Interferon Treatment in Hepatitis C: Necessary or Not in Future Aspects?

The Asian-Pacific Viewpoint

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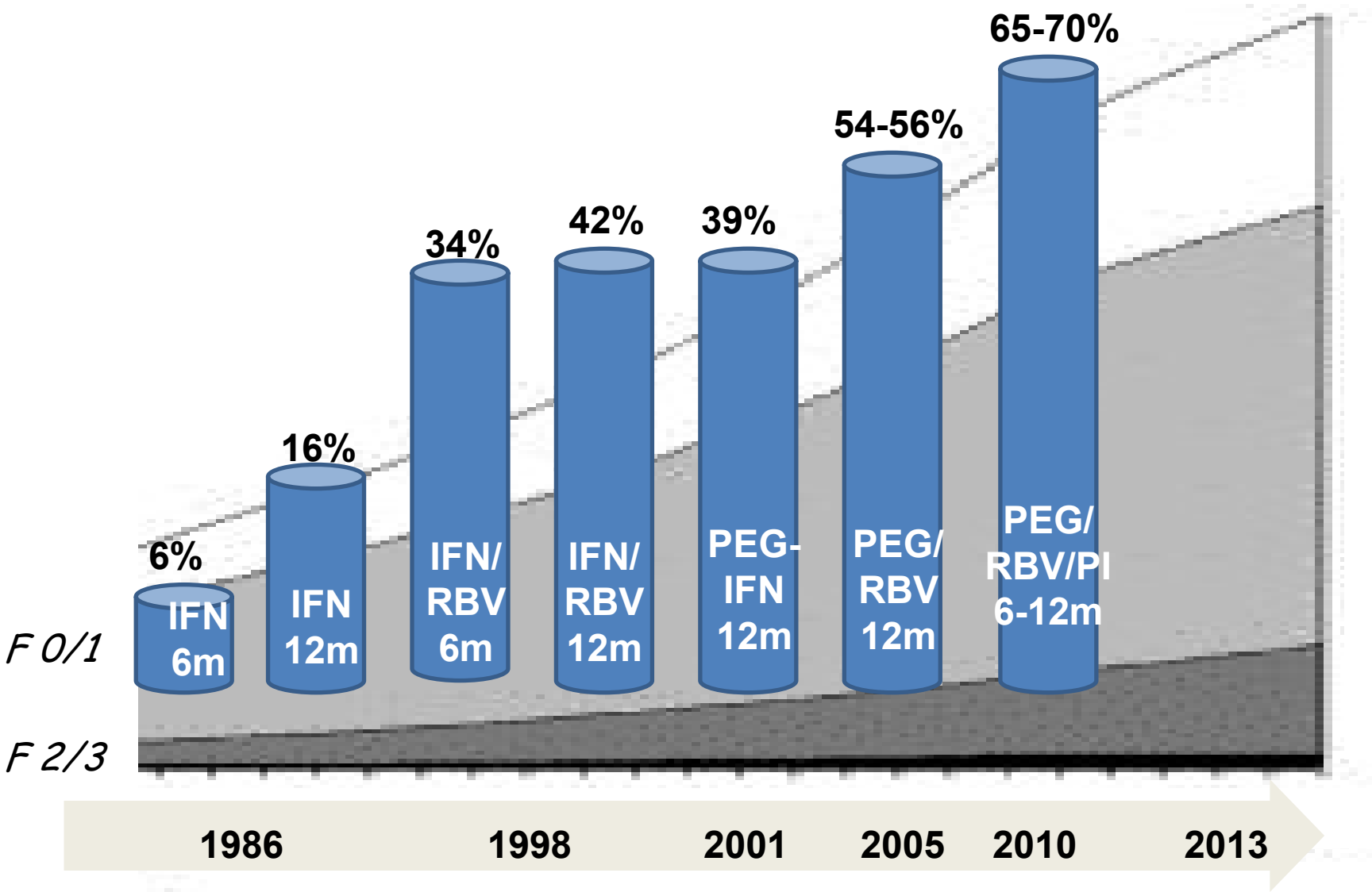
Interferon has been a good colleague for almost 30 years



