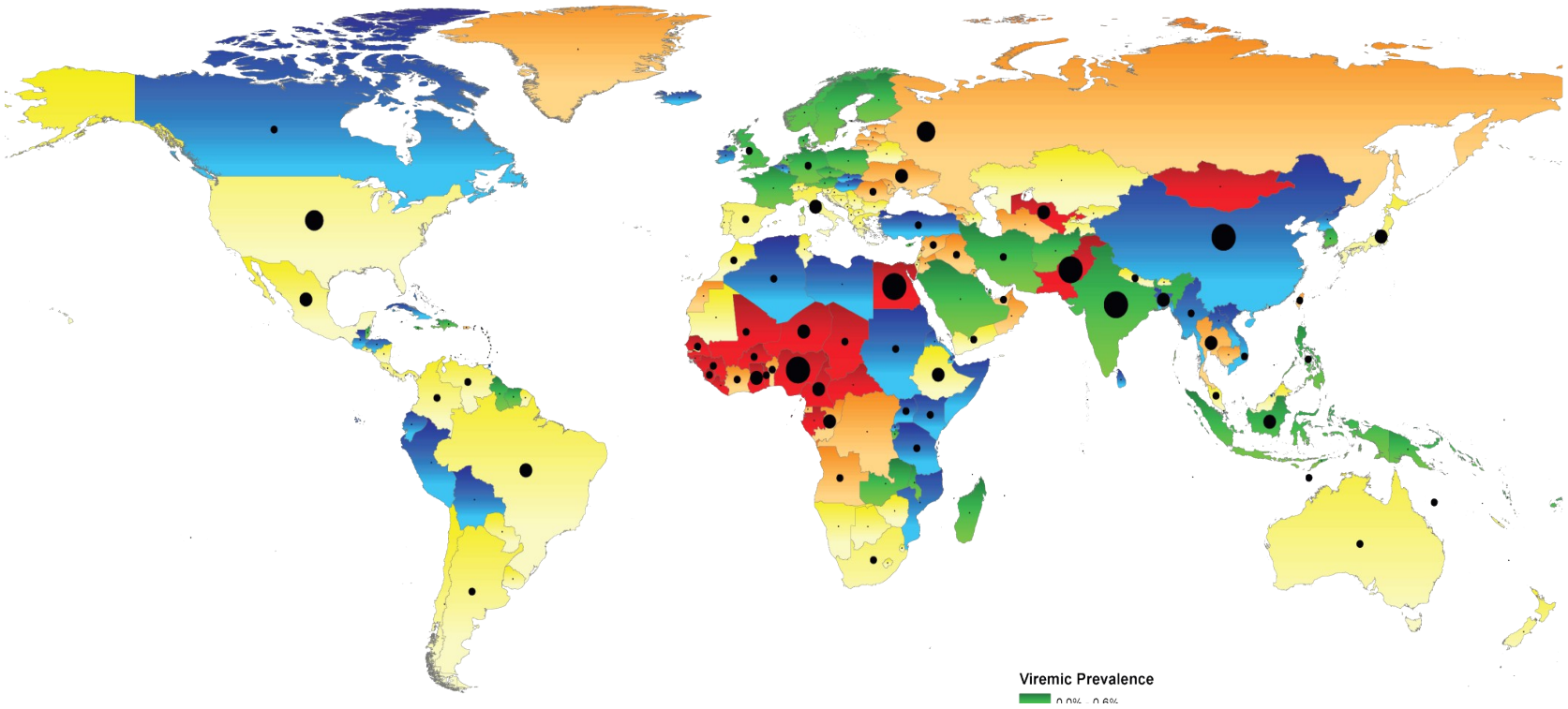
2016 9th PARIS HEPATITIS CONFERENCE
11th & 12th January 2016

Can we expect eradication in HCV G4?

What Still Needs to Be Done?

