



Elimination of Hepatitis C Virus

What PE Evaluation Can Do?

Shanlian Hu. MD. MSc. Professor

School of Public Health, Fudan University

Shanghai Health Development Research Center

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Outlines



Anti-Hepatitis B Drugs



Anti-Hepatitis C Drugs



Policy Suggestion

Background

- More than 185 million people around the world infected with HCV (WHO, 2014)
- Elimination of viral hepatitis is a global strategy by the year of 2030, the incidence rate will reduce 90%
- In 2015, China reported:

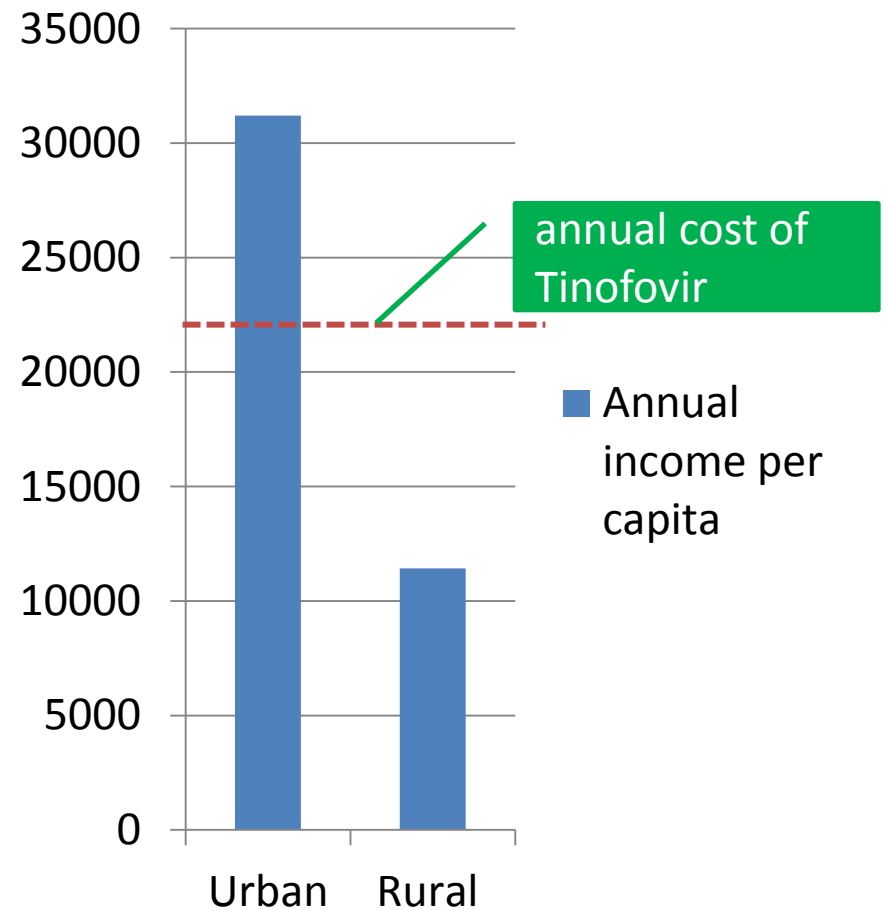
Hepatitis A	22,000 cases
Chronic hepatitis B	28 million cases
Chronic hepatitis C	8.85 million cases
Hepatitis E	27,000 cases
HBsAg carriers	74.6 million
HB vaccination rate	95%
- 56.8% gene of hepatitis C in China are 1b type

Price Negotiation in China in 2016

Drugs	Diseases	Pharma Co.	Cost per month (RMB)	Negotiation Price (RMB)	Price Reduction (%)
Gifinib (Iressa) 25mg x21	NSCLC	AstraZeneca	15,000	7000	55
Erlotinib (Tavceva)	NSCLC	Roche	19,000		
Icotinib (Conmana) 0.25mg x 10	NSCLC	Zhejiang Betta	12,000	5500	54
Tinofovir (Viread) 300mg X 30	Hepatitis B	Glaxo Smith Kline	1470	490	67
Lenalidomide (Revlimid)	Multiple myeloma	Celgene			

The Cost of Tenofovir

- The monthly cost of Tenofovir after negotiation is ¥1470 (RMB)
- The annual cost of Tenofovir is ¥ 22,464 (RMB)



Calculation of Incremental Cost-Effectiveness Ratio Under MET

- Most efficacious treatment (MET)

$$ICER_{MET} = \frac{(\text{Cost}_{MET} - \text{Cost}_{\text{Other antivirus drugs}})}{(\text{LYS/QALY}_{MET} - \text{LYS/QALY}_{\text{Other antivirus drugs}})}$$