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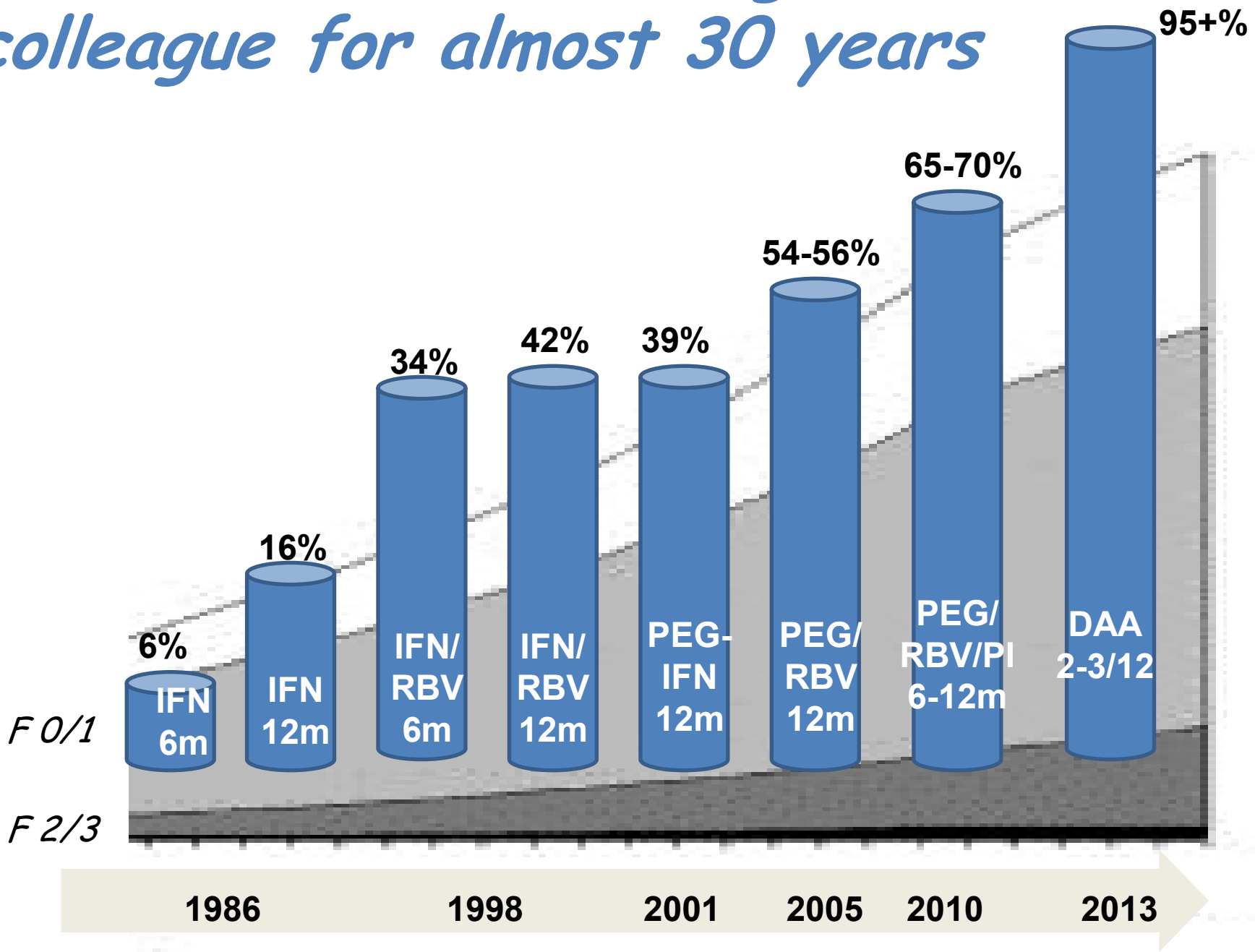


The Interferon Era: What was Gained?

- First antiviral therapy for hepatitis C
- Cured many patients of their liver disease, halted disease progression and markedly reduced risk of HCC in those patients with SVR
- Limited activity made others explore the role of additional antiviral agents eg ribavirin, or alter the characteristics of interferon via pegylation
- Better understanding of host and viral determinants of response and particularly the polymorphisms near IL28-B gene