Imam Waked
National Liver Institute
Egypt

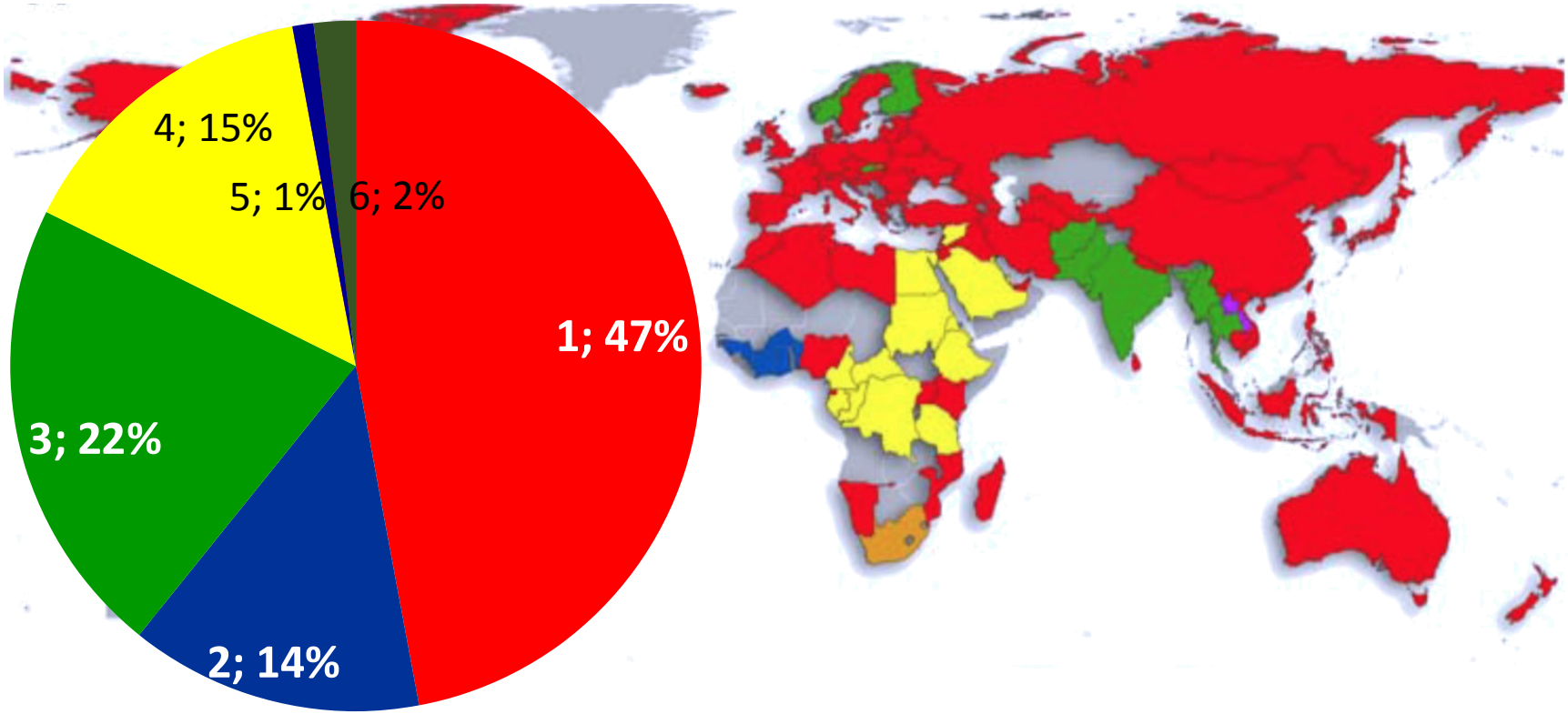
Global HCV Prevalence



Razavi H, Gower E, Estes C, Hindman S. Global HCV Genotypes. AASLD 2013; 2013 Nov 1-5; Washington, DC, United States.

HCV Genotype Distribution Globally

- HCV a global health challenge with ~150 Million chronic HCV
- ~ 3 - 4 Million new infections annually

