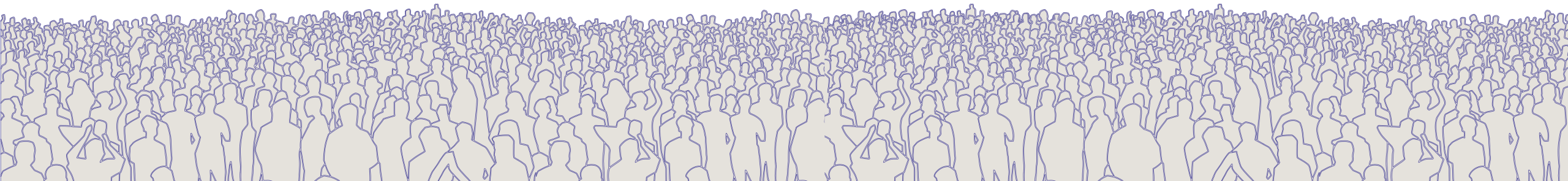
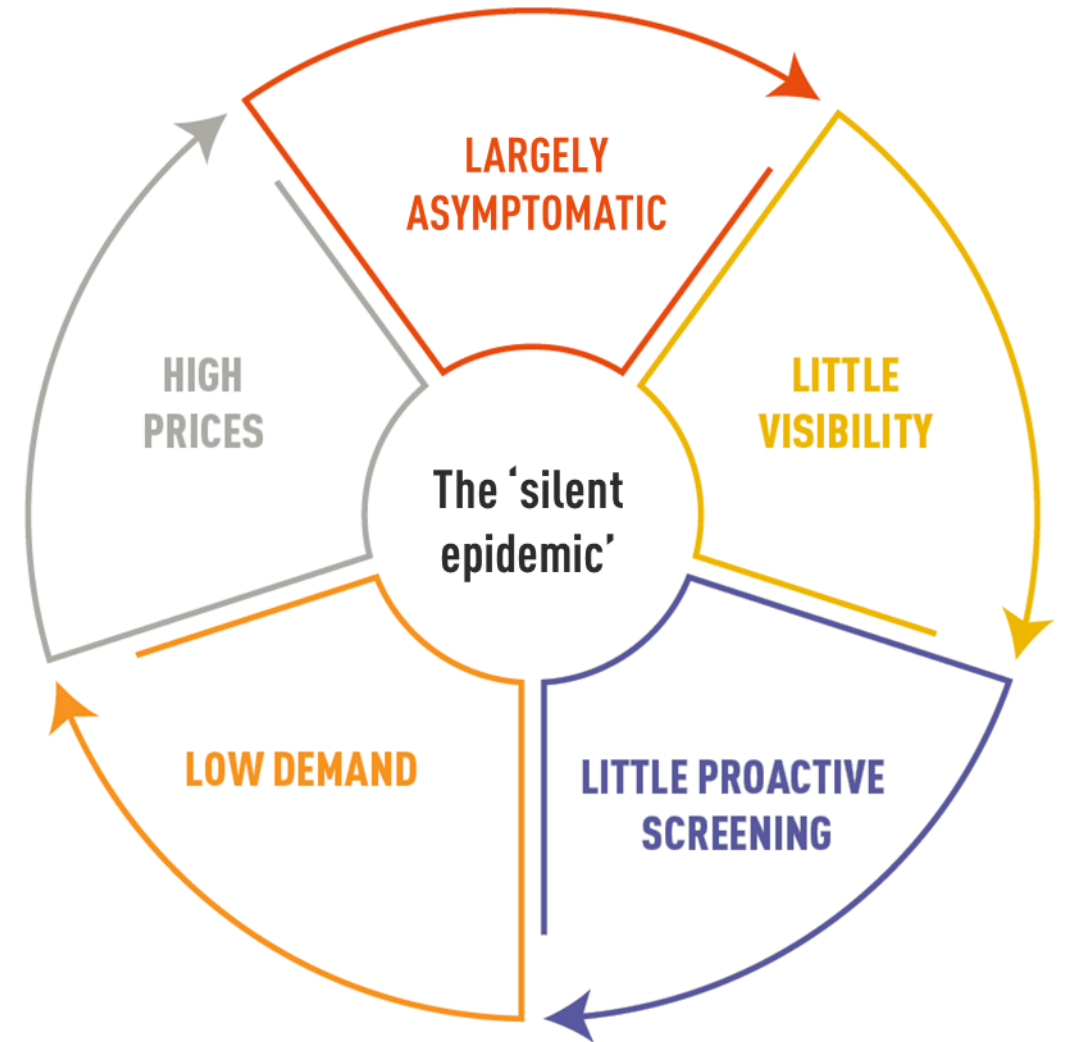




# Hepatitis C is a 'silent epidemic'

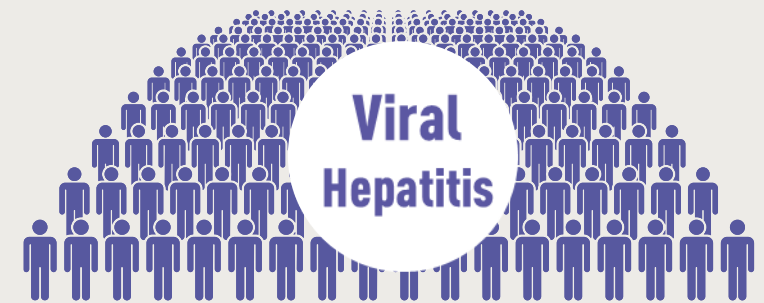
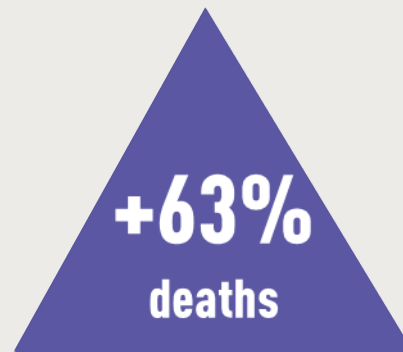
~300,000 deaths due to hepatitis C each year

- About **70%** of people infected **develop chronic disease**
- **15%-30%** of people with chronic hepatitis C develop **liver cirrhosis** within 20 years
- **75%** of people with hepatitis C live in **low- and middle-income countries**

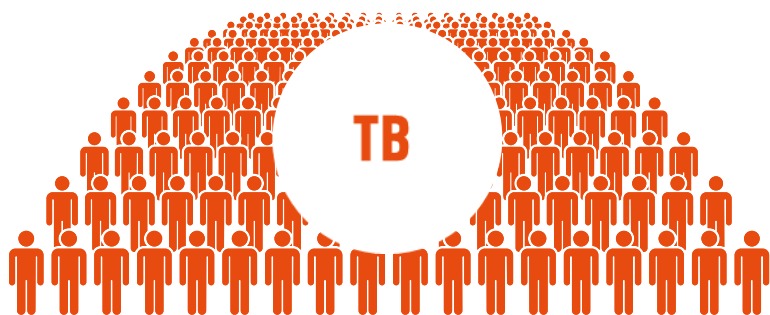


# Viral hepatitis has become one of the leading causes of deaths and disability across the globe

2016 study shows that viral hepatitis (A, B, C, D, E) deaths increased by 63% in 23 years (1990-2013)



Killing at least as many people annually as:

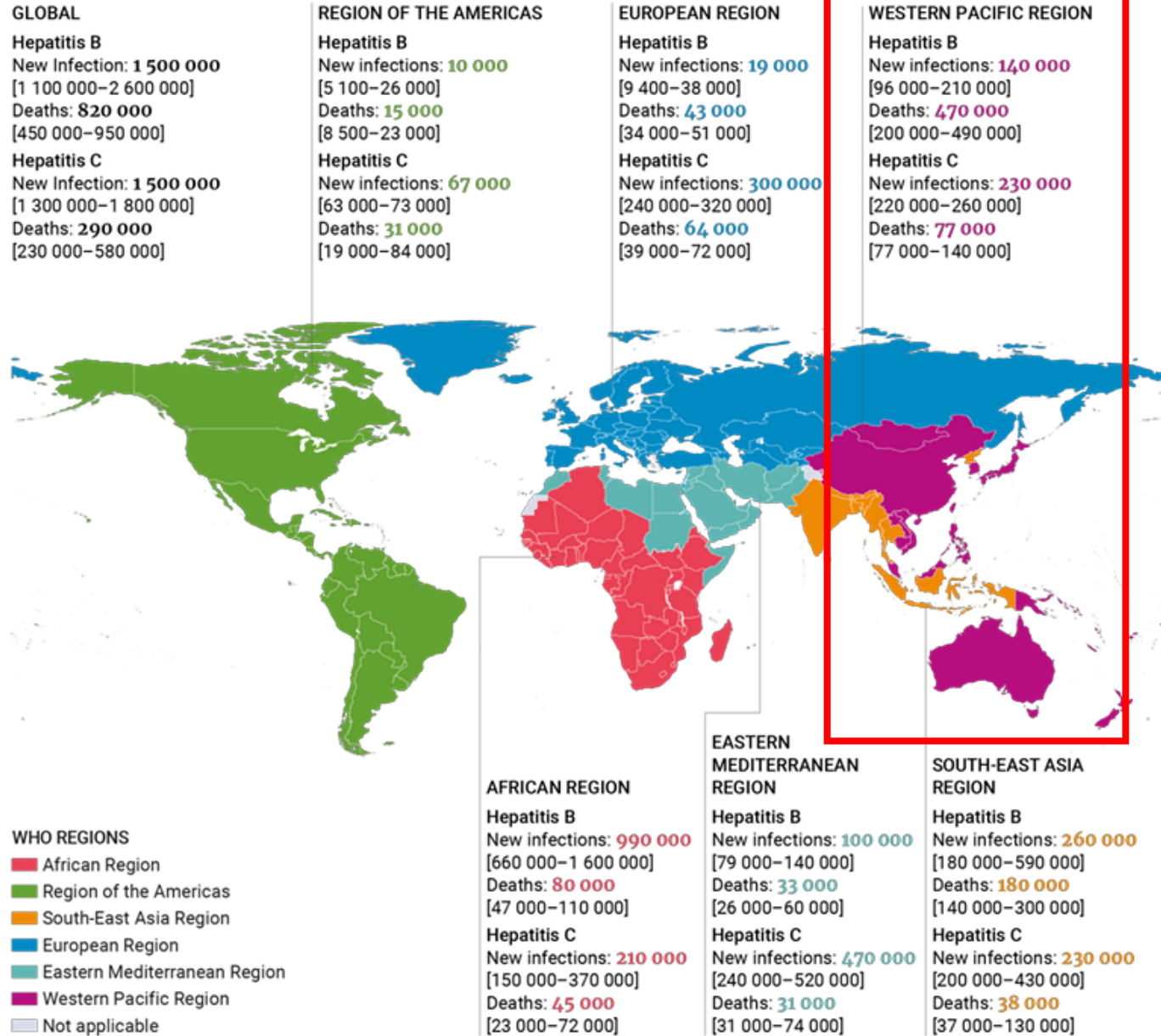


The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013.

The Lancet, July 2016 DOI: 10.1016/S0140-6736(16)30579-7



# Hepatitis B and C new infections and mortality by WHO region, 2019



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.

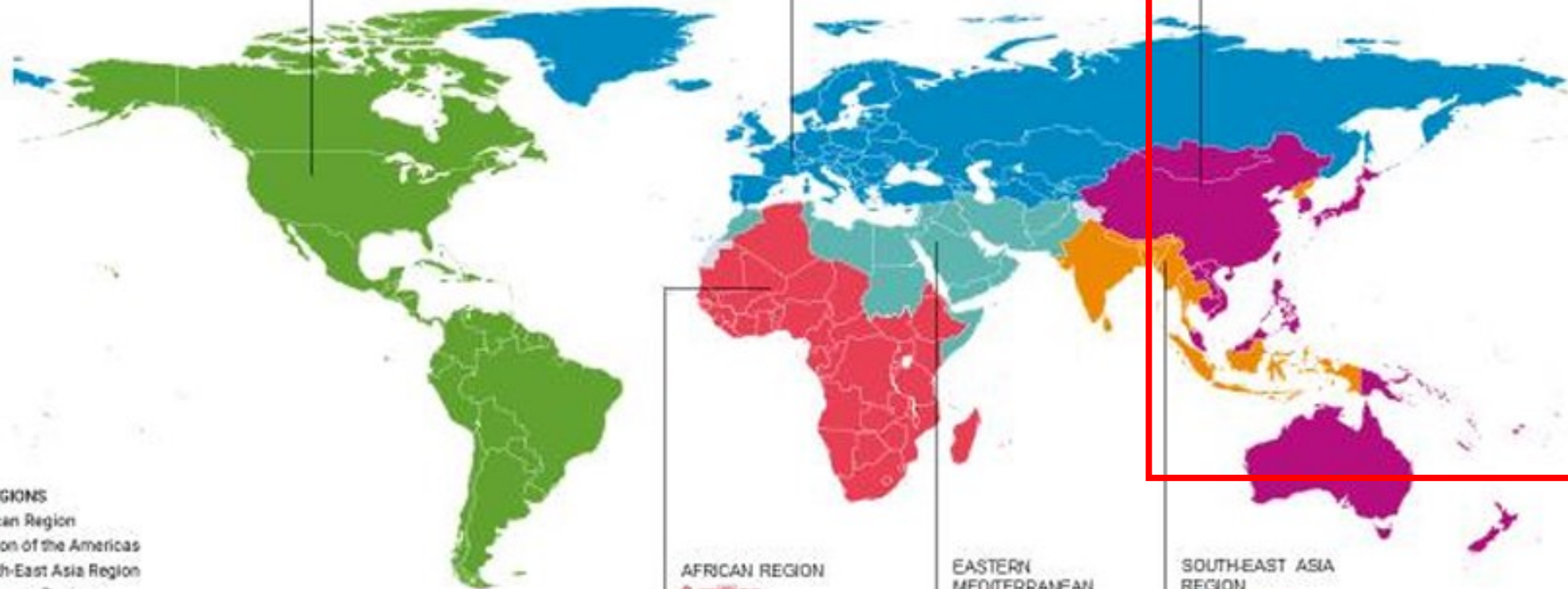
# Burden of chronic hepatitis C viraemic infection by WHO Region, 2019

GLOBAL  
**58 million**  
[46 million–76 million]

REGION OF THE AMERICAS  
**5 million**  
[4 million–6 million]

EUROPEAN REGION  
**12 million**  
[10 million–14 million]

WESTERN PACIFIC REGION  
**10 million**  
[8 million–14 million]



## WHO REGIONS

- African Region
- Region of the Americas
- South-East Asia Region
- European Region
- Eastern Mediterranean Region
- Western Pacific Region
- Not applicable



# Burden of chronic hepatitis B infection (HBsAg positivity) by WHO Region, 2019

GLOBAL  
**296 million**  
[228 million–423 million]

REGION OF THE AMERICAS  
**5 million**  
[3 million–12 million]

EUROPEAN REGION  
**14 million**  
[10 million–22 million]

WESTERN PACIFIC REGION  
**116 million**  
[95 million–142 million]

AFRICAN REGION  
**82 million**  
[62 million–115 million]

EASTERN MEDITERRANEAN REGION  
**18 million**  
[14 million–24 million]

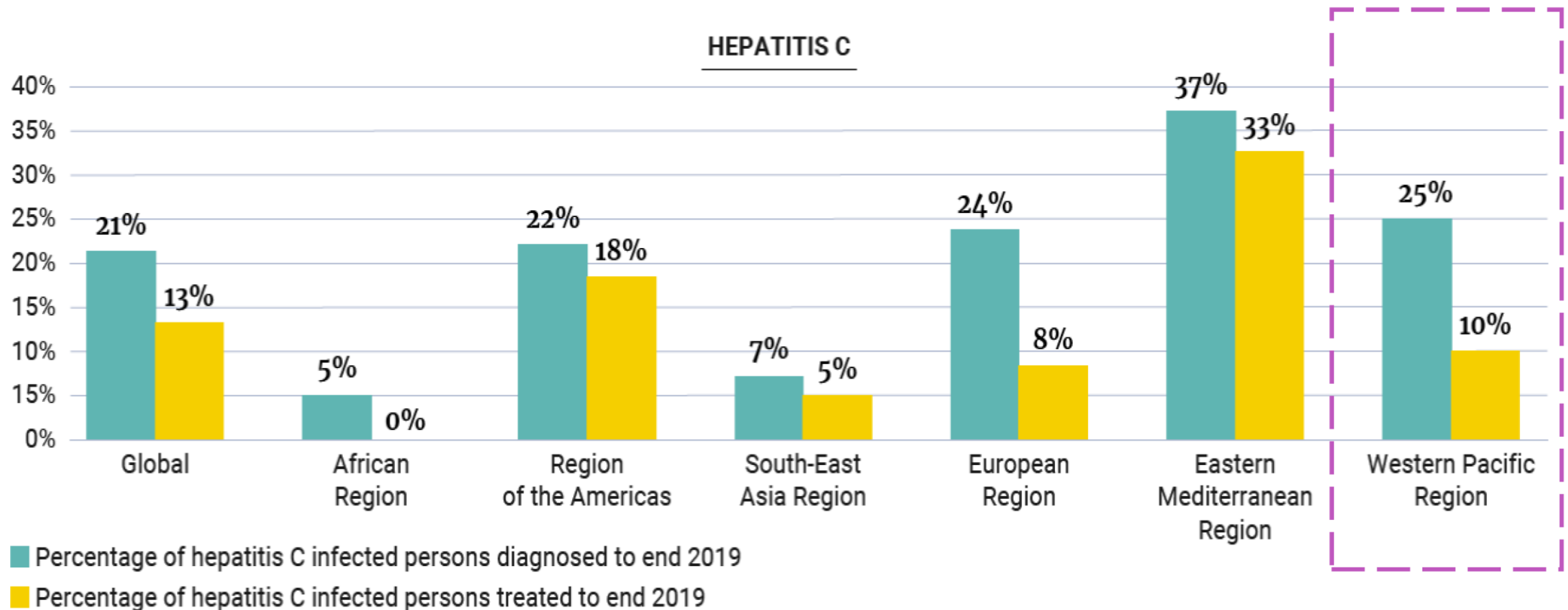
SOUTHEAST ASIA REGION  
**60 million**  
[45 million–121 million]