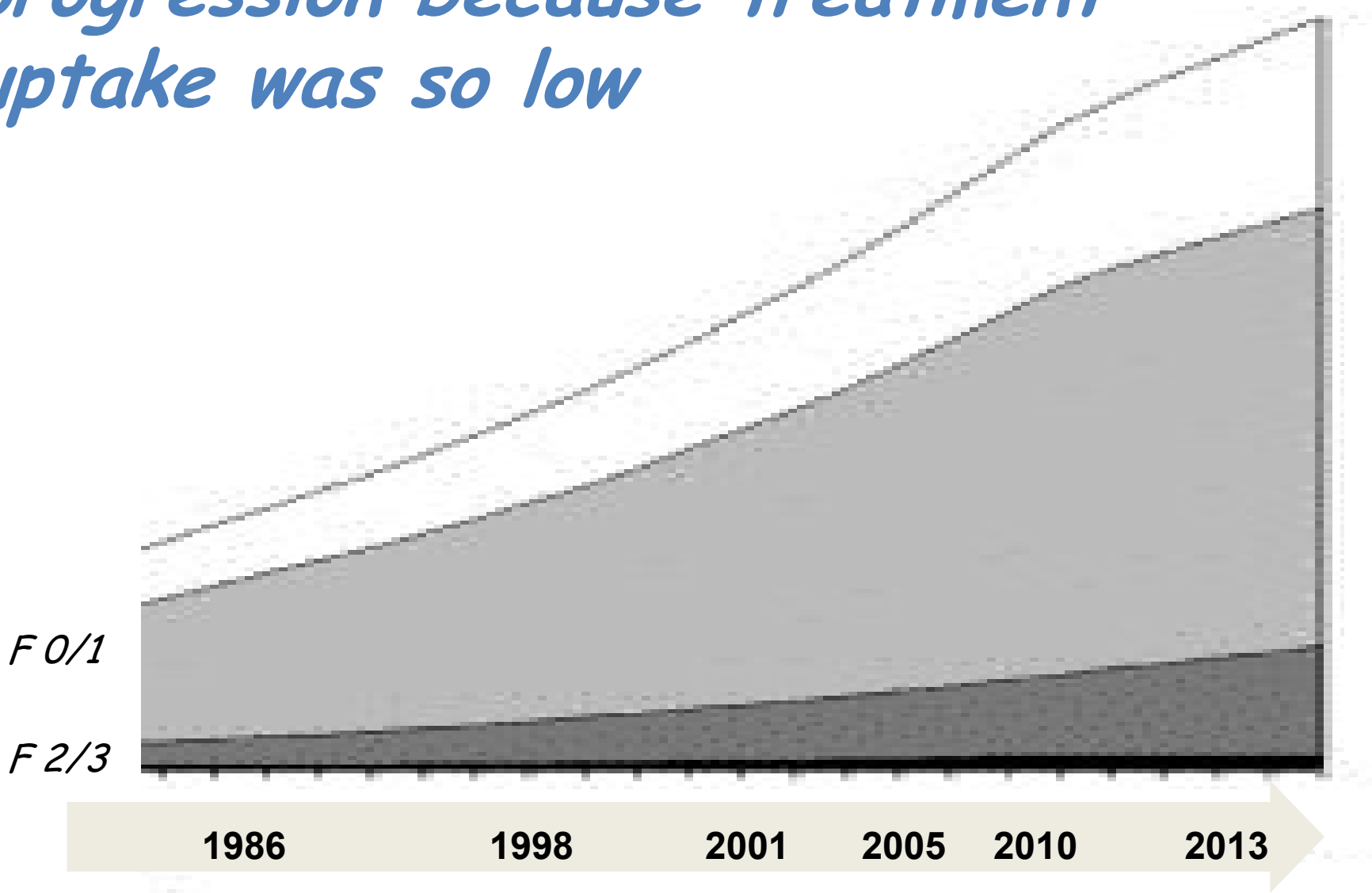
Down Sides to Interferon Therapy

- Low response rates
- Prolonged duration of therapy
- Infrastructure required for safe delivery of care
- Patient education
- Repeated clinic visits with intensive monitoring of patient well being, blood tests, and viral responses to optimise care
- Many patients in whom interferon was contraindicated, or were intolerant after treatment commenced
- Side effects virtually universal

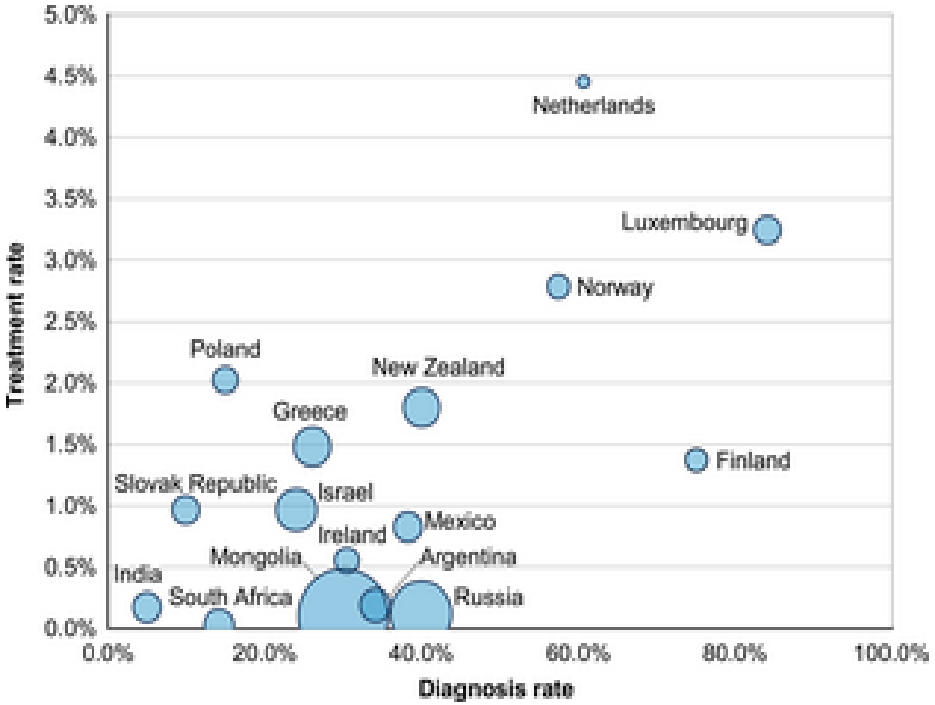
Downsides of Interferon Resulted in:

- Limited availability in areas of the world with limited health infrastructure
- Treatment limited to specialist centres
- Poor uptake of therapy in more affluent parts of the world
- Reluctance of many patients to come forward for therapy

Interferon had minimal effect on population rates of disease progression because treatment uptake was so low



Treatment Rate and Diagnosis Rate



Existing treatment rates only up to 4.5%, even when >60% of patients diagnosed

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Viral Eradication with Interferon Based Regimes was Never Going to Occur

But, DAAs Provide an Opportunity to Eradicate HCV

Inevitability About the Fate of Interferon

All Oral (Interferon Free)Therapies are Effective in Most HCV-Related Scenarios

- ✓ Treatment Naive – Genotype 1 - 6
- ✓ Treatment Experienced – Genotype 1 - 6
- ✓ Treatment Naive Compensated Cirrhosis
- ✓ Treatment Experienced Compensated Cirrhosis
- ✓ Decompensated Cirrhosis
- ✓ Pre and Post Liver Transplant
- ✓ HIV/HCV Co-Infection

On Increasing Access

- Increasing efficacy without increasing access to therapy means that the new treatments will not have any major impact on the disease burden of HCV

- Ease of all oral regimes eliminates some of the barriers to increasing access to care that were inherent in interferon-based treatments

Increase Access Within a Very Heterogeneous Region of the World

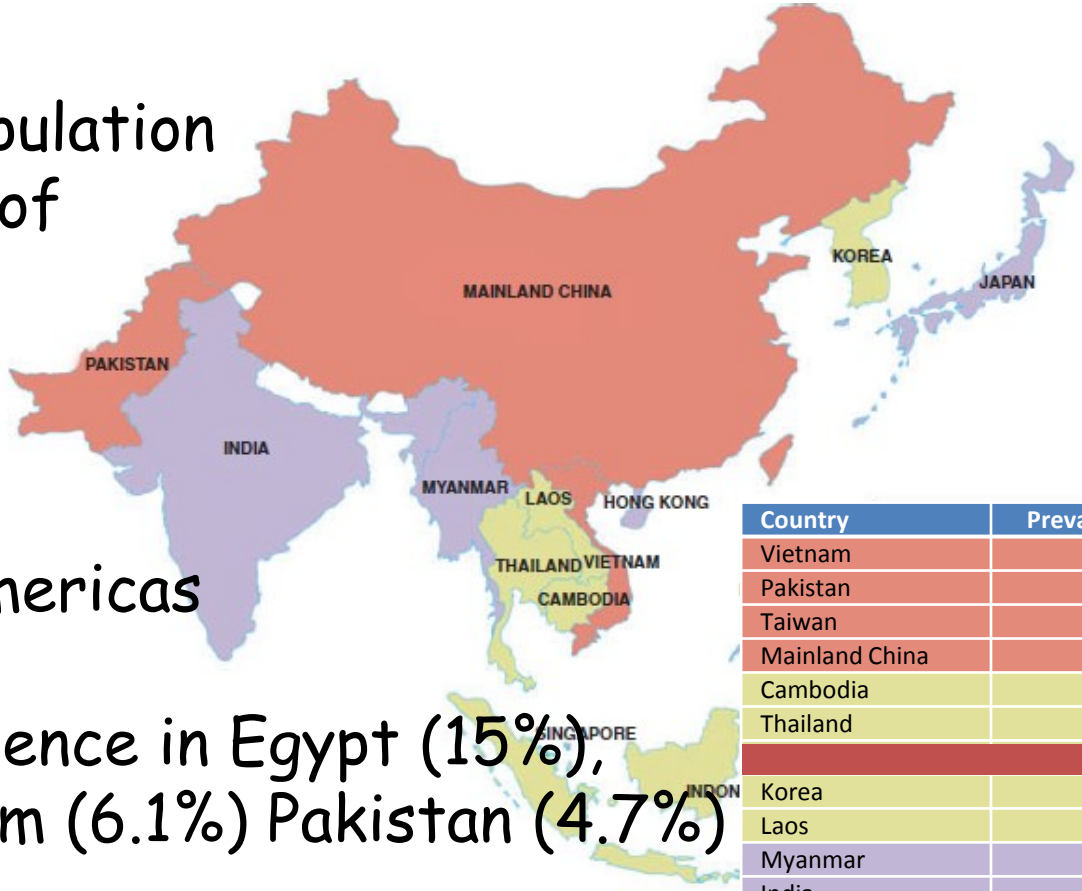
- Size and Population of Asian-Pacific Countries varies enormously:
  - 500,000 ⟶ 1.3 billion (China)
- Other countries with huge populations: India – 1.2 billion, Indonesia – 235 million
- 55 Official languages
- Gross Domestic Product (GDP) from $US 0.50 million in some countries to $US 8,000 million in others
- Nature of Health Care Systems varies