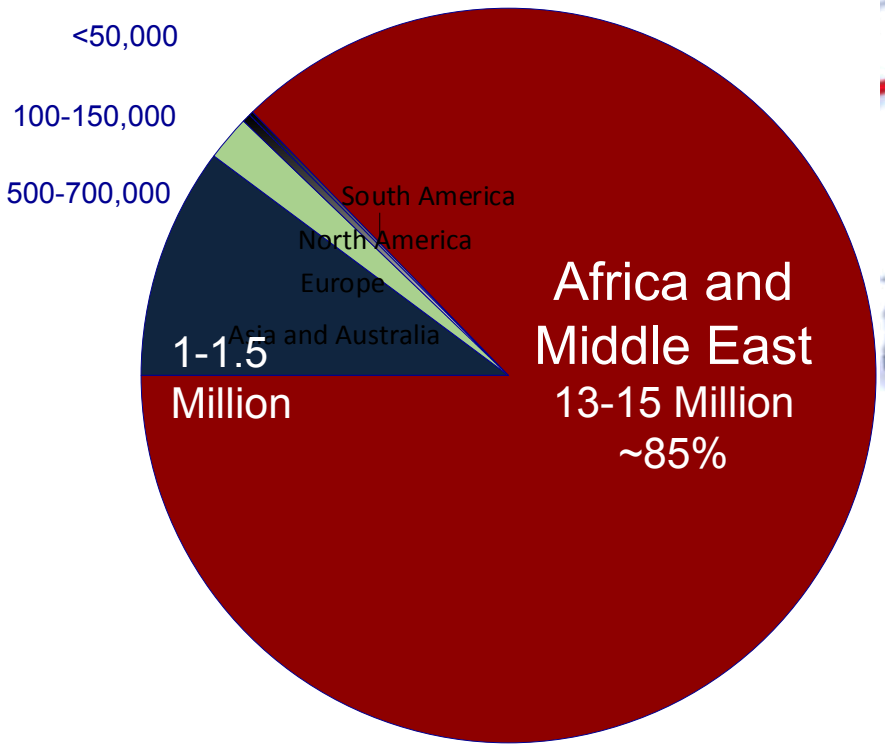


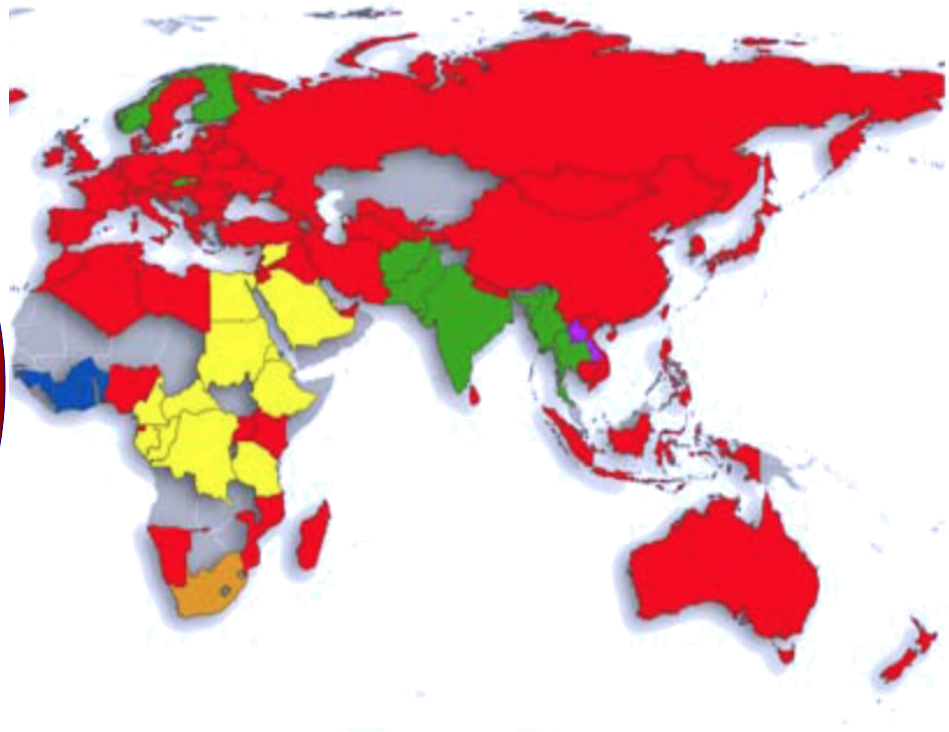
- Genotype 4: 12%-15% (15-18 Million) of total global HCV infection

1. Gower, E., et al., J Hepatol 2014; 61:S45–S57; 2. Messina J. et al. Hepatology, 2015;61:77-87

HCV Genotype Distribution Globally

Global Total ~15-18 Million

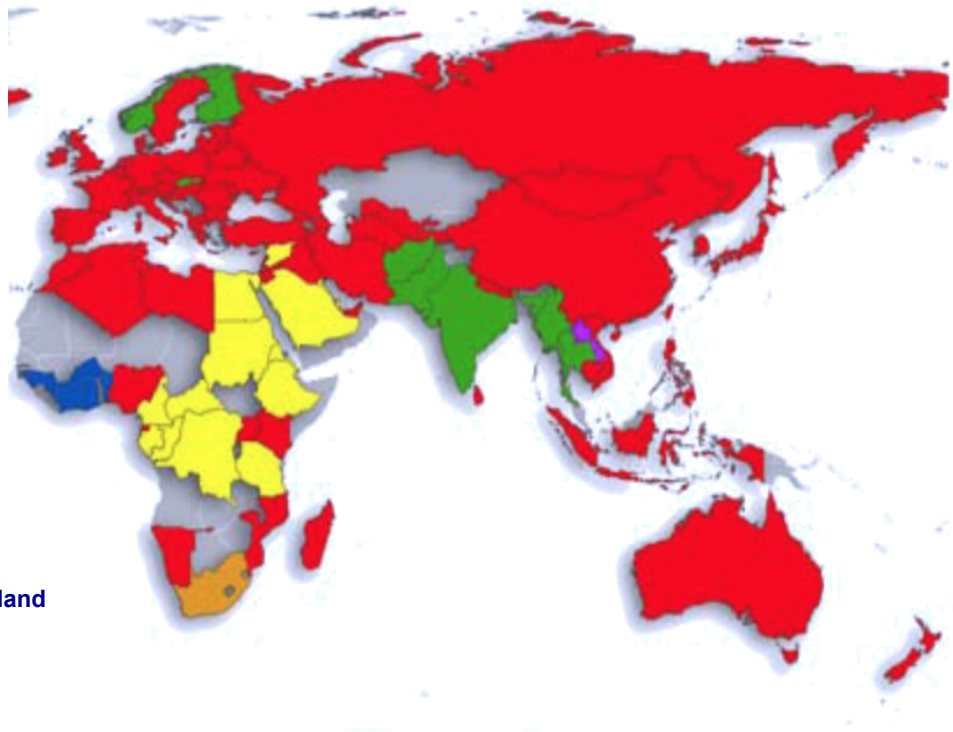




1. Gower, E., et al., J Hepatol 2014; 61:S45–S57; 2. Messina J. et al. Hepatology, 2015;61:77-87

Genotype 4 Distribution by Country Europe

France
Belgium
Netherlands
Switzerland
Germany
Portugal
Spain
Greece
Italy
Austria