## WHO REGIONS

- African Region
- Region of the Americas
- South-East Asia Region
- European Region
- Eastern Mediterranean Region
- Western Pacific Region
- Not applicable



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



## The objective: elimination by 2030



WHO Global Objective:  
Eliminate hepatitis by  
2030

- Reduce incident of viral hepatitis infections by 90%
- Decrease deaths due to viral hepatitis by 65%
- Diagnose 90% of chronic HCV infections
- Treat 80% of eligible persons

## The opportunity: elimination is achievable



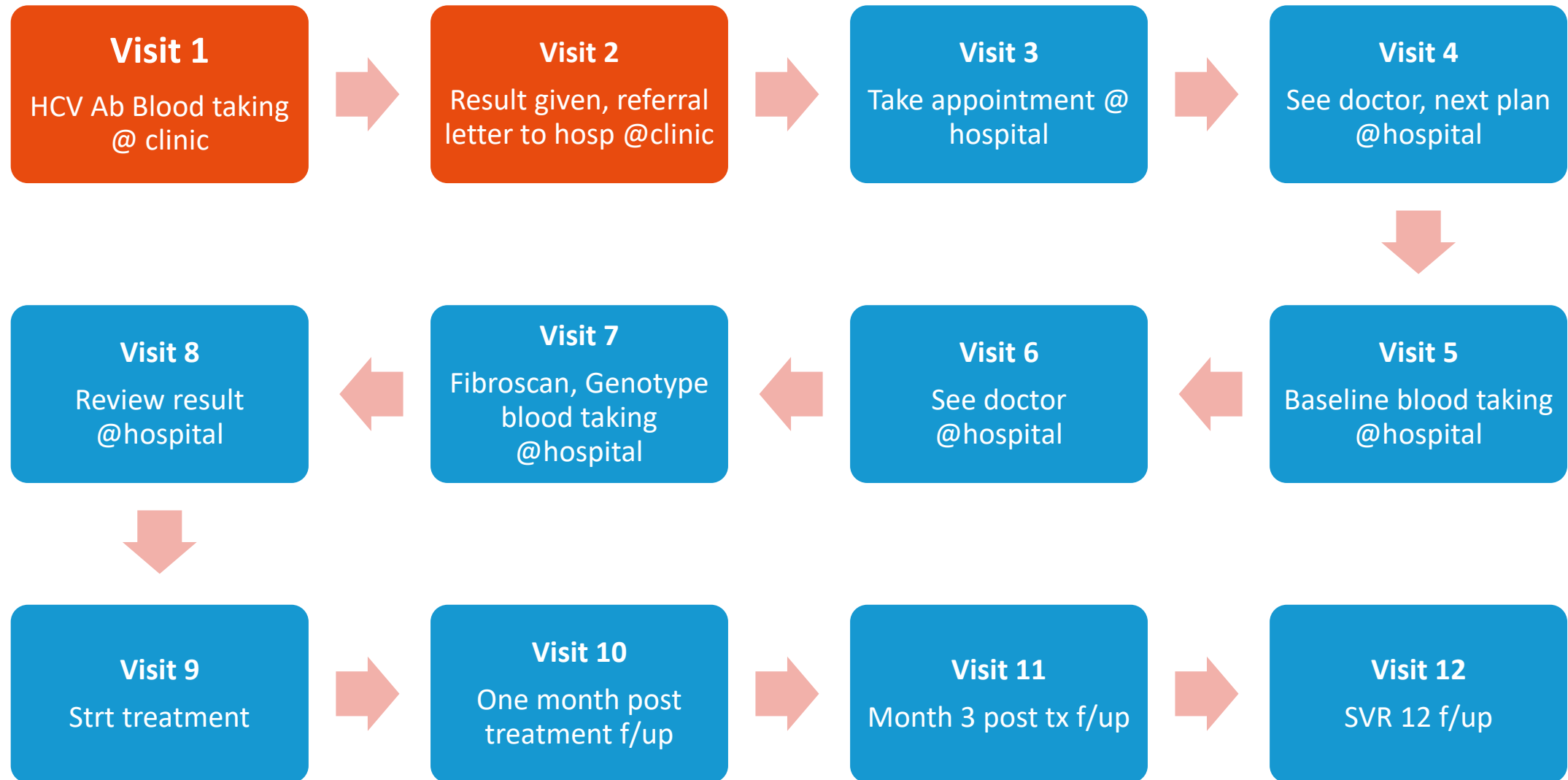
In contrast to many other infectious diseases, Hepatitis C can be completely cured with low-cost screening and direct acting antivirals (DAAs) in just 12-weeks





# Hepatitis C Model of Care: Simplification & Integration

# HCV Patient Flow Management (Pre-Simplification)





# Simplified HCV Service Delivery (1)



## Simplified service delivery

**Decentralization:**<sup>1</sup> 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.

*(strong recommendation; certainty of evidence:<sup>2</sup> moderate (people who inject drugs, prisoners); low (general population, people living with HIV)*

New

UPDATED RECOMMENDATIONS ON  
**TREATMENT OF ADOLESCENTS AND  
 CHILDREN WITH CHRONIC HCV INFECTION,  
 AND HCV SIMPLIFIED SERVICE DELIVERY  
 AND DIAGNOSTICS**

## Simplified HCV Service Delivery (2)



**Integration:**<sup>3</sup> 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), prisons and HIV/ART services.  
*(strong recommendation; certainty of evidence: moderate (people who inject drugs, prisoners); low (general population, people living with HIV))*

**Task sharing:**<sup>4</sup> 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)*

New

New

UPDATED RECOMMENDATIONS ON  
**TREATMENT OF ADOLESCENTS AND  
 CHILDREN WITH CHRONIC HCV INFECTION,  
 AND HCV SIMPLIFIED SERVICE DELIVERY  
 AND DIAGNOSTICS**

# 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

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

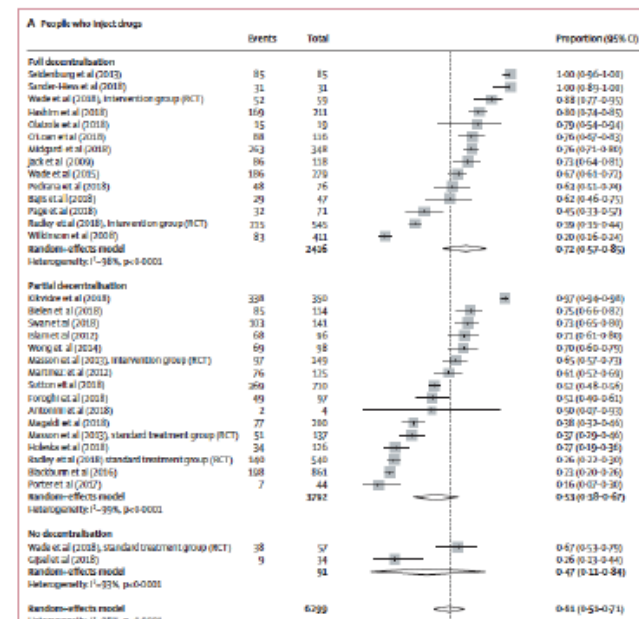
Eric Ota, Ashwini Teekay, Rohan Shrivastava, Simeon Karim, Philipp Easterbrook

### 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 domain 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 8058 reports, of which 332 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 (28 [14%] studies from low-income and middle-income countries) and a total of 489 956 patients (239 444 [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 (>80%) 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 48% of studies, and heterogeneity across studies tended to be very high ( $I^2 > 90\%$ ).





