Local HCV epidemiology & DAA data

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Queen Elizabeth Hospital, Hong Kong
**WHO goal of HCV elimination...**

<table>
<thead>
<tr>
<th>Metric</th>
<th>By 2020</th>
<th>By 2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>30%</td>
<td>90%</td>
</tr>
<tr>
<td>Rx rate</td>
<td>3 million</td>
<td>80%</td>
</tr>
<tr>
<td>Mortality</td>
<td>10% ↓</td>
<td>65% ↓</td>
</tr>
</tbody>
</table>

*WHO Global Health Sector Strategy on viral hepatitis, 2016 – 2021*
Hong Kong HCV Registry

HKASLD Research Grant (ultimate sponsor - AbbVie Limited)

Timeline

- Aug 2015  Send invitation to all clusters
- Apr 2016  REC approval completed
- May 2016  Start data collection
- May 2019  End of data collection
Method

- Territory-wide retrospective review
- **12 years data** (Jan 2005 to Mar 2017)
- All anti-HCV+ patients within HA
- Divided into 2 parts
  1. Epidemiology
  2. Real-life DAA data (in progress)
<table>
<thead>
<tr>
<th>Clusters</th>
<th>15 Hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hong Kong East</td>
<td>Pamela Youde Nethersole Eastern Hospital</td>
</tr>
<tr>
<td>Hong Kong West</td>
<td>Queen Mary Hospital</td>
</tr>
<tr>
<td>Kowloon Central</td>
<td>Queen Elizabeth Hospital</td>
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<tr>
<td>Kowloon East</td>
<td>Tseung Kwan O Hospital</td>
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<tr>
<td></td>
<td>United Christian Hospital</td>
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<tr>
<td>Kowloon West</td>
<td>Caritas Medical Centre</td>
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<td></td>
<td>Kwong Wah Hospital</td>
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<td>Our Lady of Maryknoll Hospital</td>
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<td>Princess Margaret Hospital</td>
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<td>Yan Chai Hospital</td>
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<tr>
<td>New Territories East</td>
<td>Alice Ho Miu Ling Nethersole Hospital</td>
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<tr>
<td></td>
<td>North District Hospital</td>
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<tr>
<td></td>
<td>Prince of Wales Hospital</td>
</tr>
<tr>
<td>New Territories West</td>
<td>Pok Oi Hospital</td>
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<tr>
<td></td>
<td>Tuen Mun Hospital</td>
</tr>
</tbody>
</table>
1. Epidemiology of 15 Major Regional Hospitals
Our diagnosis rate is **57.6%**

1. Whole HA
   - 12747 anti-HCV+ patients
   - Diagnosis rate = **57.6%** (assume 0.3% prevalence in HK)

2. Within 15 participating hospitals
   - 11309 anti-HCV+ patients (88.7% of HA)
   - Chinese (91.4%), Pakistan (1.1%), Vietnamese (0.8%), Nepalese (0.5%), Indian (0.4%)
   - Public assistance (29.5%)
Our HCV are ageing with significant diseases

• 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%
Our predominant genotypes are 1b and 6

Available in 2397 patients

- G1 (50.4%) - 1b 95.7% 1a 4.3%
- G6 (35.2%)
- G3 (10.9%)
- G2 (3.4%)
Genotype predominance in other groups

Ethnicity
- Pakistan, Indian, Napelese – 3, 1
- Vietnamese – 6, 1

Special populations
- People who inject drugs (PWID) – G6 (43%), G1b (38%)
- HIV – G1 (43%), G3 (35%), G6 (14%)
Mostly acquired through PWID & Transfusion

- People who injects drug (PWID): 36.7%
- Transfusion: 30.0%
- Unknown: 27.2%
- Unsafe sexual practice: 1.9%
- Tattoo: 1.4%
- Body piercing: 1.4%
- Organ transplant: 1.1%
- Maternal: 0.1%
- Needle-stick: 0.1%

Total: 66.7%
Diabetes is commonest extra-hepatic manifestations

- DM 23.6%
- Autoimmunity 1.7%
- Cryoglobulinaemia 0.5%
- Non-Hodgkin’s lymphoma 0.4%
- MPGN 0.3%
- Vasculitis 0.1%
- Porphyria cutanea tarda 0.1%

Total extra-hepatic manifestations: 3.2%
Special populations

- **HBV co-infection** (7.8%)
- **Renal impairment** (eGFR <30 = 7.1%)
- HIV co-infection (1.4%)
- Hemophilia (0.8%)
- Cooley’s anemia and Hemoglobin H disease (0.8%)
- Organ transplantation (kidney 1.0%, liver 0.9%)
Our treatment rate is **24.3%**