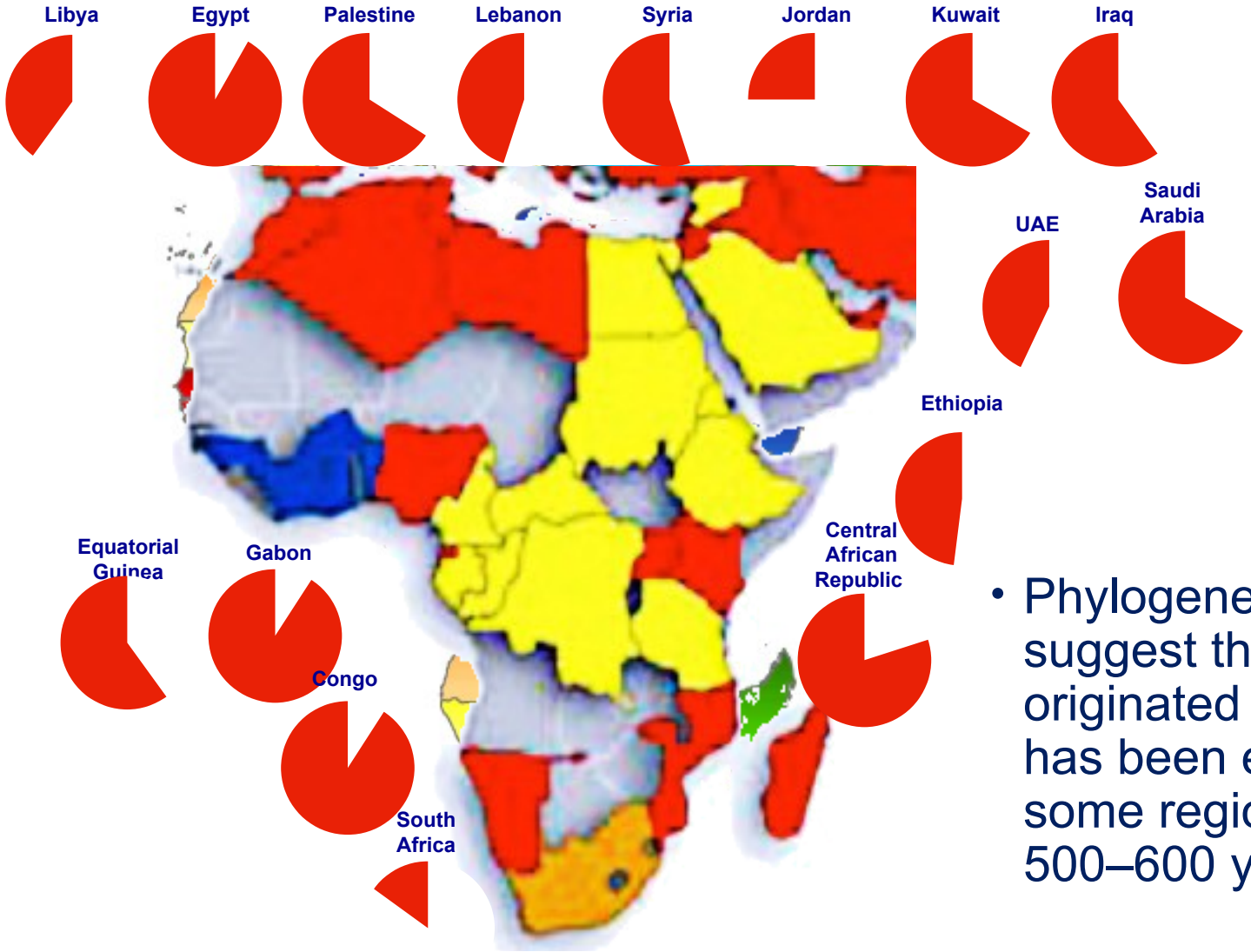


- HCV G-4 is increasing in Europe due to prevalence in PWID and migration
- Increasing in France (>10%), Spain (>15% in South Spain) and Italy

Ireland
United Kingdom
Norway
Denmark
Sweden
Finland
Czech Republic
Slovakia
Georgia
Russia
Belarus
Poland
Turkey
Hungary
Armenia
Estonia
Lithuania
Latvia

1. Gower, E., et al., J Hepatol 2014; 61:S45–S57; 2. Messina J. et al. Hepatology, 2015;61:77-87
3. Asselah et al. J Hepatol. 2012; 56:527-32; 4. Cifuentes C Et al. Enferm Infecc Microbiol Clin 2012; 30:452-7;
5. Sariguzel et al. Clin Lab. 2013; 59:1403-8