# Cambodia: A Gift to the World on HCV Care Model



UPDATED RECOMMENDATIONS ON  
**TREATMENT OF ADOLESCENTS AND  
CHILDREN WITH CHRONIC HCV INFECTION,  
AND HCV SIMPLIFIED SERVICE DELIVERY  
AND DIAGNOSTICS**

**BOX 6.1 Case study: CAMBODIA – Médecins Sans Frontières (MSF) – simplified model of decentralized HCV care in a rural health operational district in Battambang province, Cambodia (169-171)**

In LMICs, increasing overall access to HCV care remains an ongoing issue, particularly for populations outside of urban centres. MSF implemented a simplified model of decentralized HCV care in a rural health operational district in Battambang province, Cambodia.

## **Model of care**

The pilot project was implemented from June 2020 among the adult residents ( $\geq 18$  years of age) of two operational districts (ODs) in Battambang province with 27 participating rural health centres. Voluntary HCV antibody screening was undertaken through both active case finding (testing people in villages) and passive case finding (patients presenting to rural health centres). Serology testing was done with an RDT (SD Bioline®). If HCV-Ab serology positive, testing for HIV via rapid test, blood glucose, and blood pressure were also offered. Blood draw for HCV viral load (HCV-VL) test was done weekly at each health centre due to cold chain considerations for HCV viral load testing at the district referral hospital lab, using GeneXpert – a near POC molecular technology. Health center staff (primarily nurses) were trained in and assessed for competency to identify signs of decompensated liver cirrhosis and provided two-day training in the nurse-led initiation model. To expedite DAA initiation for HCV viraemic patients, pre-treatment assessment was performed by nurses. Viraemic patients who did not have additional complications received all HCV care follow-up with

# HCV Patient Flow Management (Pre-Simplification)

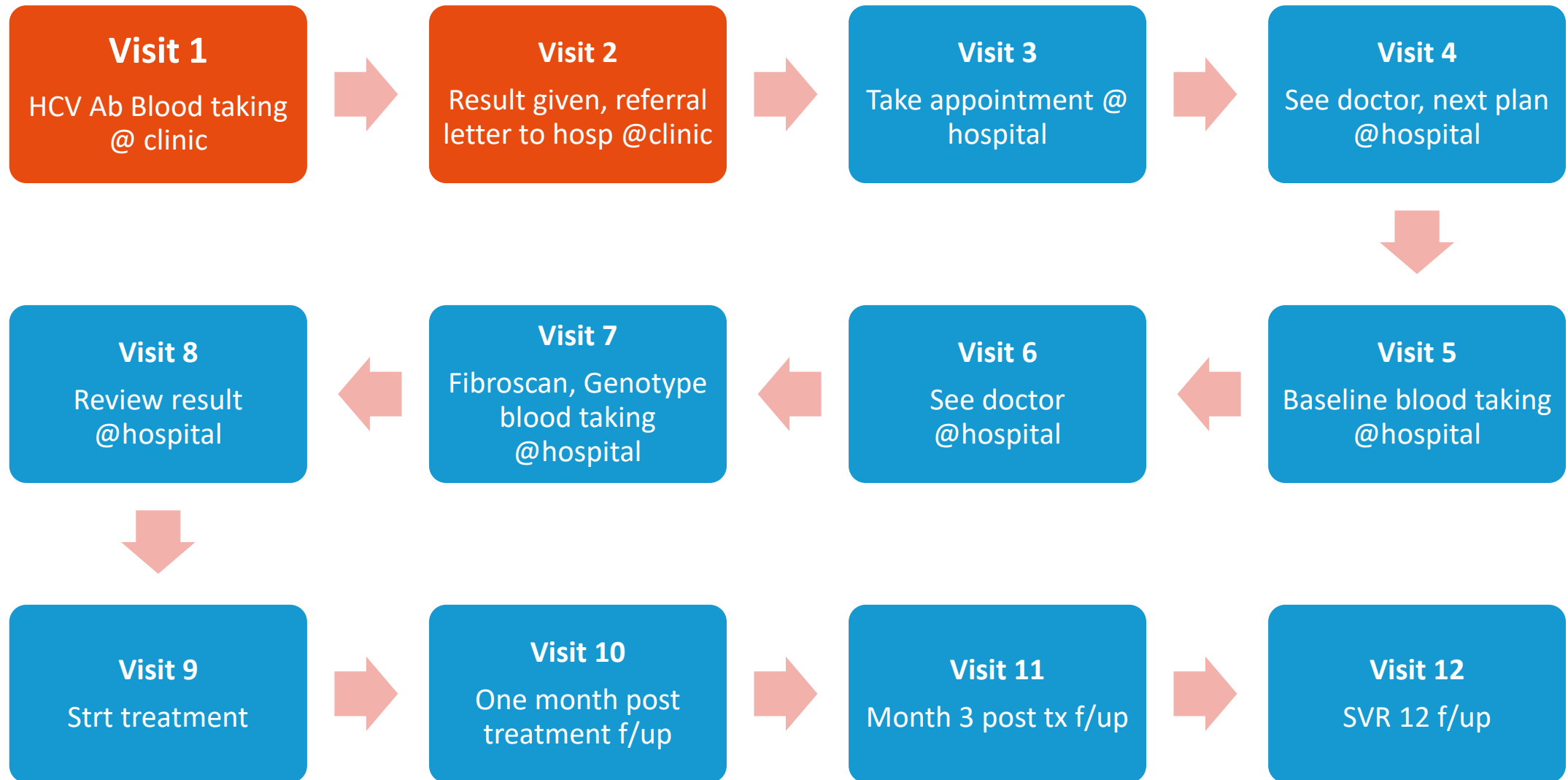
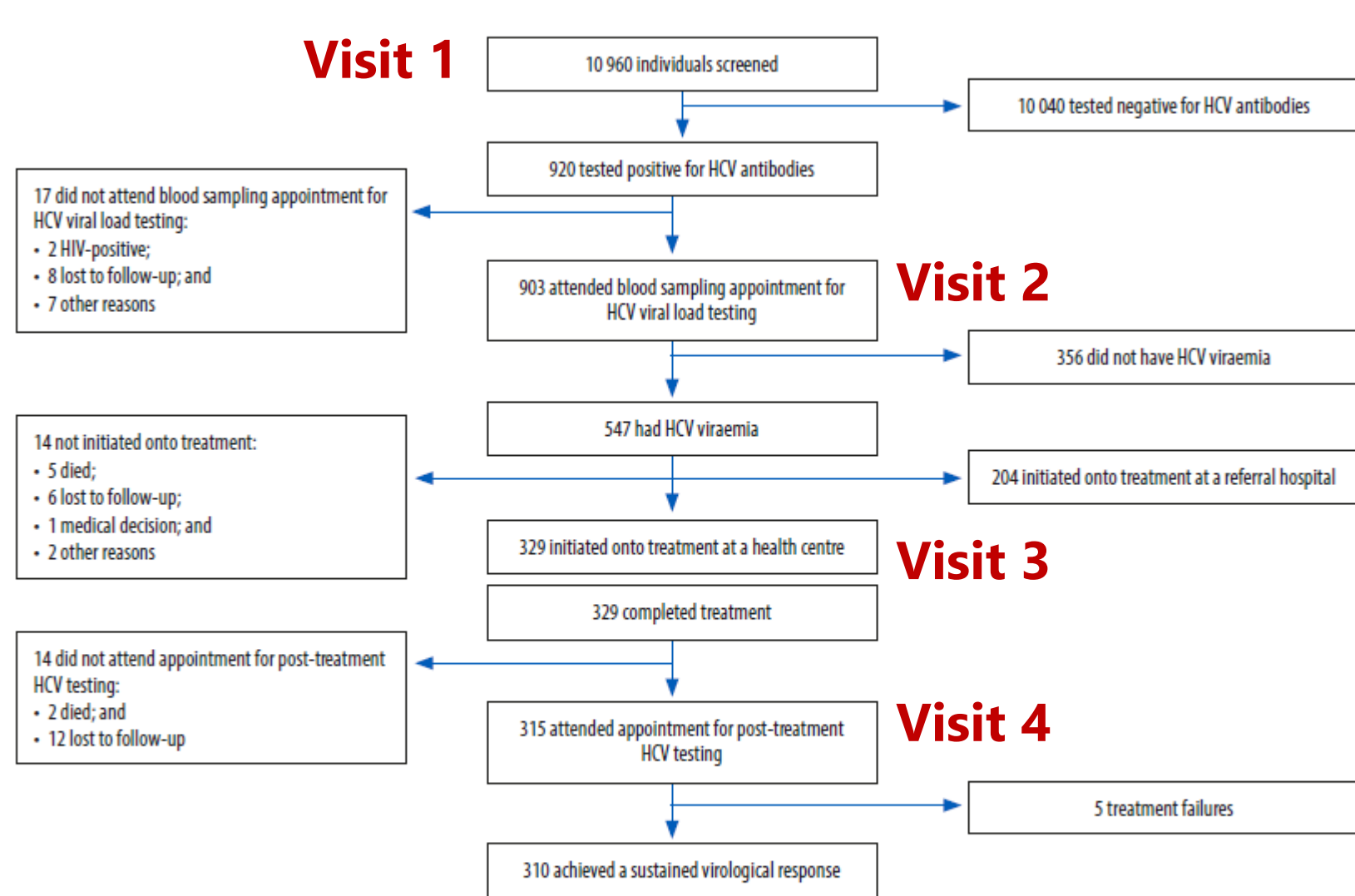


Fig. 2. Screening, testing, treatment and outcomes, nurse-led hepatitis C care pilot project, Cambodia, 2020



HCV: hepatitis C virus; HIV: human immunodeficiency virus.