HCV prevalence across Asia Pacific: Disease Burden > 100 million

> 40% of the global population and largest population of HCV-infected persons

- China alone has more HCV infections than all of Europe or the Americas

- Especially high prevalence in Egypt (15%), Mongolia (10%), Vietnam (6.1%) Pakistan (4.7%) and Taiwan (4.4%)



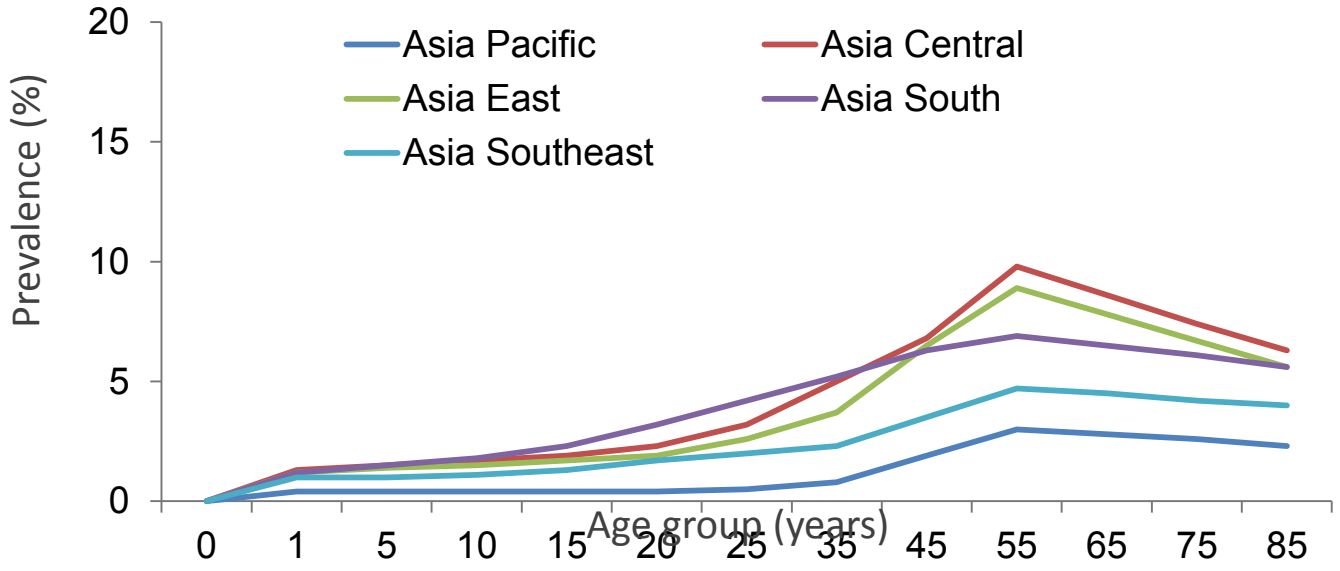
Country	Prevalence (%)
Vietnam	6.1
Pakistan	5.31
Taiwan	4.4
Mainland China	3.2
Cambodia	2.3
Thailand	2.2
Korea	1.3
Laos	1.1
Myanmar	0.95
India	0.87
Japan	0.49
Philippines	0.474
Singapore	0.37
Hong Kong	0.08

Nguyen LH, Nguyen MH. Aliment Pharmacol Ther 2013;37:921–36

Improving Access in this Environment

- Intervention, Policy Development and Policy Implementation by International Agencies
- Cooperation and Commitment of Governments at all Levels
- Supported by Pharmaceutical Industry (Gilead HCV Treatment Expansion Program)
- Plus, an improvement in Implementation of Primary Prevention Strategies