Genotype 4 Distribution by Country
Africa & Middle East

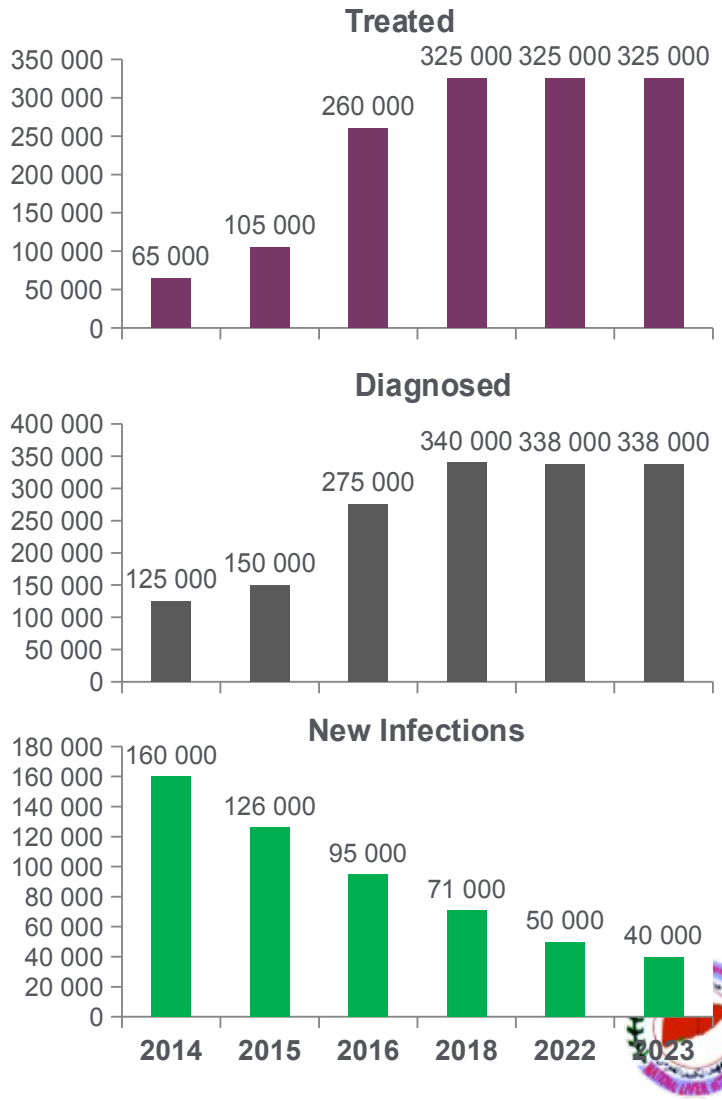


- Phylogenetic studies suggest that HCV originated in Africa and has been endemic in some regions for at least 500–600 years.

1. Gower, E., et al., J Hepatol 2014; 61:S45–S57; 2. Messina J. et al. Hepatology, 2015;61:77-87

The situation in Egypt:
Can we eradicate the disease? What needs be done?

- **To achieve disease elimination, we need to:**
  - Increase annual number of treated patients
  - Increase diagnosed patients accordingly
  - Reduce new infections by ~20% annually

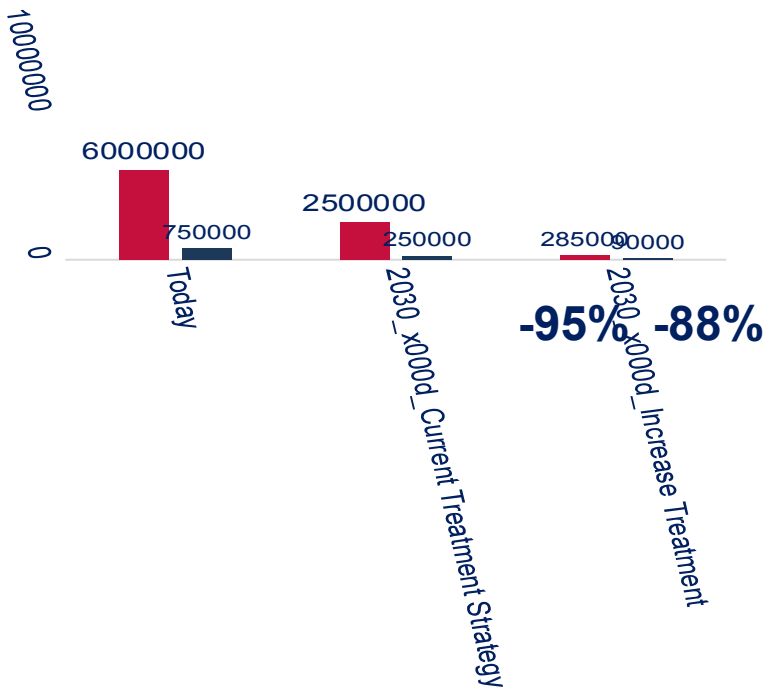


- Waked I, et al. Arab J Gastro. 2014; doi:10.1016/j.ajg.2014.04.003

The situation in Egypt:
Can we eradicate the disease?
What needs be done?

Impact of Disease Control Strategies

	Today	2030	
		Current Strategy	**Control Strategy**
Treated (Annual)	150,000	150,000	325,000
Treatment rate	3.5%	3.5%	7.1%
Average SVR	90%	90%	90%
Newly diagnosed (Annual)	125,000	125,000	340,500
Common treatment age	18 - 70	18- 70	All
Impact			
# Total infected	6,000,000	2,500,000	280,000
Change (%)		-55%	-95%
# Total with cirrhosis	750,000	300,000	90,000
Change (%)		-55%	-88%



Waked I, et al. Arab J Gastro. 2014; doi:10.1016/j.ajg.2014.04.003

Is current therapy for HCV effective? Can it Improve?

Efficacy in Clinical Trials and Research Centers ≠ **Effectiveness in Community Practice**

↓

Efficacy
x Access
x Acceptance
x Adherence

El-Serag HB. Gastroenterology. 2007;132:8.

Is current therapy for HCV effective? Can it Improve?