Notes: Only patients without signs of decompensated liver cirrhosis or another comorbidity initiated treatment at a health centre; others were referred to hospital.

Patients initiated onto treatment at a health centre were prescribed combined sofosbuvir, 400 mg/day, and daclatasvir, 60 mg/day, orally daily for 12 weeks.

Hepatitis C virus (HCV) viraemia was defined as an HCV viral load  $\geq 1000$  IU/mL and a sustained virological response was defined as an HCV viral load  $< 1000$  IU/mL 12 weeks post-treatment.



Research

### Nurse-led initiation of hepatitis C care in rural Cambodia

Daniel O'Keefe,<sup>1</sup> Keo Samley,<sup>2</sup> Voeurng Bunreth,<sup>3</sup> Tonia Marquardt,<sup>4</sup> Serge Eric Bobi,<sup>5</sup> Kien Antharo,<sup>6</sup> Chanroen San Kim,<sup>7</sup> Hem Sothy,<sup>8</sup> Thoang Sokha,<sup>9</sup> Chor Samnang,<sup>9</sup> Yan Sokchea,<sup>9</sup> Farah Hossain,<sup>9</sup> Sana Balkan,<sup>9</sup> Mickael Le Pailh<sup>9</sup> & Jean-Philippe Dousset<sup>9</sup>

**Objective** To determine whether a nurse-led model of care for patients with hepatitis C virus (HCV) infections can provide safe and effective diagnosis and treatment in a resource-poor setting in rural Cambodia.

**Methods** The nurse-led initiation pilot project was implemented by Médecins Sans Frontières in collaboration with the Cambodian health ministry in two operational districts in Battambang Province between 1 June and 30 September 2020. Nursing staff at 27 rural health centres were trained to identify signs of decompensated liver cirrhosis and to provide HCV treatment. Patients without decompensated cirrhosis or another comorbidity were initiated at health centres onto combined treatment with sofosbuvir, 400 mg/day, and daclatasvir, 60 mg/day, orally for 12 weeks. Treatment adherence and effectiveness were assessed during follow-up.

**Findings** Of 10 960 individuals screened, 547 had HCV viraemia (i.e. viral load  $> 1000$  IU/mL). Of the 547, 329 were eligible for treatment initiation at health centres through the pilot project. All 329 (100%) completed treatment and 310 (94%; 95% confidence interval: 91–96) achieved a sustained virological response 12 weeks post-treatment. Depending on patient subgroups, this response varied from 89% to 100%. Only two adverse events were recorded; both were determined as unrelated to treatment.

**Conclusion** The safety and effectiveness of direct-acting antiviral medication has previously been demonstrated. Models of HCV care now need to enable greater access for patients. The nurse-led initiation pilot project provides a model for use in other resource-poor settings to scale up national programmes.

Abstracts in العربية, 中文, Français, Português and Español at the end of each article.

### Introduction

Given the demonstrated safety and effectiveness of current, direct-acting antiviral treatments for hepatitis C virus (HCV) infection and the validity of rapid, point-of-care tests,<sup>1–3</sup> international discussions and investigations are now focusing on the best models of care for HCV-infected patients. Several implementation studies have evaluated simplified models of HCV care provided in decentralized settings that involve substantial task-shifting to less-specialized staff (e.g. treatment initiation and follow-up by nursing staff).<sup>4–6</sup> Furthermore, innovations in rapid, point-of-care testing have enabled same-day diagnosis and, potentially, same-day treatment initiation.<sup>4,5</sup> Importantly, the ability to decentralize HCV testing and treatment facilitates the implementation of a so-called one-stop-shop model of HCV care, whereby diagnosis, treatment and follow-up are provided at a single location, with specialist referral for patients with cirrhosis.<sup>4,6</sup>

Nurse-led models of HCV treatment have been implemented internationally in a variety of contexts, including community, hospital and custodial settings.<sup>7–11</sup> However, there have been no high-income countries with developed HCV

For Cambodia, there are no robust estimates of the prevalence of HCV infection, which historically was mainly iatrogenic. However, recent geographical and subpopulation seroprevalence estimates range from 2.6% to 14.7%.<sup>12–14</sup> Access to HCV testing and treatment is limited across the country.<sup>15</sup> Since 2016, Médecins Sans Frontières has implemented HCV testing and treatment projects in: (i) urban Phnom Penh, using a progressively simplified care model in a government hospital; and (ii) rural areas, involving basic primary health outposts with non-specialist staff.<sup>16</sup> In 2020, Médecins Sans Frontières expanded on these projects: the nurse-led initiation pilot project was implemented to evaluate pre-treatment assessment, treatment initiation and follow-up by nursing staff in a resource-constrained rural setting in Battambang Province, Cambodia. The pilot project involved minimal resources – there were no medical doctors on-site in health centres and no transient elastography machines for liver assessment, and laboratories did not have the capacity to perform some pre-treatment assessments, such as deriving aspartate aminotransferase-to-platelet ratio index scores.

The aim of this paper was to report the outcomes of the nurse-led initiation pilot project, including patient retention,