- Tenofovir vs Lamivudine

$$ICER_{MET} \text{ LYS} = (87615 - 87134) / (18.39 - 17.65) = 481 / 0.74 = 650$$

$$ICER_{MET} \text{ QALY} = (87615 - 87134) / (15.43 - 14.67) = 481 / 0.76 = 633$$

ICER Value in Different Treatment of Anti-Virus Drugs on HBV HBeAg(+)

	Tinofovir (TDF)	Entecavir (ENT)	Telbivudine (TEL)	Adefovir (ADV)	Lamivudine (LAM)
Annual treatment costs (\$)	87615	90273	90721	91199	87134
Life Year Saving (LYS)	18.39	18.18	17.94	17.67	17.65
QALY	15.43	15.21	14.96	14.68	14.67
ICER(LYS)	4764.3	4965.5	5056.9	5161.2	4936.8
ICER(QALY)	5678.2	5935.1	6064.2	6212.5	5939.6

(Darkin H et al: Pharmacoeconomics 29(12): 1075-1091, 2011)

Tenofovir Reduced Price in Different MIs at Provincial Level

Drug	URBMI/ EBMI	RCMS	Catastrophic MI
Tenofovir (Viread)	Xinjiang	Yunnan, Hainan, Guangxi, Liaoning, Jiangxi Guizhou, Helongjiang, Jiangsu, Beijing, Sichuan, Xinjiang, Jilin, Gansu, Henan	Yunnan, Hainan, Liaoning, Jiangxi, Jiangsu, Jilin
Icotinib (Conmana)	Xinjiang, Neimongguo Zhejiang	Yunnan, Hainan, Guangxi, Liaoning, Jiangxi, Jilin, Helongjiang, Guizhou, Beijing, Xinjiang, Zhejiang	Yunnan, Hainan, Liaoning, Jiangxi, Jiangsu, Hunan, Jilin, Henan
Gifinib (Iressa)	Xinjiang, Neimongguo Helongjiang Xizhuang	Yunnan, Hainan, Guangxi, Liaoning, Guizhou, Helongjiang, Beijing, Xinjiang, Qinghai, Ningxia, Jilin	

URBMI = Urban resident basic medical insurance

EBMI = Employee basic medical insurance

RCMS = Rural cooperative medical system

Catastrophic MI = Catastrophic illness medical insurance

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Icotinib (Conmana)	Xinjiang, Neimongguo Zhejiang 3	Yunnan, Hainan, Guangxi, Liaoning, Jiangxi, Jilin Helongjiang, Guizhou, Beijing, Xinjiang, Zhejiang 11	Yunnan, Hainan, Liaoning, Jiangxi, Jiangsu, Hunan Jilin, Henan 8
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The Barrier of Price Negotiation Implementation in China

Provider side

- Pricing strategies (off-patent, generics competition, price-volume agreement)
- Price reduction and market access
- Accepted by MoHRSS's drug reimbursement list
- Establishing a special financial account, those revenue of negotiated drugs could not account in the proportion of pharmaceutical revenue in hospitals (<30%)

Demand side

- Release the economic burden of patients who use the patent and innovative drugs
- Depend on the attitude of different stakeholders
- Purchasing from national drug supply information platform
- Conducting patient registry and clinical guideline

Outlines



Anti-Hepatitis B Drugs



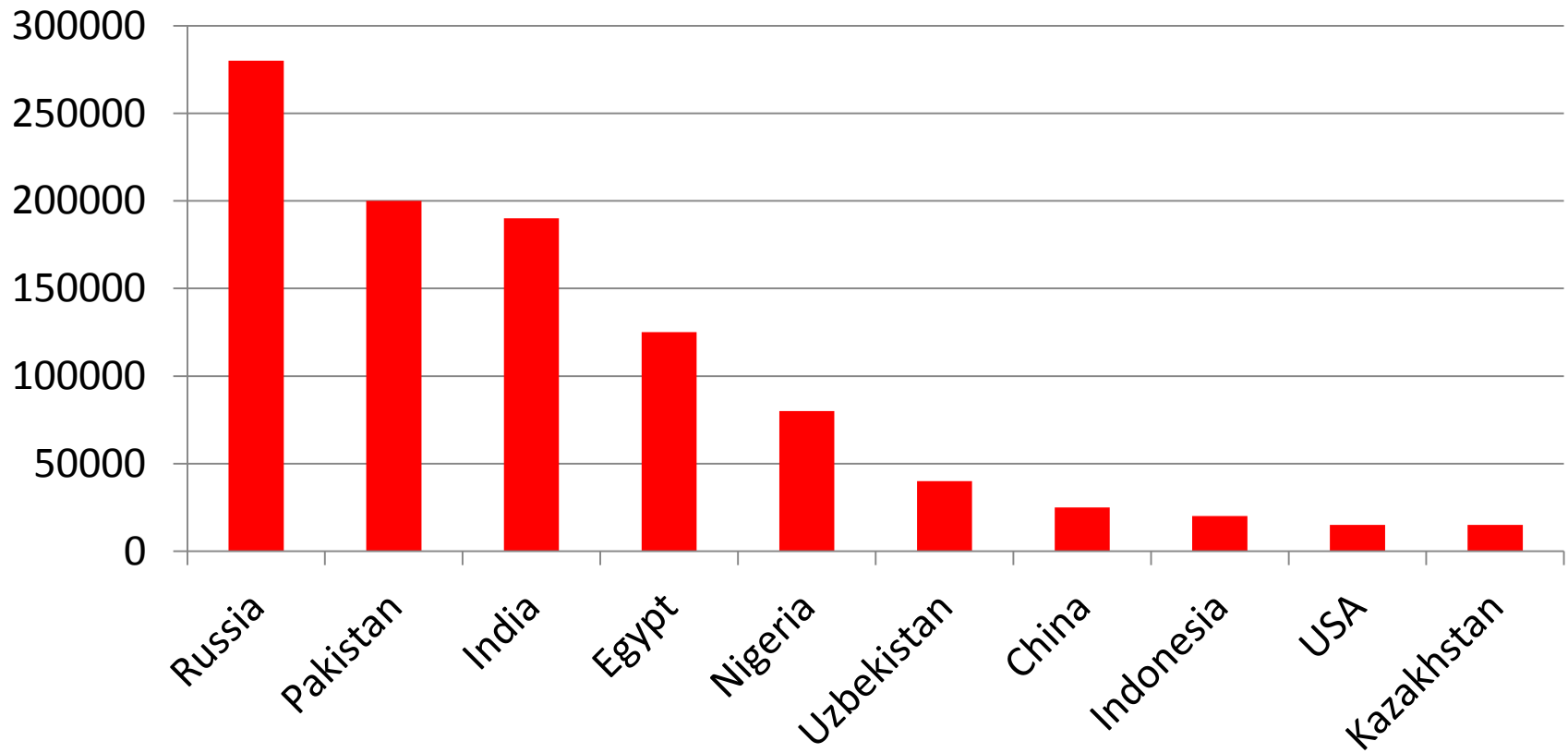
Anti-Hepatitis C Drugs



Policy Suggestion

Top 10 Countries with the Highest New HCV Infections in 2015

No. of cases



<http://www.polarisobservatory.com>

Sufferers of Hepatitis C Await Cure

- China has nearly 10 million hepatitis C sufferers but only about 1% of them have ever received treatment
- WHO estimated 400,000 people died each year in China from hepatitis-related complications. The global target is to treat at least 80% of HC patients by 2030
- The most effective medicines, direct-acting antivirals that cure hepatitis C are available globally, except in China
- The medicine costs > \$50,000 in US and \$1,000 in India to cure the patient due to a tiered pricing

HCV Treatment Landscape

- Landscape of HCV treatment is changing from traditional interferon-based therapies to oral interferon-free direct acting agents (DAAs)
- DAAs have shorter durations, minimal side effects and cure rates approaching 90-100%
- Comparator usually is the combined pegylated interferon and ribavirin (干扰素和利巴韦林联合用药), and cure rates were averaging between 40-50%, and associated with many side effects

Recent DAA Drug for HC

- Innovative HCV Treatments:
 - Sovaldi (索非布维)
 - Harvoni (哈维尼)
(Sofosbuvir/
Ledipasvir雷迪帕韦)
 - Daklinza (daklatasvir 达卡他韦)
 - Viekirax (维克瑞克斯)
(Ombitasvir 翁比他韦/
Pantaprevir 帕利瑞韦/
Ritonavir 利托那韦)
 - Exviera(达萨布韦dasabuvir)
- India will produce generic Epclusa (Sofosbuvir and Velpatasvir compound drug), no need to do gene test
- China Geli (歌礼) pharma reported using ASC08 +ASC16 to run the clinical trial