Current therapy

Efficacy of current therapy	85%
Access	x 20%
Acceptance	x 90%
Adherence	x 90%
Effectiveness	= 14%

Improve Access to 50%

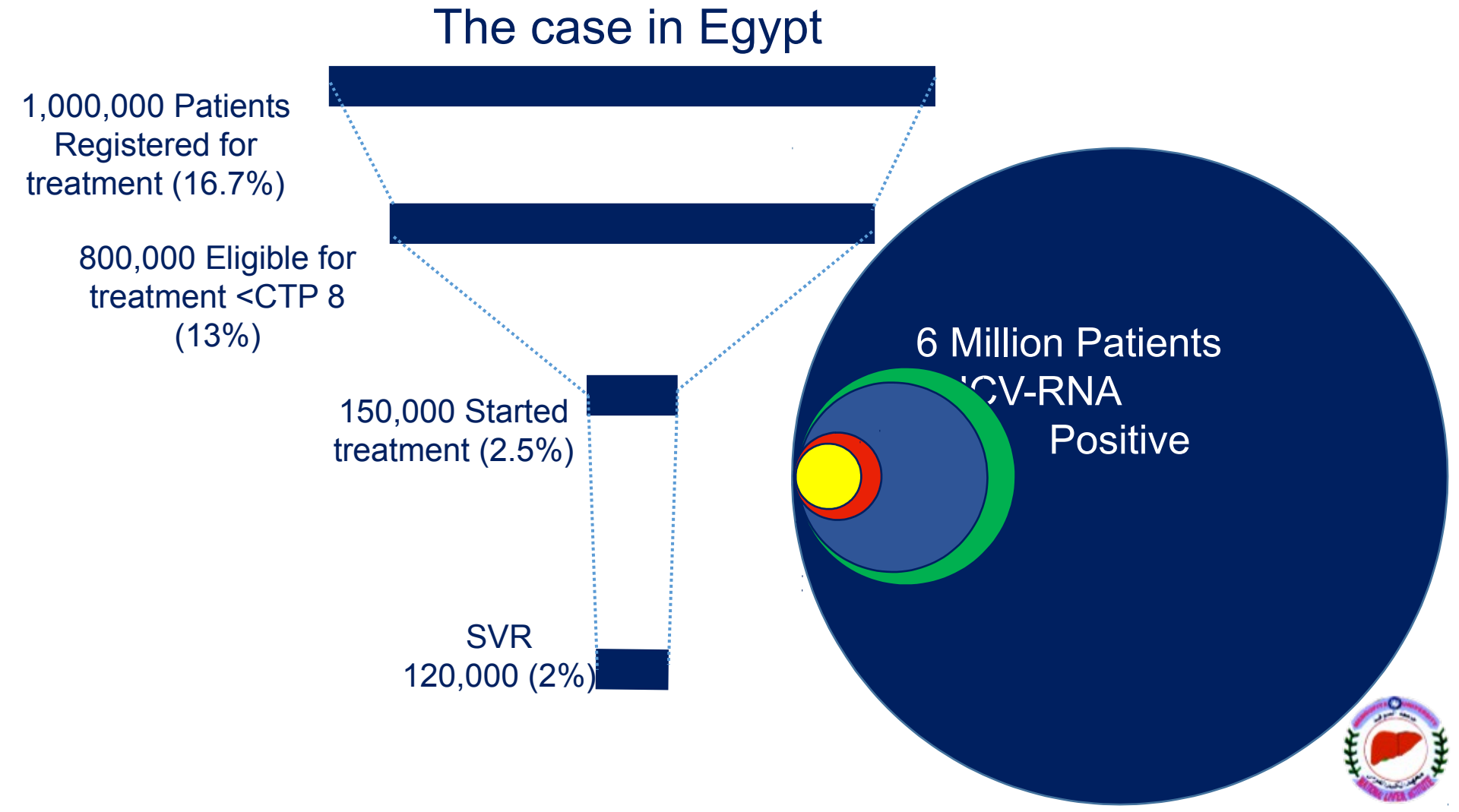
Efficacy of Future therapy	85%
Access	x 50%
Acceptance	x 90%
Adherence	x 90%
Effectiveness	= 35%

Improve Access to 90%

Efficacy of current therapy	85%
Access	x90%
Acceptance	x 90%
Adherence	x 90%
Effectiveness	= 62%

El-Serag HB. Gastroenterology. 2007;132:8.

The situation in Egypt:
Only a small proportion of HCV patients are identified and treated



HCV-G4 Prevalent in Low and Middle Income Countries (LMICs)

	% HCV	# HCV	% G4	Per Capita $
Burundi	8.2%	830,000		270
Cameroon	13.8%	2,750,00		50
Central African Republic	3%	15		0
Democratic Republic of the Congo	6.4%			
Djibouti				
Egypt				3,050
Eritrea				917
Ethiopia			50%	550
Gabon		,000	97%	9,720
Kenya		450,000	27%	1,180
Liberi			100%	370
	12%	480,000	60%	2,700
	2.5%	300,000	100%	680
S	1.5%	150,000	50%	600
So	1.7%	700,000	15%	6,800
Sud	3%	1,200,000	100%	1,670
Tanz	3.6%	1,500,000	50%	850
Uganda	6.6%	2,250,000	100%	670

LMIC in Africa: ~14 Million HCV-G4 cases

Lancet Infect Dis 2002; **2:** 293–302 , World Bank: http://data.worldbank.org/indicator/NY.GNP.PCAP.CD

Other HCV G4 Prevalent Countries

Countries	HCV	Interferon Availability	National Policy
Senegal1	0.25%	Yes	Yes
Benin 2	4.12%	No	No
Mali2	2–4%	No	No
Burkina Faso2	2–5%	No	No
Côte d'Ivoire2	2–4%	Yes	Yes
Burundi2	8.2%	Yes	No
Chad2	1.5–3%	No	No
Cameroon3	13%	Yes	Yes

1. Dieya TN et al. Dakar Med. 2006;51:47-52; 2. WHO Estimate 2008; 3. Njoya O. Hépatites Virales. Harmattan; 2013.

Do you think HCV-G4 will be globally eradicated?