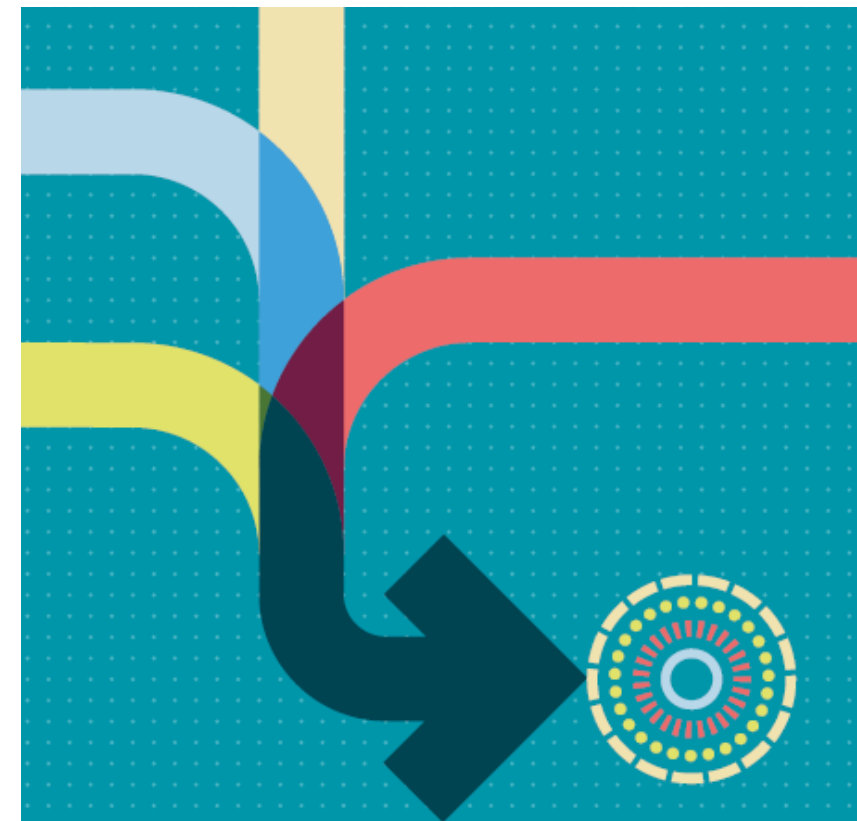
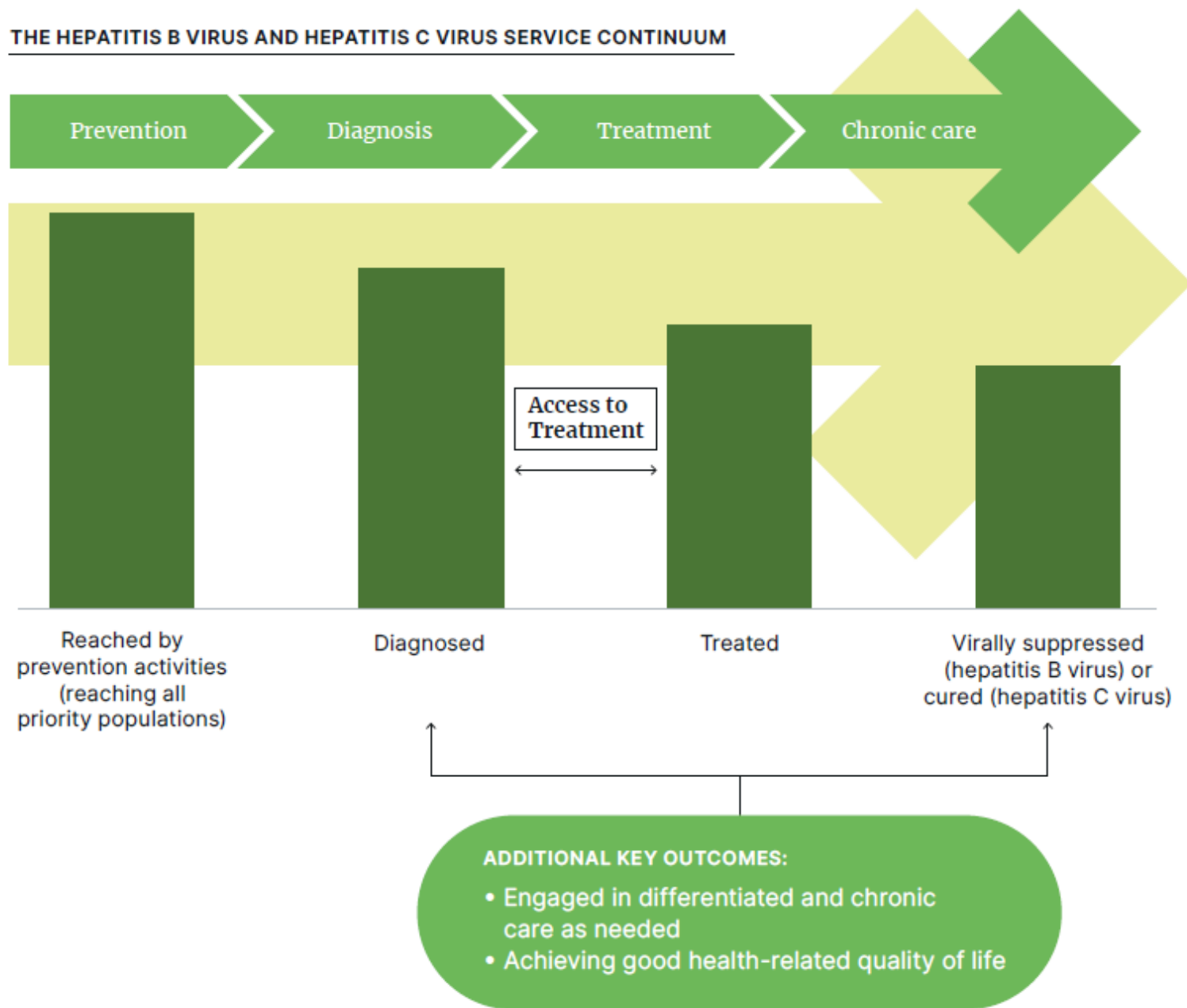
# Working with Partners on HCV

- CDC MOH
- WHO Country Office
- CHAI
- HACC, KHANA
- Hep C PACT (MSF, DNDi, TAG, FIND)
- We need more partners!



Fig. 5.1. The service engagement cascade for hepatitis B virus and hepatitis C virus

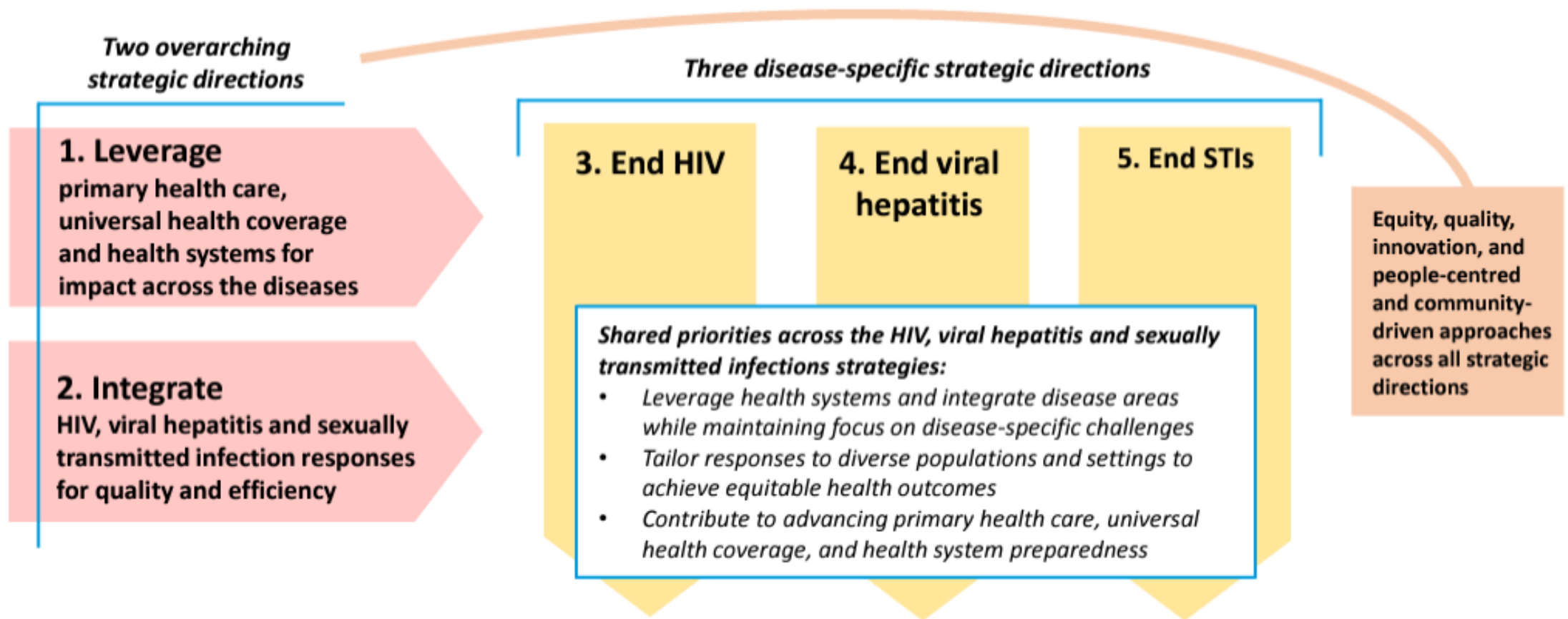
**THE HEPATITIS B VIRUS AND HEPATITIS C VIRUS SERVICE CONTINUUM**



**Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022–2030**

# Global Health Sector Strategies on HIV, Viral Hepatitis and Sexually Transmitted Infections, 2022–2030

*Ending Epidemics and strengthening primary health care and health systems*



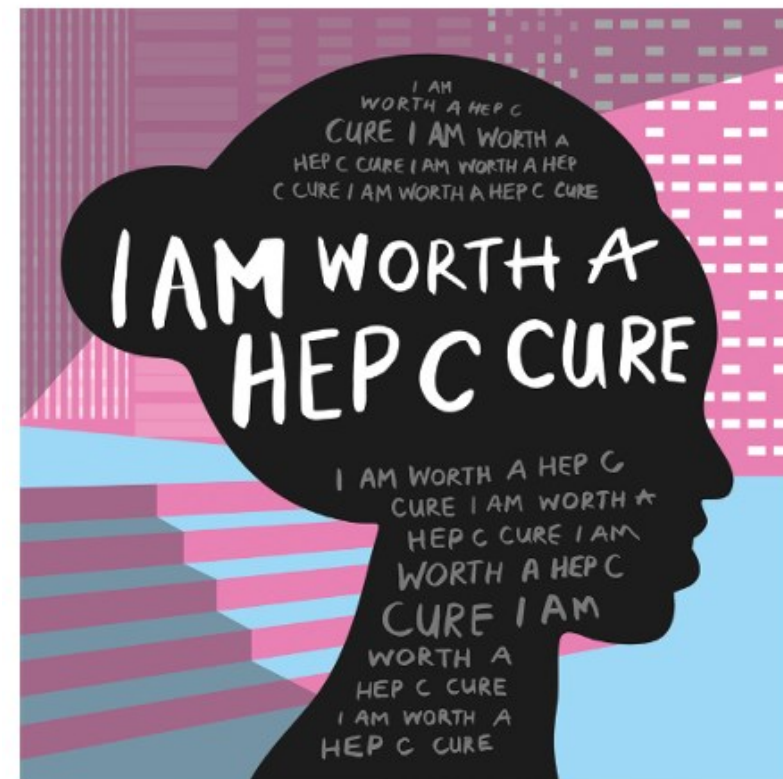
- *Sustainable Development Goal 3: Ensure healthy lives and promote well-being for all at all ages*
- *All other Sustainable Development Goals*