N = 2201

- PegInterferon Ribavirin (2061)
- Ombitasvir/Paritaprevir/Dasabuvir (116)
- Boceprevir triple therapy (54)
- Ledipasvir/Sofosbuvir (37)
- Sofosbuvir-based therapy (23)
- Daclastavir/Asunaprevir (7)

~ 10% treated by DAA

*From Jan 2005 to Mar 2017*
Many subgroups have low treatment rates

<table>
<thead>
<tr>
<th>Sub-groups</th>
<th>Overall Rx uptake (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassemia major</td>
<td>85.7</td>
</tr>
<tr>
<td>Hemophilia</td>
<td>50.0</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>49.4</td>
</tr>
<tr>
<td>HIV</td>
<td>38.0</td>
</tr>
<tr>
<td>HCC</td>
<td>33.1</td>
</tr>
<tr>
<td>PWID</td>
<td>27.4</td>
</tr>
<tr>
<td>Dialysis</td>
<td>17.2</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>16.7</td>
</tr>
<tr>
<td>Age &gt;= 70</td>
<td>13.9</td>
</tr>
</tbody>
</table>
Our diagnosis and treatment rate are not bad

HK
Dx rate 57.6%
Rx rate 24.3%

Australia
2016 Rx rate ~17%

GJ Dore et al. J Viral Hep 2014
Mortality is rising despite HCV treatment

26% mortality were liver-related
Estimated disease burden within HA < 6000 pts

1. Within 15 hospitals
   A. Viremic cases ~ 11309 x 80% = 9047
   B. Patients treated (no. x genotype prevalence x SVR) = 1604
   C. Untreated cases (A - B) = 7443
   D. Alive untreated cases = C x (1 – 30.6% mortality) = 5165

2. Alive untreated cases within whole HA (D ÷ 88.7%) = 5823
PEG-IFN/R quite effective but not the solution to HCV elimination

- Overall SVR 74.8%
- Contra-indicated 33.5%; Refused treatment 35.7%
- Premature termination 28.5% (83.4% AEs, 16.6% non-responder)
- Not effective in many subgroups
PR is not very effective in many subgroups

<table>
<thead>
<tr>
<th>Genotype</th>
<th>SVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>88.9</td>
</tr>
<tr>
<td>6</td>
<td>87.9</td>
</tr>
<tr>
<td>2</td>
<td>77.8</td>
</tr>
<tr>
<td>1b</td>
<td>63.9</td>
</tr>
<tr>
<td>1a</td>
<td>50.0</td>
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</table>

<table>
<thead>
<tr>
<th>Sub-groups</th>
<th>SVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWID</td>
<td>86.0</td>
</tr>
<tr>
<td>Age &lt; 60</td>
<td>80.0</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>75.8</td>
</tr>
<tr>
<td>Age &gt;= 60</td>
<td>65.3</td>
</tr>
<tr>
<td>HIV</td>
<td>61.5</td>
</tr>
<tr>
<td>Hemophilia</td>
<td>50.0</td>
</tr>
<tr>
<td>HCC</td>
<td>50.0</td>
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Suboptimal SVR
2. DAA real-life data (interim analysis)
DAA-treated patients with SVR data

N = 86

• Ombitasvir/ Paritaprevir/ Dasabuvir (40)
• Sofosbuvir-based therapy (32)
• Boceprevir (14)

As of Sept 2017
Results of Boceprevir are **POOR**

- Null-responder 50.0%, partial responder 35.7%, Rx failure 14.3%
- Premature termination **36.4%** (60% futility rule, 20% AEs)
- Overall SVR **30.8%**
IFN-free DAA has excellent real-life efficacy

- 56.8% IFN-experienced; 45.9% cirrhosis
- G1b (63.4%), G1a (12.2%), G6 (8.5%), G3 (4.9%), G2 (2.8%)
- 2 treatment failures:
  - G1a cirrhosis TE HIV hemophilia – SOF/LED/R 12 wks
  - G1b TN – SOF/R 24 wks
- Overall SVR12 = 97.3% (G1a 90%, G1b 97.6%, G2, 3, 6 = 100%)
Ombitasvir/ Paritaprevir/ Dasabuvir (N=40)

Overall SVR 100%

TN – Rx naïve
TE – Rx experienced

SVR12 (%)

G1a
(Cirrhosis = 3)

G1b
(Cirrhosis = 16)

TN  TE  TN  TE

3/3  7/7  11/11  19/19

100  100  100  100
Sofosbuvir / Ledipasvir (N=14)

Overall SVR 92.9%

SVR12 (%)

<table>
<thead>
<tr>
<th></th>
<th>TN</th>
<th>TE</th>
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<tbody>
<tr>
<td>G1a</td>
<td>2/6</td>
<td>2/6</td>
</tr>
<tr>
<td>G1b</td>
<td>3/6</td>
<td>3/3</td>
</tr>
<tr>
<td>G6</td>
<td>3/3</td>
<td>3/3</td>
</tr>
</tbody>
</table>

TN – Rx naïve
TE – Rx experienced

(Cirrhosis = 1)
(Cirrhosis = 5)
(Cirrhosis = 0)
Sofosbuvir / PEG-IFN / Ribavirin (N=4)

Overall SVR 100%

SVR12 (%)

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<thead>
<tr>
<th></th>
<th>TN</th>
<th>TE</th>
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<tbody>
<tr>
<td>G2</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>G3</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>G6</td>
<td>1/1</td>
<td>1/1</td>
</tr>
</tbody>
</table>

TN – Rx naïve
TE – Rx experienced
Sofosbuvir / Ribavirin (N=14)

Overall SVR 92.9%

- **Overall SVR**
  - TN – Rx naïve
  - TE – Rx experienced

<table>
<thead>
<tr>
<th>Cirrhosis</th>
<th>TN</th>
<th>TE</th>
<th>TN</th>
<th>TE</th>
<th>TN</th>
<th>TE</th>
<th>TN</th>
<th>TE</th>
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<tbody>
<tr>
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SVR12 (%)
DAA is highly effective across all subgroups

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<td>100</td>
</tr>
<tr>
<td>PWID</td>
<td>100</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>100</td>
</tr>
<tr>
<td>Age &lt; 60</td>
<td>98</td>
</tr>
<tr>
<td>Post-transfusion</td>
<td>97.6</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>96.4</td>
</tr>
<tr>
<td>Age &gt;= 60</td>
<td>95.7</td>
</tr>
<tr>
<td>HIV</td>
<td>91.7</td>
</tr>
<tr>
<td>Hemophilia</td>
<td>88.9</td>
</tr>
</tbody>
</table>
IFN-free DAA is well tolerated

- Malaise 20%
- Skin rash 6.5%
- Nausea 4.8%
- Insomnia 4.8%
- Grade 3, 4 ↑ ALT 3.2%
- Premature termination 1.4% (1 patient)
HK has the potential to eliminate HCV in 2030

- Low disease burden
- Better diagnosis and treatment rate
- DAA susceptible genotypes - 1b & 6 (83.4%)
- Excellent DAA real-life efficacy
What do we need to do before 2030?

1. **Improve diagnosis rate**
   (targeted screening of at-risk populations)

2. **Improve treatment access**
   (advanced diseases, low Rx uptake groups, viral transmitters)
To achieved the goal, we need potent, well-tolerated treatment.
Prof. Sophia Chan, JP  
Secretary for Food and Health  
18/F, East Wing, Central Government Offices  
2 Tim Mei Avenue, Tamar  
Hong Kong  

Dear Prof. Chan,  

An opportunity to eliminate hepatitis C virus from Hong Kong  

Background  
Hepatitis C virus (HCV) infection is one of the leading chronic liver diseases worldwide. Left untreated, around a quarter of infected patients may eventually die from liver cancer or end-stage liver disease. In the past, the standard treatment for chronic hepatitis C was peginterferon-alfa plus ribavirin, which carries numerous side effects and has a low treatment success rate of 50-70%. In recent years, the development of direct-acting antivirals (DAAs) has transformed clinical practice. A 12-week course of oral DAA therapy can cure HCV in over 95% of cases with minimal side effects. As a result, both the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver recommend DAA as first-line treatment for chronic hepatitis C.
Disease Prevention and Control

- Set up a steering committee to formulate strategies to effectively prevent and control viral hepatitis. The steering committee will review local and international trends and developments in the prevention and control of viral hepatitis; advise the Government on policies and cost-effective targeted strategies for prevention and control of viral hepatitis; and conduct and co-ordinate the surveillance and evaluation of viral hepatitis control and recommend appropriate response. (FHB) (New Initiative)
Acknowledgement

Prince of Wales Hospital - GLH Wong, SD Liu, K Liu, S Cheung, HLY Chan, VWS Wong

Tuen Mun Hospital - YK Ma, W Yau, KL Lui, K Lee, KK Li

Queen Elizabeth Hospital - WY Mak, JTW Lam

Princess Margaret Hospital - J Chan, K Lam, WF Luk, OTY Tsang

United Christian Hospital - KB Lai, KN Kung

Kwong Wah Hospital - CK Loo, YH Ho, YM Kan

Caritas Medical Centre - A Ng, E Shan, R Tong, YK Chan

Queen Mary Hospital - DYK But, JYY Fung, MF Yuen

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Pok Oi Hospital - CY Lam, LSW Lai

Our Lady of Maryknoll Hospital - WI Cheung