HCV prevalence rises with increasing age and peaks at age 55-64 in Asia



High prevalence in these age groups infers:

- More advanced disease and more urgency for therapies with better drugs to improve survival

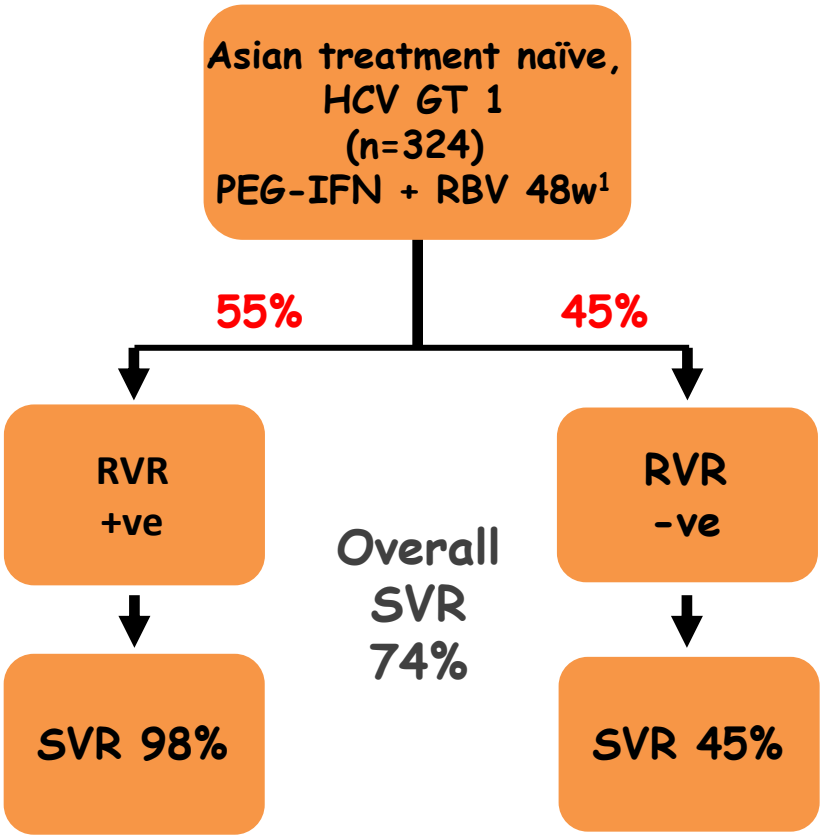
Hanafiah KM, et al. Hepatology 2013;57:1333–42

In the meantime: Squeeze out the last drop

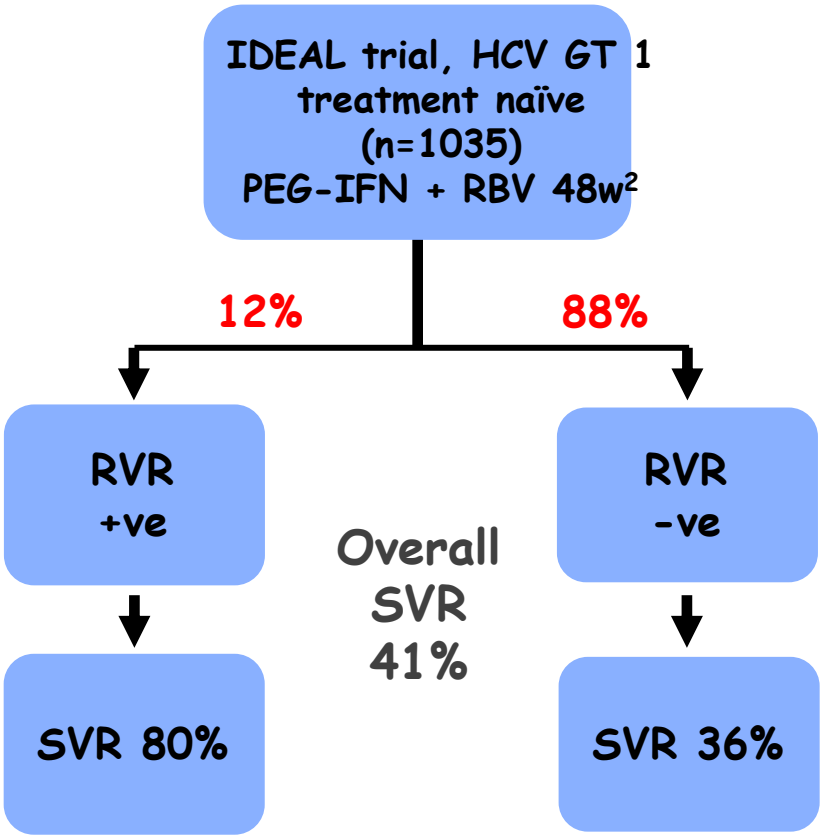
Five Issues Relevant to Asia Pacific that May Impact on Treatment Availability