# Key Recommendations for Cambodia

**Community and national governments work together** to raise funding for HCV elimination, to find the missing thousands of people living with HCV, and to scale up HCV diagnostics

**Integration to existing health system & services** (especially HIV, STI, TB, Malaria & Hepatitis) will need to happen

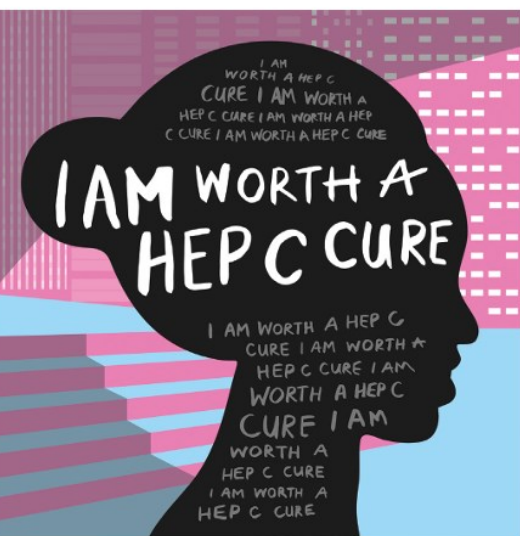
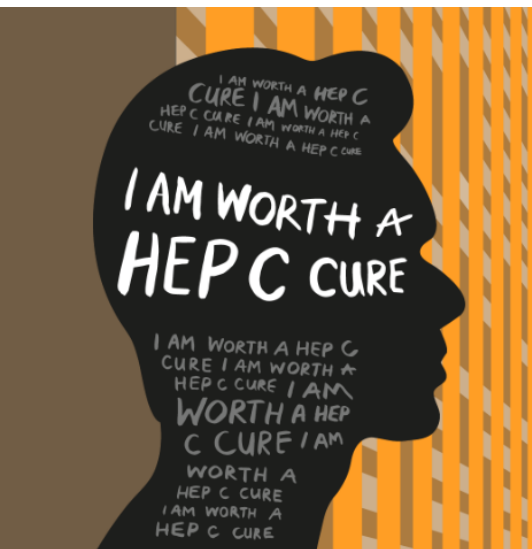
National hepatitis programs should continuously **raise awareness about HCV**, subsidize HCV screening programs to encourage more people to screen [e.g. **Starts with our family campaign**]



**TAG**  
Treatment Action Group







Awareness & Community Response is key



# Thank you!

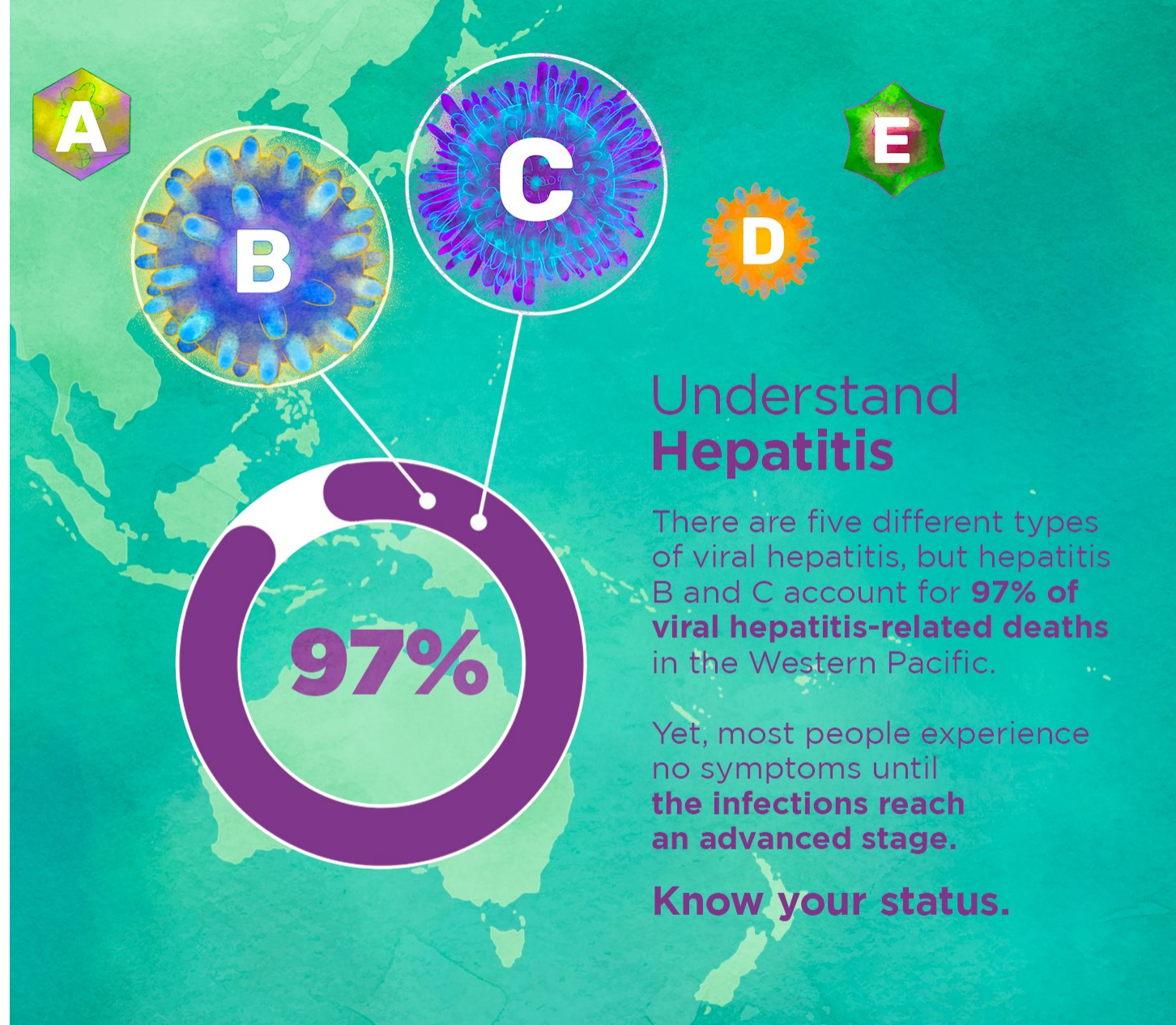
*[hychung@dndi.org](mailto:hychung@dndi.org)*





- 5 types of hepatitis virus
- Hep B & Hep C most commonly seen & generally no symptoms in early stage of infection

**DNDi**



## Understand Hepatitis

There are five different types of viral hepatitis, but hepatitis B and C account for **97% of viral hepatitis-related deaths** in the Western Pacific.

Yet, most people experience no symptoms until **the infections reach an advanced stage.**

**Know your status.**

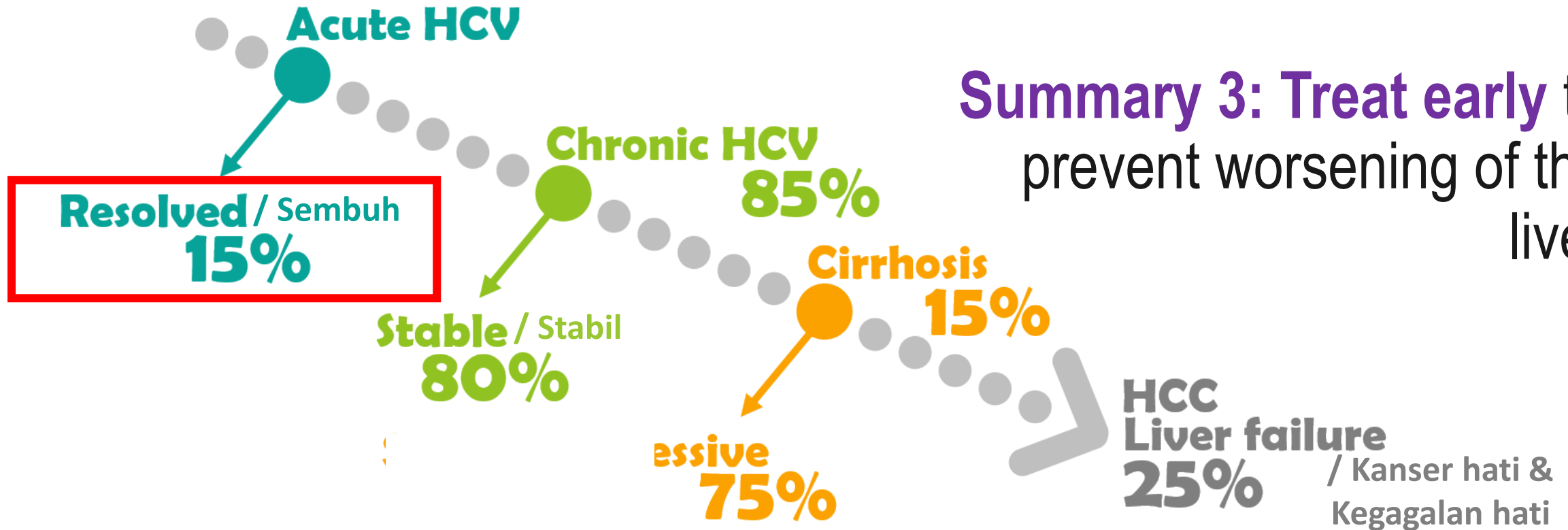
SEEK **HEP.** SEEK **HELP.** Get tested today.

