Global & Regional Epidemiology of HCV: Pathways to Its Elimination by 2030.

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University Department of Medicine,
Queen Mary Hospital, HK
• I am on the Advisory Committee of Gilead Sciences HK Limited. I have given sponsored lectures for Gilead Sciences and Abbvie.
• Introduction
• HCV global burden / incidence
• HCV treatment guidelines and benefits
• The global goal of HCV elimination by 2030
Introduction
INTRODUCTION

• RNA virus
• Replication entirely cytoplasmic
• Resides only in the liver
• Transmission: parental only, mainly through transfusion or intravenous drug use
• Most hepatocellular carcinoma (HCC) due to underlying cirrhosis; not an oncogenic virus unlike HBV
• >95% cure with 8–12 weeks of DAAs
HCV global burden/incidence
HCV: Incidence

## HBV vs HCV (WHO Report 2017)

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<td><strong>Cirrhosis</strong></td>
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**Total deaths by viral hepatitis 1.34 million**

Global annual mortality 2000-2015

No. of Deaths

Year

Hepatitis
Tuberculosis
HIV
Malaria

Mortality from viral hepatitis up by 22% since 2000

- 1.1 million deaths in 2000
- 1.34 million deaths in 2015

HK Data from 11309 HCV patients (2017)

- People who injects drug (PWID) 36.7%
- Transfusion 30.0%
- Unknown 27.2%
  - Unsafe sexual practice 1.9%
  - Tattoo & body piercing 2.8%
  - Organ transplant 1.1%
  - Maternal

YT Hui et al. Liver Int 2018
HK Data from 11309 HCV patients (2017)

Median age 59

Delayed review of diseases
(Median time from infection to first review for HCV 26 years)

Liver stiffness data:
- Cirrhosis 26.8%
- Significant fibrosis 12.2%
- Gray zone 17.4%
- Insignificant fibrosis 43.6%

YT Hui et al. Liver Int 2018
Global Distribution of HCV Genotypes

WHO 2013
EXAMPLE OF THE INCREASE IN HCV INCIDENCE

Studies from Yunnan Province of China:
• 67% of IDUs in China HCV+ve
• Incidence of subtype 6a increased from 5% to 15% in 5 years
• Subtype 6a originated from Vietnam; then spread to the 3 southern China provinces Guangdong, Guangxi and Yunnan

EXAMPLE OF THE INCREASE IN HCV INCIDENCE

Studies from Yunnan Province of China:

• In Guangxi and Yunnan:
  - Genotype 6a much more common in IDUs than general population

• In Guangdong:
  - Genotype 6a same in IDUs and general population!!
  - Postulation: Guangdong became very prosperous, stimulating pornography!!!
  - Sexual transmission may be major risk factor, especially for MSM and prostitutes

HCV Treatment Guidelines
The Goal

to reduce all-cause mortality, including end-stage disease and HCC through CURE as evidenced by SVR
AASLD and EASL Guidelines 2018

• Who to treat?
  - ALL patients with chronic HCV, except those with short life expectancy due to non-HCV disease(s)
  - Patients with end-stage liver disease due to HCV should still be treated
• IFN-free, ribavirin-free, DAA-based regimens because of their efficacy, safety and tolerability

• Simplified pangenotypic regimes recommended

• Pre-treatment assessment:
  - proof of HCV replication
  - assess presence or absence of cirrhosis by non-invasive methods, eg, Fibroscan
Treatment Benefits
Cirrhosis registry study (DALTON-C): Interim results
Shift in CPT classification with DAAs

• 1066/1067 patients maintained SVR throughout follow-up period of 2-44 months (21 months)

Reduction of HCC with SVR to Treatment

US VA experience ( n = 25,000)  Japanese experience( n = 1,170)

p = <0.001 (log-rank test)

p = 0.007 (log-rank test)

Kanwal et.al , Gastroenterology . 2017
Fumihiro Ogata et, al. Oncology . DOI: 10.1159/000470910
CLINICAL OUTCOME OF HCV WITH DAA-TREATMENT

All Cause Mortality

DAA-treated (n=7344)

Untreated (n=2551)

Burden of HCV in China: 2004 to 2050

• Markov Models for 4 different scenarios:
  - Natural history
  - Pre-DAAs
  - DAAs for ≥ F3
  - DAAs for ≥ F0

Scenario
Natural history
Pre-DAAs
DAAs for ≥ F3
DAAs for ≥ F0

Incidence (millions)

Year
2004 2010 2020 2030 2040 2050

Burden of HCV in China: 2004 to 2050

- To avert the increasing burden of HCV in China;
  - start launching DAAs rapidly
  - F0 patients should also be treated
  - expanded screening to identify cases

The global goal of HCV elimination by 2030
HCV elimination by 2030

Problems to overcome

• Prevention of new infections

• For the existing chronic carriers
  – access to testing
  – access to treatment
  – sustainability
  – identification of cases
  – reluctance to seek medical advice
  – patient compliance
HCV elimination by 2030

Problems to overcome

• Prevention of new infections

• For the existing chronic carriers
  – access to testing
  – access to treatment
  – sustainability

* – identification of cases
* – reluctance to seek medical advice
* – patient compliance

* Personal opinion: Likely to remain persistent problems!
HCV Elimination Targets 2017

http://cdafound.org/polaris 2018
Prevention of new HCV infection

Transmission persists!!

• Compared to the second half of the 20\textsuperscript{th} century, several countries reported lower incidence of HCV in historical epidemiology studies\textsuperscript{1,2,3}

• WHO reports 1.75 million \textit{new} infections in 2015 (incidence rate 23.7 per 100,000), exceeding the number being treated\textsuperscript{4}

Prevention of new HCV infection

Transmission persists!!

• Main routes
  
  - IV drug use: accounts for 23% of new HCV infections
  
  - unsafe health care practices
    
    - distribution of syringes for IVDUs 27/person/year (instead of the target 200/year)
    
      [ ZERO syringes in the HK Methadone Clinics!!]
    
    - in low-income countries, 34% donated blood not screened with basic quality procedures
    
    - in 2010, 5% injection with unsterilized, reused devices:
      
      4% in E Mediterranean and 5% in SE Asia regions!!

The existing HCV carriers
The First 3 Public Health Issues
The 3 public health issues

1. Access to testing
   • Rapid tests including dried blood spot, oral fluids
   • Who to test?
     – where incidence is ≥2% or ≥5%, all adults\(^1\)
     – HCV: IVDUs
     – Funding??

The 3 public health issues

2. Access to treatment

HCV with the 8–12 weeks of DAA treatment

• VERY variable in different countries
  – Canada: free treatment including prisoners
  – USA: based on income & insurance
  – Taiwan: only for IFN+ ribavirin failures with F3
  – China: for those with state insurance 60% reimbursement
  – HK: for patients with F2 (prisoners not included)
The 3 public health issues

2. Access to treatment

"The number of low- and middle-income countries with a scaled-up response is limited...Global fund to fight AIDS, TB and malaria does not provide for viral hepatitis”

The 3 public health issues

3. Sustainability of funding
   • Reducing the price of diagnostics and drugs
   • Global funding?
The 3 most difficult problems
The 3 Most Difficult Problems

1. Identification of cases
   - According to WHO Global Report 2017, only 9% of the 257 millions of HBV carriers and 20% of the 71 millions of HCV carriers know their Dx
   - The estimations of global carrier rates are dependent on population surveys. Data often obtained through extrapolation. Under-estimations are to be expected
2. Reluctance to seek medical advice

• What are the percentages of known carriers who have sought medical advice and have preliminary blood tests?

• This applies also to non-high risk groups. HCV carriage is asymptomatic until the late stages
3. Patient compliance

- Drug compliance, even for the 8-12 course of DAAs for HCV, need strong doctor-patient relationship, which may be difficult especially in low income countries.

- Compliance to life-long 6 monthly ultrasonography
Conclusions
Conclusions

Global incidence
New infections
Effects of globalization
Prevention of new infections

71 million
Increasing because of unsafe injections
Transmission of rare genotypes
1.75 million new infections (2015):
IVDUs, re-used syringes
Conclusions

• Problems with existing carriers of HCV
  - access to testing
  - access to treatment
  - Sustainability
  - identification of cases
  - reluctance to seek medical advice
  - patient compliance

  Likely to be persistent

  Dependent on country &
  global efforts
Thank you!