- Yes, By
  - 5 years?
  - 10 years?
  - 20 years?
- Never?

Access to Therapy in G-4 Prevalent Countries

- The gap between HCV drug development and access to treatment is great in low- and middle-income countries (LMIC) where 80% of the global burden of HCV and 95% of HCV-G4 infection and mortality exists.
- Major challenges include
  - Finding and diagnosing cases
  - Linking cases to care
  - Access to DAAs for all patients.
- This needs.
  - Assuring governmental and societal commitment
  - Improving low-cost diagnostic tests
  - Affordable access to treatment in LMICs

Diagnosis and Finding Patients

- WHO HCV guidelines suggest that countries where much of HCV transmission is in health-care settings need to consider screening the general population
- This requires access to high quality inexpensive tests.
- Cost for serological tests should be similar to HIV serological tests(<$1)

Diagnosis and Finding Patients

- Access to HCV NAT (RNA) or direct viral antigen detection is essential.
- Need for developing rapid, point-of-care assays for immediate detection of active HCV infection in the price range of HIV viral load
- A qualitative assay that detects the presence of HCV could be used to diagnose active infection and confirm cure
- A quantitative HCV RNA value will not impact any clinical management decisions.

Access to DAAs

- Agreements that resulted in 100-fold reduction in the US price of DAAs have been announced.
- Egypt has negotiated access to sofosbuvir at a cost of $900 for 12 weeks
- Gilead announced licensing agreements with Indian companies to manufacture generic hepatitis C medicines for 91 developing countries,
- Tiered pricing in developing countries as well as differential pricing for public and private markets
- Followed (In Egypt) by J&J, BMS, AbbVie

www.reuters.com/article/2014/03/21/us- hepatitis-egypt-gilead-sciences-idUSBREA2K1VF20140321
www.gilead.com/~/media/Files/pdfs/ other/HCVGenericAgreementFactSheet.pdf

Access to DAAs

- DAAs be used in LMIC should be safe, easy to use, not needing expert hepatologist evaluation, not needing viral load monitoring, or precise fibrosis assessment and be pan-genotypic.
- The combination of sofosbuvir and an NS5a inhibitor, (daclatasvir or ledipasvir) is suitable for LMIC
- These are effective in patients with compensated and decompensated cirrhosis, HIV/HCV coinfection, and those who have failed previous Peg-IFN and RBV.
- Could minimize total testing requirements for treatment and management

Access to DAAs

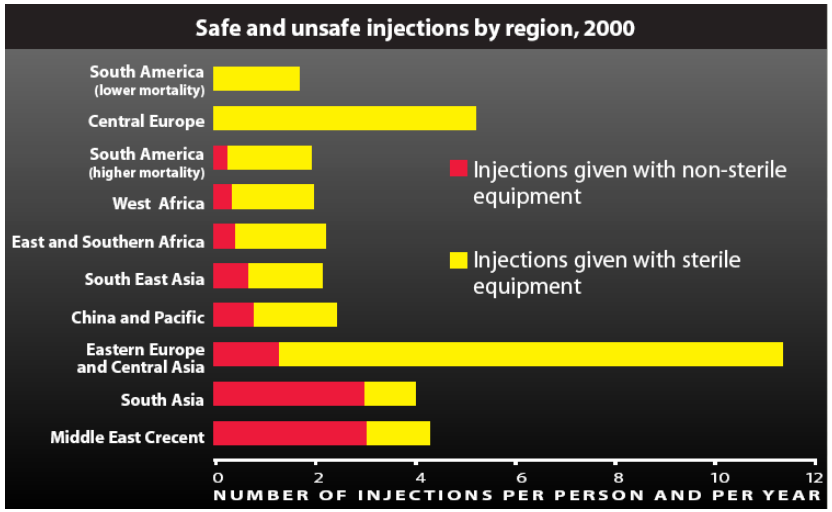
- Up to 90% of patients in LMIC pay for medications out of pocket.
- Insurance does not always cover HCV treatment, diagnostic tests, or monitoring.
- All countries must have affordable drug pricing across the population if they are to provide treatment for HCV infection.

Access to DAAs

- The actual production costs for a 12-weeks DAA regimen is estimated at less than US$250, so this should be an achievable goal
- In Egypt, generic combination DAA prices for public offers is EGP 1600 for 12 weeks ($ 195)
- WHO should institute prequalification program for HCV diagnostics and DAAs generics

Transmission
Parenteral, Unsafe injections

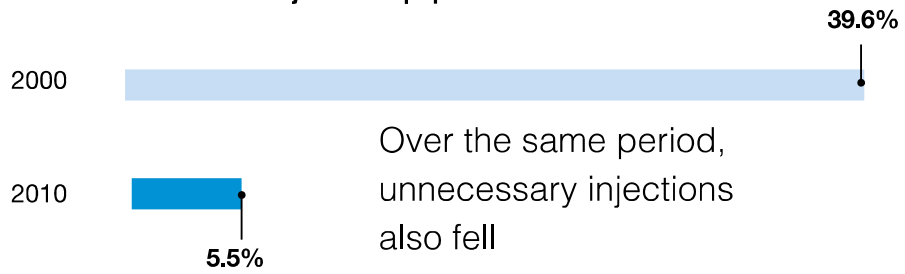
- Injection safety has improved
- LMIC need further support to eliminate healthcare-associated HCV transmission.