DAA Treatment in Asia

- Availability of DAAs in Asia is lagging behind of Western Countries
- DAAs pricing in Asia will vary widely given the diversity in epidemiology, economic priorities and reimbursement policies
- DAAs are more expensive and efficacious, but will have budget impact to the payer and choice among DAAs

PE Evaluation of Sofosbuvir (Sovaldi)

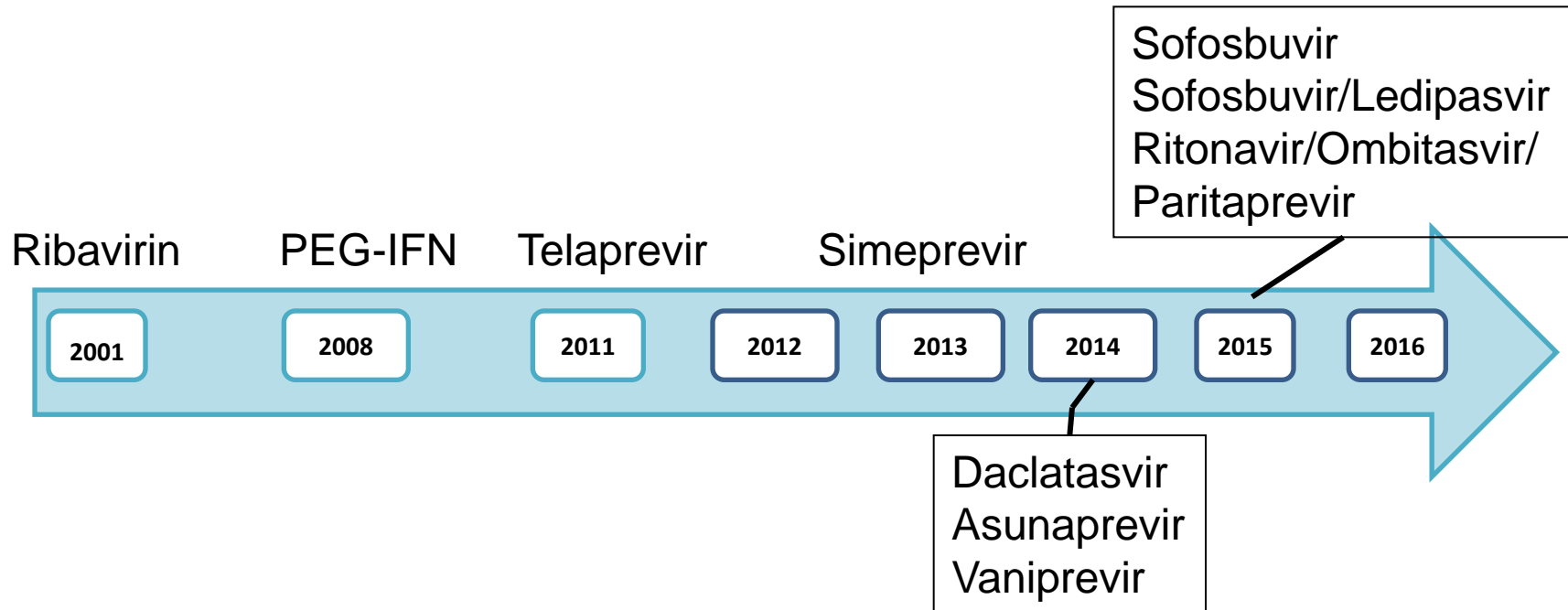
	France	Germany
Disease	Viral Hepatitis C	Viral Hepatitis C
HTA	ASMR II, ASMR III (genotype 3)	Except genotype 2
ICER	€ 5866-75518/QALY	
Price	€13667/#28	€16270 (not including VAT)
Price reduction	24%	10.75%
Reimbursement	100%	
Condition	Discount is kept under secret	

DAA Reimbursement Decision in Taiwan

	Harvoni Ledipasvir 90mg, sofosbuvir 400mg	Viekirax Ombitasvir 12.5mg 75mg {artota[revor. Ritonavir 50mg	Daklinza Daclatasvir 60mg
Daily dose	#1 qd	#2 qd + #1 bid	#1 qd + #1 bid
Duration	3 months	3 months	6 months
Cure rate (%)	94.99	91-100	82-92
Self pay cost/course	USD \$39,062	USD \$46,562 (+ Exvera Dasabuvir)	USD \$10,312 (+Sunvepra Asunaprevir)

- NHIA will negotiate drug cost/course, plans to have an independent budget for this category of drug treatment for ten year
- Treat 10,000 patients/year, budget: US\$ 80 million

DAAs Availability in Japan



Effect on Existing Drug Price in Japan

- Chuikyo 7 drugs subject to cost-effectiveness review, re-pricing will be conducted in 2018
- Prices forecast to drop by an average of 6.8% in April 2016, price cuts range from -0.1% to 53.2%
- Patent drugs are impacted: Sovaldi/Harvoni -31.7%; Xarelto/eliquis -28%; Apidra -16.3%; Tysabri -47%; Reyataz – 13.9%

(Floriane Reinaud: Principal Analyst. HIS Life Sciences)

Chronic Hepatitis C Data from Two Real-World Population-based Studies in Japan

	Medical Data Vision (MDV)	Japan Medical Data Center (JMDC)
Data source	Administrative data from 242 acute care hospitals (15%) and 13.93 million patients	Employer-based health insurance claims
No. of CHC cases	29702	3950
Age	63.2 ± 13.4	51.6 ± 11.9
Charlson co-morbidity index (CCI score)	1.9 ± 2.1	1.3 ± 1.7
No. cases treated with Interferon & DAAs	1620 (5.5%)	365 (10.2%)

- Both databases showed low treatment rates for CHC
 - Current treatment regimen 64-67% interferon, 25-27% DAA with telaprevir
- (Crawford B: 2014)

Utility Score (QOL) for Various Health States for Hepatitis C

Health State	QOL Score	Data Source
Chronic hepatitis (Inactive)	0.876	EQ-5D-5L score from patient Study (N= 2875)
Chronic hepatitis (active)	0.821	
Compensated cirrhosis	0.737	
Decompensated cirrhosis	0.671	
HCC(I/II)	0.675	EQ-5D-5L score from HCC expert (N=3)
HCC (III/IV)	0.428	
Transplantation	0.651	

(Source: Hirao et al: MHLW 2014)

Cost-effectiveness of Sofosbuvir

Treatment option	Cost (JPY)	QALY	LY
Sof + RBV	8,460,000	28.76	25.82
IFN + RBV	4,520,000	27.00	23.64
Difference	+ 3,940,000	+1.76	+ 2.18

ICER: JPY 2.2MIL/QALY, JPY 1.8 MIL/LY

Hypothetical Threshold: JPY 5ML/QALY (USD 50,000)

ICER would get lower under reimbursement price JPY 5,000,000

(source: Igarashi et al, ISPOR EU 2014)

Results of Viekirax for Non-Cirrhosis Patients

Treatment IFN naive	Cost (JPY Mil)	QALY	LY	ICER
Veikirax	5.41	16.41	17.80	
DCV/ASV	4.44	15.83	17.40	1.68/QALY
No Treatment	7.76	11.34	14.24	Dominant
Treatment IFN treat	Cost (JPY Mil)	QALY	LY	ICER
Veikirax	5.32	16.22	17.58	
DCV/ASV	4.30	15.66	17.20	1.84Mil/QALY
No Treatment	7.66	11.23	14.09	Dominant

(Source: Virabhak et al. JME 2016)

Selected Drugs among Existing Ones

Target		
Cost-markup	Sales	Opdivo (melanoma, Lung Cancer) Kadcyla (Breast cancer)
	Premium	
Similar Drug Comparison	Sales	Sovaldil (Hepatitis C) Harvoni Viekirax Daklinza/Sunypepra
	Premium	

Reducing Price of DAA in France

- France conducts progressive contribution scheme to ensure the access of PAA in HC patients
- The expenditure for paying Sovaldi was €450 millions in 2014, the threshold was increased to €700 millions in 2015, if the sale value is beyond the threshold, Gilrad Co. will be charged by selected taxation
- France has 200,000 HC cases, the treatment cost will be reached to one billion Euro
- The cost of Sovaldi is €56,000 (\$84,000) in 12-week course

Reducing Price of DAA in USA

- The high price of Harvoni is \$94,500 per non-cirrhosis HC patient in 12-week treatment course in USA
- 45% patient only require 8 week treatment, the cost is \$63,000
- Several measurements have been taken by different states in US, such as pre-approval & review by PBM, liver biopsy in advance, prescribed by specialist, hepatologist and GE doctors b

Policy Suggestion

- The Path to Zero programme is advocated by WHO to address better understand the challenges of elimination of HCV
- Hepatitis C viruses will cause liver cirrhosis and liver cancer, DAAs should be used appropriateness
- DAAs should be widely used in China and put into EML and RML, their price could be reduced through negotiation



***Thank You for
Your Attention***