- Cost
- Epidemiology of HCV in Asia Pacific: Should more funding go to primary prevention?
- Response of Asians to interferon-based therapies
- Genotype distribution
- Distribution of IL-28 B polymorphisms

Asians Respond Differently to Caucasians to Interferon Based Therapies



Ethnic mix: Asians 100%

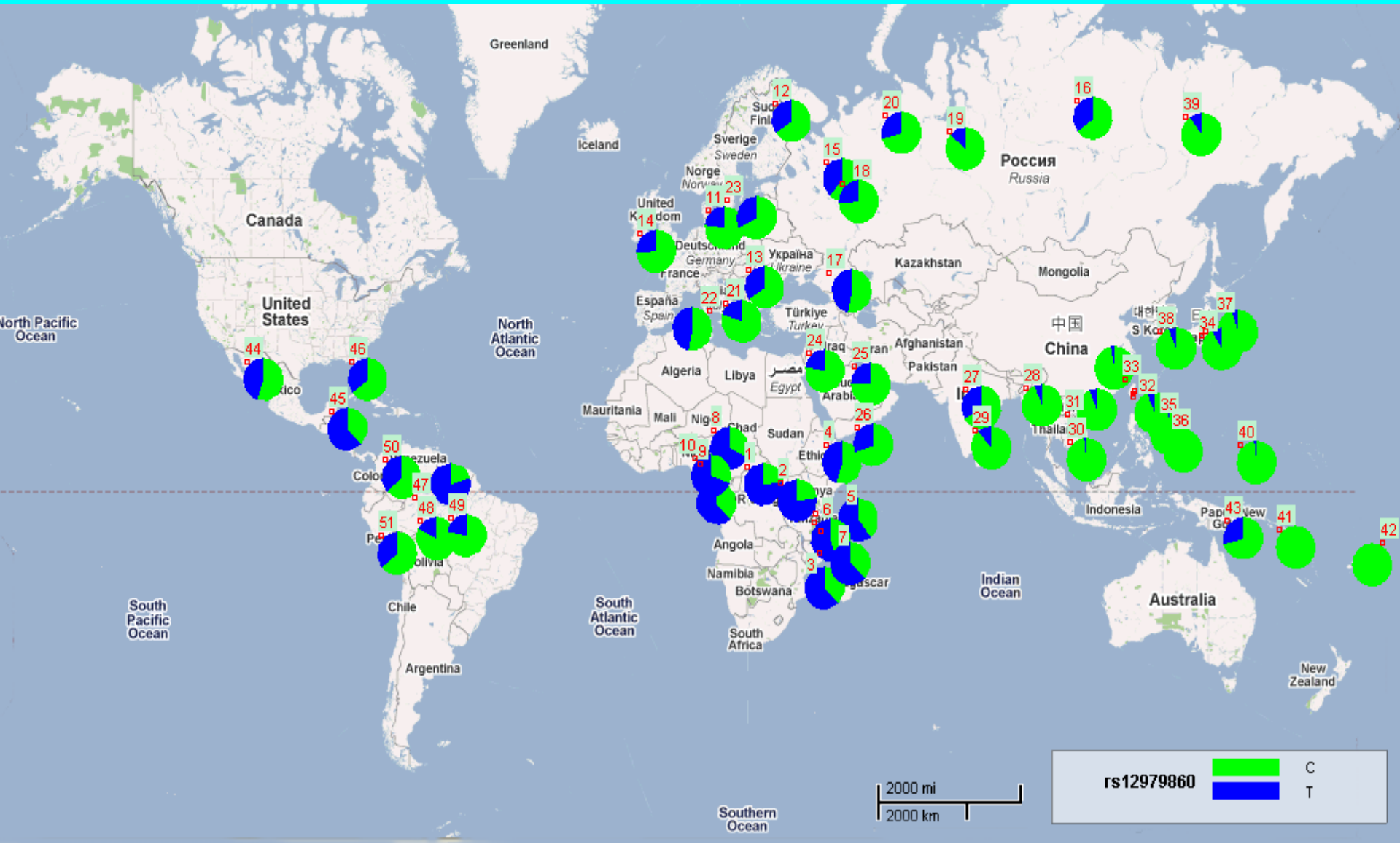


Ethnic mix: White 71%; Black 19%; Hispanic 6%, Asians 1–2%

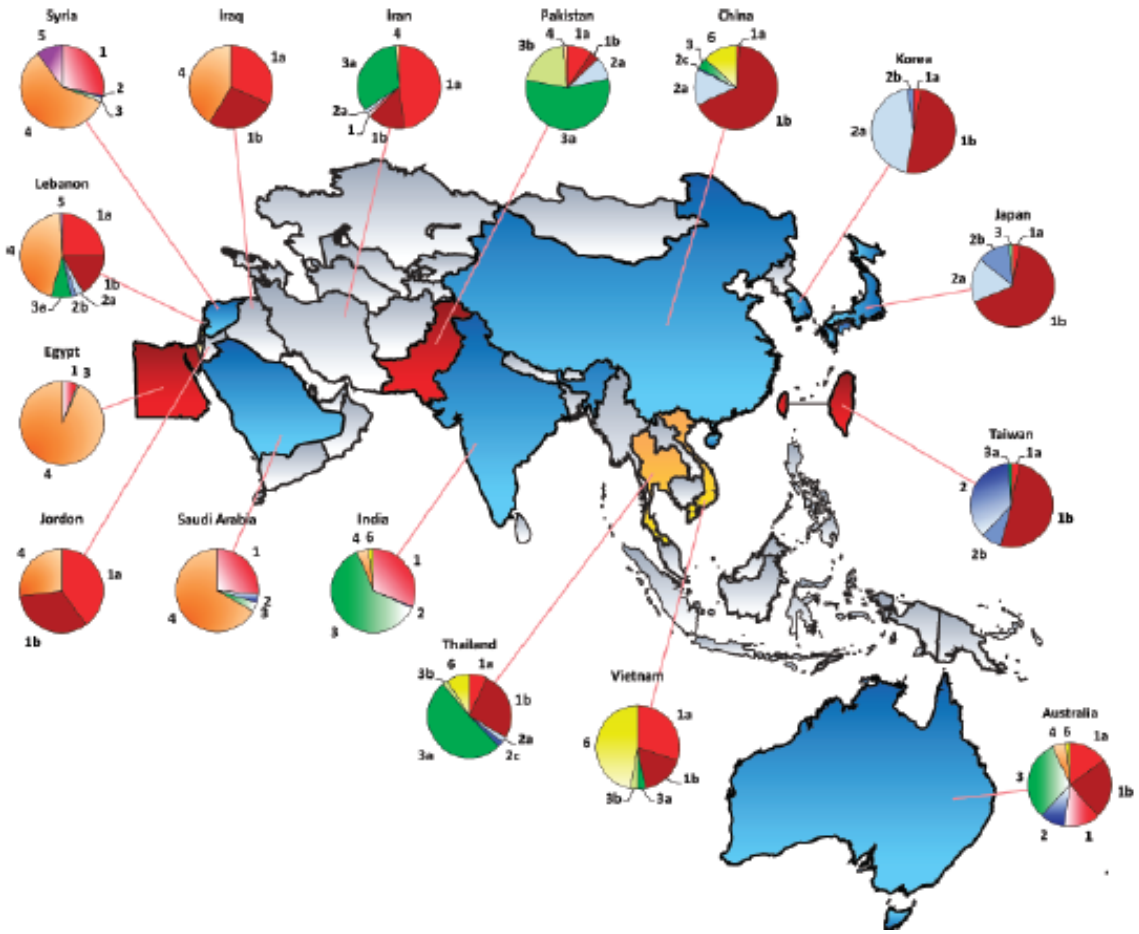
1. Liu C, et al. Antiviral Therapy 2012;17:477–84.

2. McHutchison JG, et al. N Engl J Med 2009:61:580–93.

The global prevalence of C/T alleles at SNP rs12979860 may explain the recognized geographical variation in SVR rates



HCV genotype distribution



- GT 1: Australia, China, Taiwan and North Asia
- GT 2: Japan, Korea and Taiwan
- GT 3: India and Pakistan
- GT 4: Egypt, Saudi Arabia and Syria
- GT 5: rare in Asia; small number in Syria
- GT 6: Vietnam and other Southeast Asian countries

All of the known genotypes have been documented

Sievert W, et al. Liver Int 2011;31(Suppl 2):61–80

GT: genotype

Conclusions

- All oral, interferon-free regimes provide the first real opportunity for eradication of HCV in the Asia Pacific region
- Access must be improved to reduce/eliminate the burden of the disease
- Interferon may linger longer in the region due to more favourable interferon responsiveness of Asian population to the interferon based regimes
- But its ultimate fate is well known to us all !