For more information, visit [who.int/westernpacific/health-topics/hepatitis](http://who.int/westernpacific/health-topics/hepatitis)



**Summary 2:** Hep C has no clear sign of infection for years

**Summary 3:** Treat early to prevent worsening of the liver



**Time/year**  
Masa / Tahun

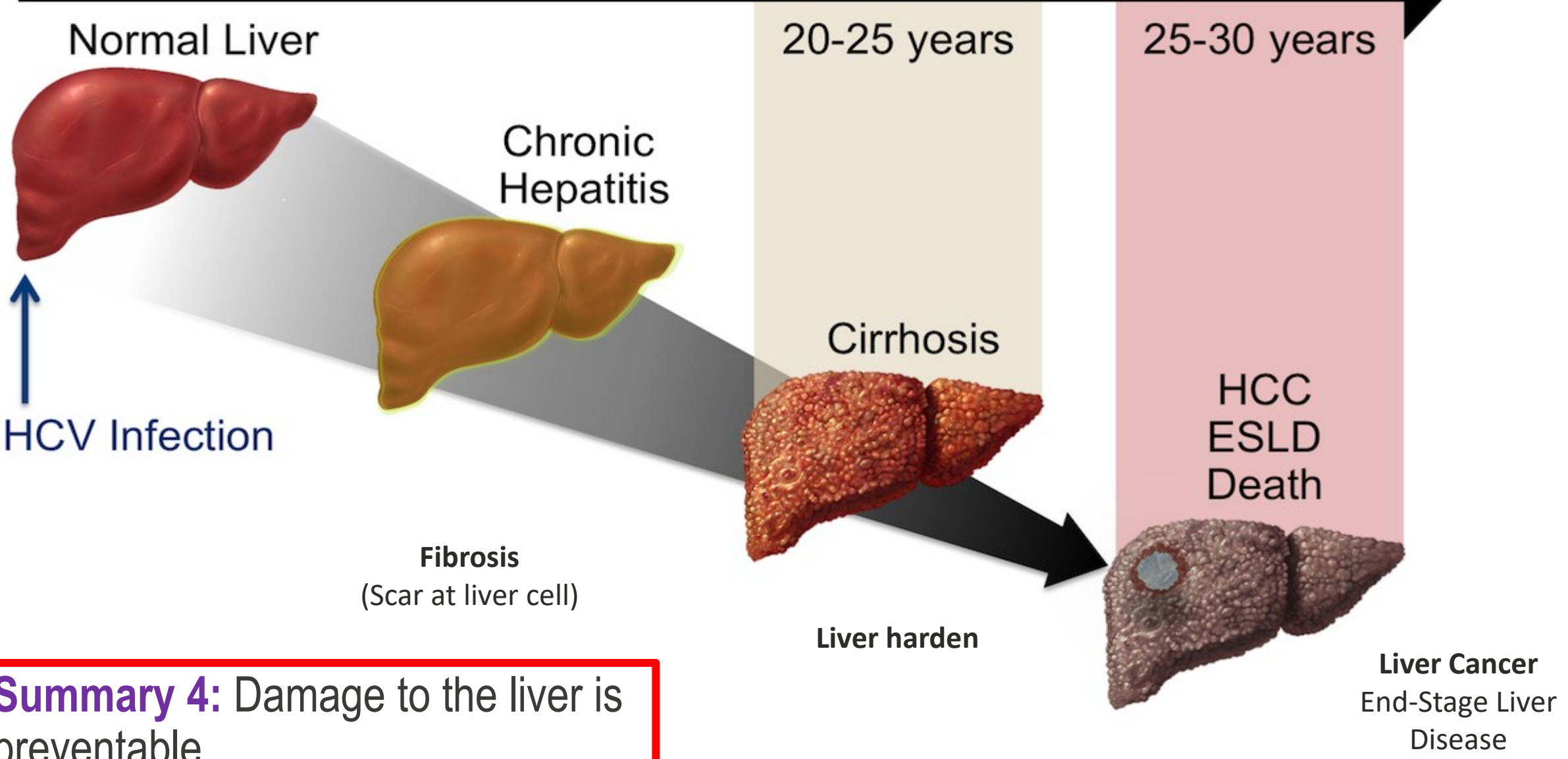
10

20

30

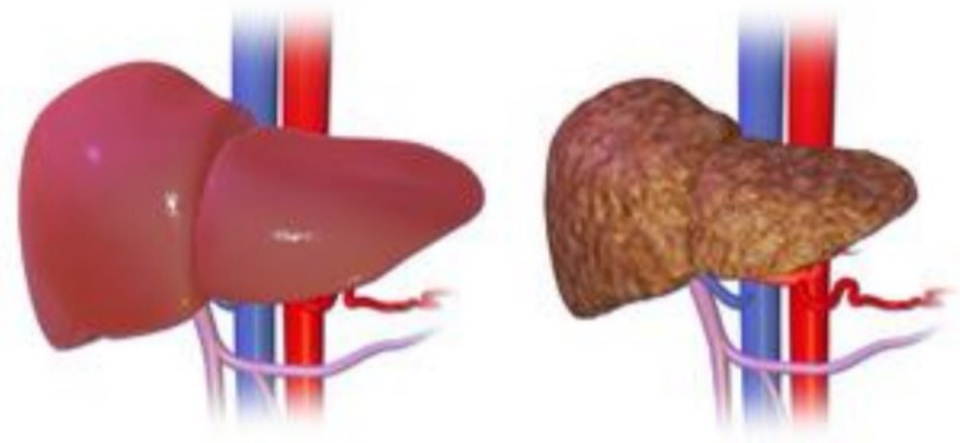


# Time






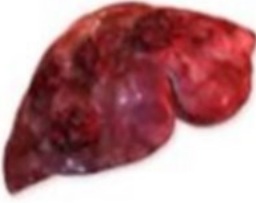
**Summary 4:** Damage to the liver is preventable

# Stages of Liver Attacked by Hepatitis C Virus



Normal Liver

Liver Cirrhosis

PROGRESSION OF LIVER DAMAGE			
HEALTHY LIVER	FIBROTIC LIVER	CIRRHOTIC LIVER	LIVER CANCER
			
A healthy liver is able to perform its normal functions effectively, e.g. aiding digestion and breaking down harmful drugs and poisons.	Continuous inflammation of the liver caused by hepatitis C can lead to fibrosis – the formation of scar tissue within the liver.	Extensive scarring can block the flow of blood through the liver and cause liver function to deteriorate over time - this is called cirrhosis.	Hepatitis C is a leading cause of liver cancer – the formation of a malignant tumour in the liver.

**Fibrosis**  
(Scarring of the  
Liver cell)

**Hati Keras**

**Kanser Hati**  
End-Stage Liver  
Disease



# Summary 5: Hep C can be Treated

**Direct-Acting Antiviral (DAA)** (vs HAART for HIV)

- **Sofosbuvir + Daclatasvir**
- Sofosbuvir + Velpatasvir
  
- 12-weeks or 24-week (3-6 months)
- Depending on liver stages (cirrhotic/non-cirrhotic)
- No serious side effect/well tolerated + **FREE\***





## To help foster an enabling environment for improved availability of HCV diagnostics and treatments in LMICs

- Developing **awareness among decision-makers** of HCV and the opportunity for elimination
- Designing **sustainable financing** mechanisms for HCV scale-up in LMICs (Cambodia & Bangladesh)
- Supporting **simplified HCV diagnostic** tools and strategies
- Supporting improved **access to all simple and affordable DAA** treatments in high-burden LMICs including ravidasvir + sofosbuvir

## HEP C PACT, PRIORITY COUNTRIES:

