# Understanding viral hepatitis C Diagnosis and Treatment : Community Training

Giten Khwairakpam
TREAT Asia/amfAR
August 2019

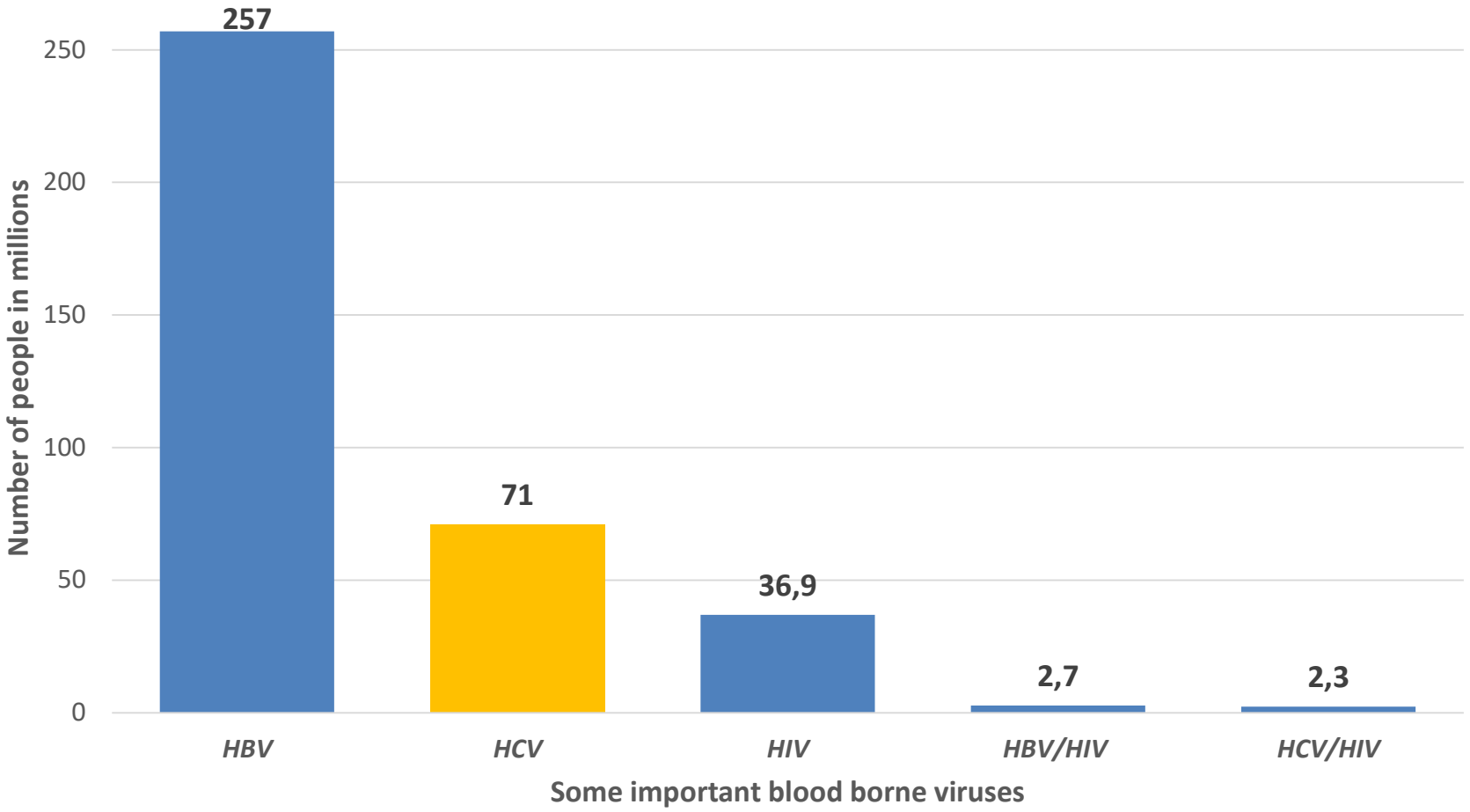
# Understanding hepatitis

- *Hepar*-itis*:* From Greek origin means inflammation of the liver
- Alcohol, medicines, chemicals and viruses can cause hepatitis
- Affects liver (*inflammation*) as a natural response to the infection
- There are 6 types of viral hepatitis

# Understanding viral hepatitis

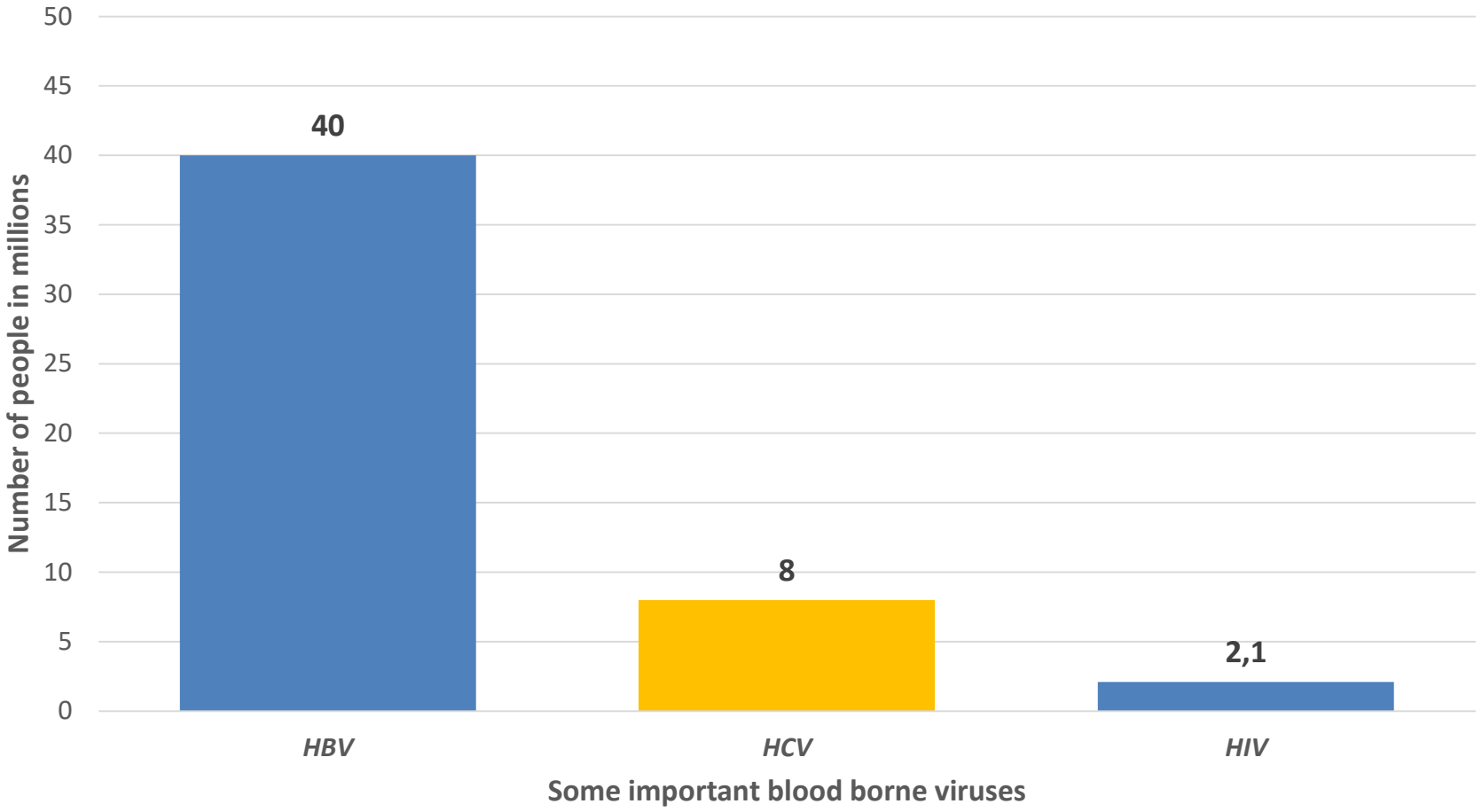
| Viral hepatitis type | Brief information |
|---|---|
| **Hepatitis A (HAV)** | - Spreads through contaminated food, water, vegetables<br>- Usually not chronic and resolves itself<br>- Preventive vaccine available for HAV |
| **Hepatitis B (HBV)** | - Spreads through blood of infected people<br>- Chronicity high when infected in birth, infancy or childhood<br>- Preventive vaccine available for HBV |
| **Hepatitis C (HCV)** | - Spreads through blood of infected people<br>- Around 15% to 25% will clear the virus on its own<br>- There is no preventive vaccine for HCV, but can be cured |
| **Hepatitis D (HDV)** | - Infects only people with HBV<br>- Makes disease progression faster when co-infected with HBV<br>- HBV Vaccine also protects from HDV. |
| **Hepatitis E (HEV)** | - Spreads mostly through contaminated water<br>- Usually resolves itself and there is no preventive<br>- HEV infection during pregnancy can lead to fatality |
| **Hepatitis G (HGV)** | - Similar to HCV; currently unclear on its impact in HIV co-infection |

# Number of people living with

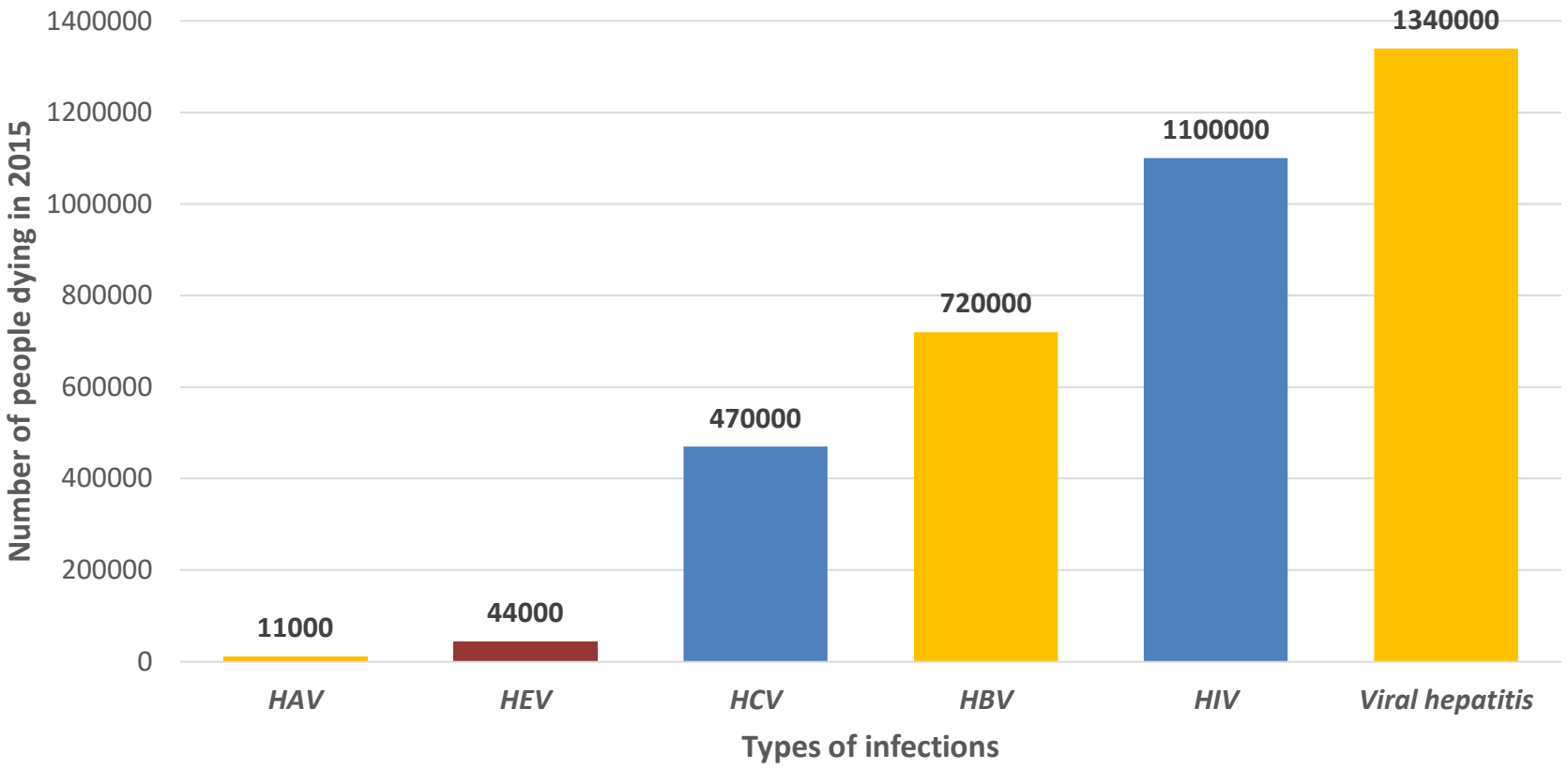



Global Hepatitis Report 2017, WHO

# Number of people living with in India



# Deaths due to viral hepatitis, HIV




Global Hepatitis Report 2017, WHO

# Hepatitis C and HIV

- 2.3 million people living with HCV/HIV co-infection
- Co-infection decreases the chances of natural clearance
- Co-infection increases the chance of mother to child transmission of HCV
- Co-infection makes higher RNA levels
- Co-infection makes liver disease progression faster
- In the absence of harm reduction services, PWID are exposed to much higher risk

# Diagnosis

- HCV Antibody tests
- HCV RNA
- *HCV genotype*

# HCV Antibody test

- Detection 2 months to 6 months post-exposure
- Detect the immune response to the virus
- Confirm exposure
- Do not confirm ongoing infection
- False negatives may occur in Chronically immunosuppressed HIV positive.

# HCV RNA testing (Quantitative)

- Also known as viral load
- Necessary to confirm active infection
- Detection: 2-6 weeks post-exposure
- Re-testing 4-6 months later recommended

# HCV Genotype Testing

- **HCV has:**
- 6 major known genotypes (designated 1-6)
- Many subtypes (a, b, c.. 67 subtypes recognized)
- All patients need not have genotype testing prior to treatment
- Treatment duration varies: 8 to 12 or 24 weeks

# Preparing for Treatment

- HCV RNA (Quantitative) Viral Load
- Stage of liver fibrosis
- CD4 count *(Optional but good to know)*
- Other hematological and serological test
- *Genotype*

# What factors affect Tx outcome

- *Genotype 2 or 3*
- *Low HCV RNA (Viral Load)*
- *Age = 40*
- *Female*
- *Weight = 75kg*
- *IL28 B genotype*
- **Minimal Fibrosis**

# Interpreting Viral Load in HCV

- Shows in two units- copies per ml or international units per ml (IU/mL).
- No standard conversion in between the 2 units.
- Treatment naïve, non-cirrhotic patients G1 patients who has viral load below **6 million IU/mL** treated for 8 weeks
- Viral load nowadays does not inform any treatment decisions

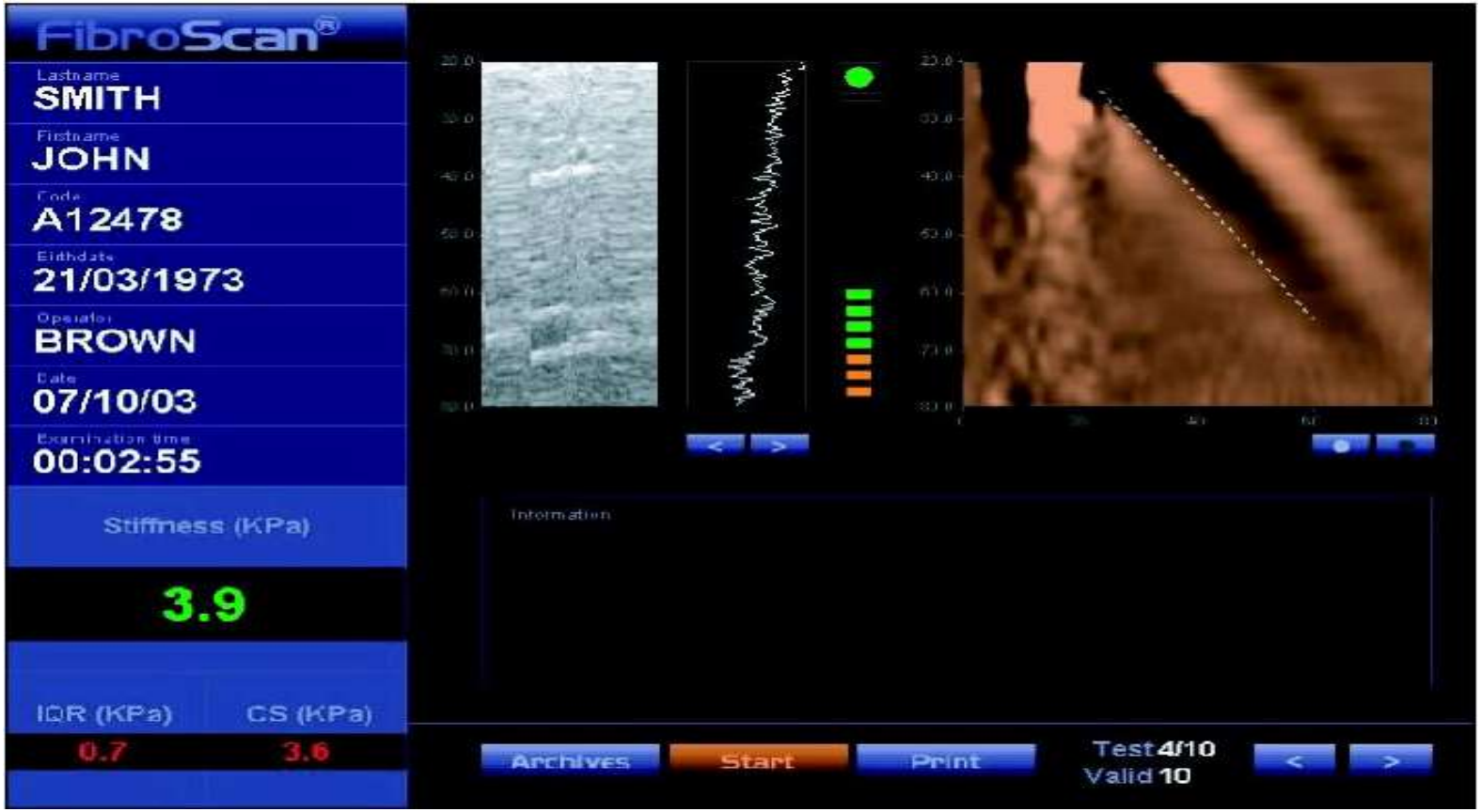
# Understanding fibrosis staging

- Non-invasive methods;
  - Transient Elastography (FibroScan, Fibrotouch)
  - APRI
  - FIB4

# Transient Elastography



# FibroScan® results



# Interpreting FibroScan results

- Fibroscan® is non invasive method and considered most convenient.
- F0: No Fibrosis (Upto 2.5 Kpa)
- F1: mild or minimal fibrosis ( 2.5 to 7.0 Kpa)
- F2: moderate or significant fibrosis (7.0 to 9.5 Kpa)
- F3: severe fibrosis (9.5 to 12 Kpa)
- F4: cirrhosis ( 12 to 75)
  - Compensated (Liver is doing some of its functions)
  - Decompensated (liver is not doing its functions properly)

# Compensated or Decompensated cirrhosis

- Indicates patients survival chances
- Score is assigned through a process called Child Pugh score calculation
  - CP needs 2 clinical symptoms and 3 blood markers
  - Symptoms: Ascites, Encephalopathy
  - Blood: Albumin, Bilirubin, Prothrombin time/INR
- Decompensated cirrhosis is divided into 2 stages;
  - Decompensated stage B and C
  - Once in this stage, without intervention, survivability decreases

# Child Pugh Score classification

| Parameter | Points assigned | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| Ascites | Absent | Slight | Moderate |
| Bilirrubin, mg/dL | </= 2 | 2-3 | >3 |
| Albumin, g/dL | >3.5 | 2.8-3.5 | <2.8 |
| Prothrombin time<br>* Seconds over control<br>* INR | 1-3<br><1.8 | 4-6<br>1.8-2.3 | >6<br>>2.3 |
| Encephalopathy | None | Grade 1-2 | Grade 3-4 |

# Child Pugh Score classification

| Grade | Points | One-year patient survival (%) | Two-year patient survival (%) |
|---|---|---|---|
| A: well-compensated disease/liver function is preserved | 5-6 | 100 | 85 |
| B: significant functional compromise/liver function impaired | 7-9 | 80 | 60 |
| C: decompensated disease/liver function severely impaired | 10-15 | 45 | 35 |

# Other liver staging biomarkers

- APRI (AST/SGOT to Platelet Ratio Index)
- http://gihep.com/calculators/hepatology/apri/
- Understanding results:
  - Less than 2 :- No Cirrhosis
  - Above 2: Cirrhotic

$$\text{APRI} = \frac{\dfrac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count } (10^9/\text{L})} \times 100$$

# Other liver staging biomarkers

- FIB4 (Fibrosis 4)
- http://gihep.com/calculators/hepatology/fibrosis-4-score/
- Understanding results:
  - Less than 1.45 = F0/F1
  - More than 3.35= F3/F4

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

# Direct Acting Antivirals (DAAs), treatment regimens, treatment duration, treatment monitoring and drug-drug interactions

# Direct-acting antivirals

- **Protease inhibitors** *"previr"*
  - simeprevir, asunaprevir etc.
- **NS5a inhibitors:** *"asvir"*
  - daclatasvir, ledipasvir etc.
- **Polymerase inhibitors also NS5b:** *"buvir"*
  - sofosbuvir, dasubuvir etc.

# Some important DAAs

- Sofosbuvir
- Ledipasvir
- Daclatasvir
- Velpatasvir
- Glecaprevir
- Pibrentasvir

# WHO 2018 recommendations

- **Who to test?**
  - **Focused testing in most-affected populations**
    - Delivered through facility or community-based testing HCV antibody test be offered with linkage to prevention, care and treatment services to adults and adolescents from populations most affected by HCV infection, who have a history of exposure and/or high-risk behaviors for HCV infection)
    - Adults, adolescents and children with a clinical suspicion of chronic viral hepatitis (i.e. symptoms, signs, laboratory markers).
  - **General population testing**
    - In settings with a ≥2% or ≥5% HCV antibody sero-prevalence in the general population, all adults have access to and be offered HCV antibody testing with linkage to prevention, care and treatment services.
    - General population testing approaches should make use of existing community- or facility based testing opportunities or programs such as HIV or TB clinics, drug treatment services and antenatal clinics
  - **Birth cohort testing**
    - This approach may be applied to specific identified birth cohorts of older persons at higher risk of infection and morbidity within populations that have an overall lower general prevalence

# What to test with?

- **Which serological assay to use?**
  - To test for evidence of past or present infection in adults, adolescents and children (>18 months of age), an antibody or antibody/antigen using either a rapid diagnostic test (RDT) or laboratory-based test that meet minimum safety, quality and performance standards
  - In settings where there is limited access to laboratory infrastructure and testing, and/or in populations where access to rapid testing would facilitate linkage to care and treatment, RDTs are recommended.
- **Detection of viraemic infection**
  - Directly following a reactive HCV antibody serological test result, the use of quantitative or qualitative Nucleic acid testing (NAT) for detection of HCV RNA is recommended as the preferred strategy to diagnose viraemic infection
- **Assessment of HCV treatment response**
  - NAT for qualitative or quantitative detection of HCV RNA should be used as the test of cure at 12 or 24 weeks (i.e. sustained virological response SVR12 after completion of antiviral treatment.

# Whom to treat and what to treat with?

- Offer treatment to all individuals diagnosed with HCV infection who are 12 years of age or older, irrespective of disease stage
- Use pan-genotypic DAA regimens for the treatment of persons with chronic HCV infection aged 18 years and above
- Treat with appropriate DAAs in adolescents aged 12–17 years or weighing at least 35 kg with chronic HCV infection
- In children aged less than 12 years with chronic HCV infection
  - deferring treatment until 12 years of age
  - treatment with interferon-based regimens should no longer be used
- **Pan-genotypic regimens**
  - Sofosbuvir/velpatasvir
  - Sofosbuvir/daclatasvir
  - Glecaprevir/pibrentasvir

# Pan-genotypic regimens and duration for adults (18 years or more) with no cirrhosis

| Daclatasvir/sofosbuvir | Velpatasvir/sofosbuvir | Glecaprevir/pibrentasvir |
|---|---|---|
| 12 weeks | 12 weeks | 8 weeks |

# Regimens and duration for adults (18 years or more) with cirrhosis

| Daclatasvir/sofosbuvir | Velpatasvir/sofosbuvir | Glecaprevir/pibrentasvir |
|---|---|---|
| 24 weeks | 12 weeks | 12 weeks |

# Regimens for adolescents (12 to 17 years)

| Genotype | Ledipasvir/sofosbuvir | Ledipasvir/ sofosbuvir/ ribavirin | Sofosbuvir/ ribavirin |
|---|---|---|---|
| Genotype 1 | 12 weeks | | |
| Genotype 2 | | | 12 weeks |
| Genotype 3 | | | 24 weeks |
| Genotype 4 | 12 weeks | 12 weeks | |
| Genotype 5 | 12 weeks | 12 weeks | |
| Genotype 6 | 12 weeks | 12 weeks | |

# Alternative regimens for persons without cirrhosis

| Genotype | Simeprevir/ sofosbuvir | Daclatasvir /sofosbuvir | Ombitasvir/ paritaprevir/ ritonavir/ dasabuvir | Ombitasvir/ paritaprevir/ ritonavir/ ribavirin | Sofosbuvir /pegylated interferon/ ribavirin |
|---|---|---|---|---|---|
| **Genotype 1** | 12 weeks | | 12 weeks | | |
| **Genotype 2** | | 12 weeks | | | |
| **Genotype 3** | | | | | |
| **Genotype 4** | 12 weeks | | | 12 weeks | |
| **Genotype 5** | | | | | 12 weeks |
| **Genotype 6** | | | | | 12 weeks |

# Indian guidelines recommendations on treatment

| Category of Patient | Recommended regimen | Duration |
|---|---|---|
| Non Cirrhotic | Sofosbuvir/ daclatasvir | 12 weeks |
| Cirrhotic (compensated) | Sofosbuvir/velpatasvir | 12 weeks |
| Decompensated cirrhosis (RBV tolerant) | Sofosbuvir/velpatasvir/ ribavirin | 12 weeks |
| Decompensated cirrhosis (RBV intolerant) | Sofosbuvir/velpatasvir | 24 weeks |

# Monitoring for treatment response

| Time | Regimen: Only DAAs (non-cirrhotic usually) | | | Regimen: DAAs and Ribavirin (cirrhotic usually) | | |
|---|---|---|---|---|---|---|
| | CBC, S.Creatinine, LFT | Adherence and side effects | HCV RNA | CBC, S.Creatinine , LFT | Adherence and side effects | HCV RNA |
| Baseline | Yes | | Yes | Yes | | Yes |
| Week 1 | | | | Yes | Yes | |
| Week 2 | | | | Yes | Yes | |
| Week 4 | Yes | Yes | | Yes | Yes | |
| Week 8 | | | | Yes | Yes | |
| Week 12 | | | | Yes | Yes | |
| Week 12 after completion of treatment ( SVR-12) | | | Yes | Yes | | Yes |

*CBC, complete blood counts; LFT, liver function tests; SVR, sustained viral response*

# Drug–drug interactions between HCV and HIV medications

| DAAs | ABC | ATZ/r | DRV/r | DTG | EFV | LPV/r | NVP | RAL | TDF | TAF | ZDV | XTC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Daclatasvir | | | | | | | | | | | | |
| Glecaprevir/pibrentasvir | | | | | | | | | | | | |
| Sofosbuvir | | | | | | | | | | | | |
| Sofosbuvir/ledipasvir | | | | | | | | | | | | |
| Sofosbuvir/velpatasvir | | | | | | | | | | | | |

*Do not co-administer.*

*May need dose adjustment for DAAs.*

*No known interaction; can be co-administered.*

ABC: abacavir; ATZ/r: atazanavir/ritonavir; DRV/r: darunavir/ritonavir; DTG: dolutegravir; EFV: efavirenz; LPV/r: lopinavir/ritonavir; NVP: nevirapine; RAL: raltegravir; ZDV: zidovudine; TDF: tenofovir disoproxil fumarate; XTC: emtricitabine or lamivudine; TAF: tenofovir alafenamide.

# THANK YOU ☺

# QUESTIONS