Between 2000 and 2010, in developing countries worldwide, re-use of injection equipment decreased from 39.6% to 5.5%

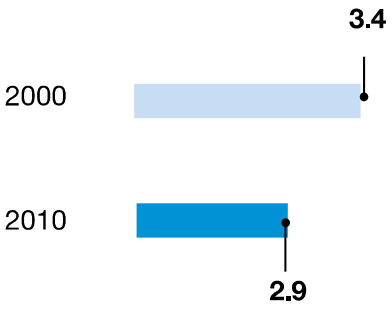
86%

Reduction in re-use of injection equipment



Over the same period, unnecessary injections also fell

Average number of injections per person in developing countries



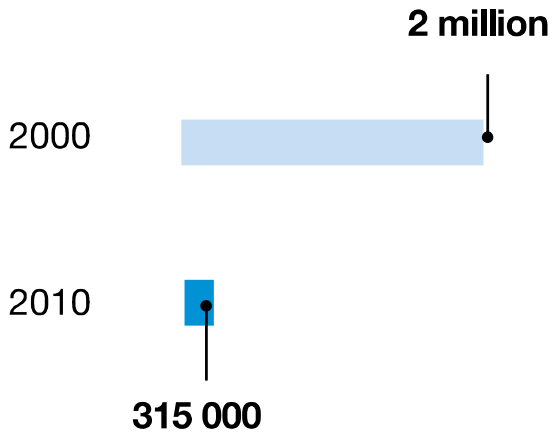
- www.injectionsafety.org - sign@who.int

Transmission
Parenteral, Unsafe injections

- Of the ~ 4 million annual new cases of HCV, unsafe healthcare practices (unscreened blood products or reused syringes), account for over 3 million
- Unsafe injections still account for ~300,000 new HCV infections

91%

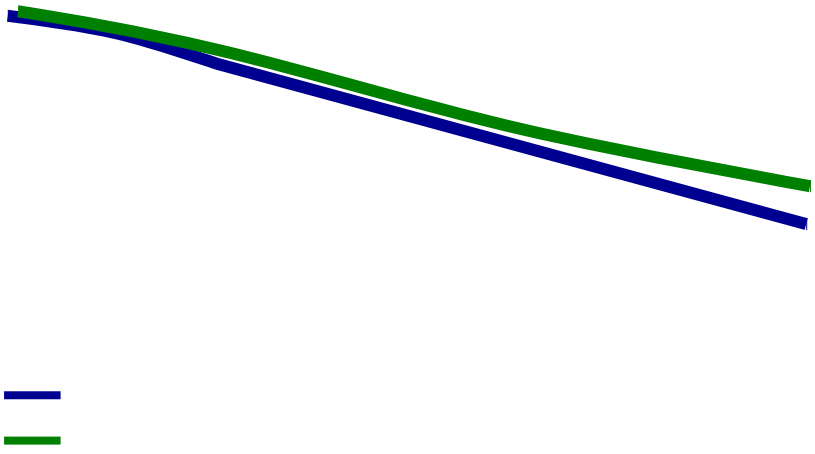
reduction in hepatitis C infections due to unsafe injections



Transmission: The Situation in Egypt

Importance of Preventing Transmission

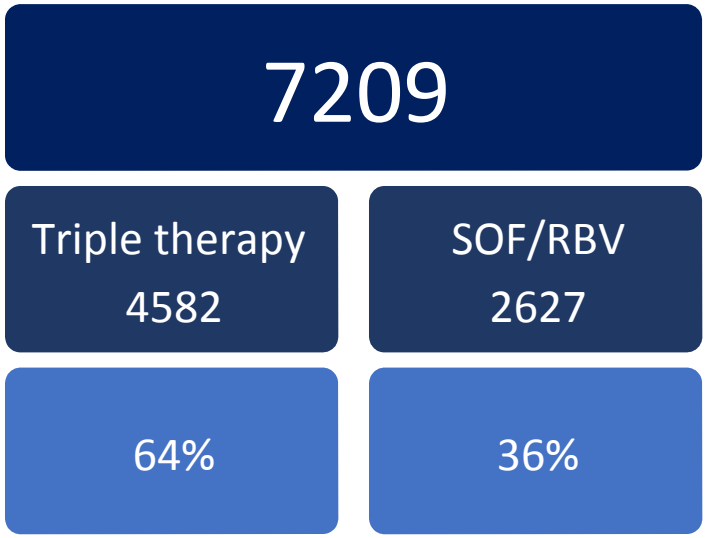
- If:
  - Effective measures are not adopted to reduce incidence
  - Number of new cases only decreases as an effect of increased cure
- There will be 1 million more cases by 2030
- Disease elimination will not be reached



	Prevalence in 2030	
Increased treatment, SVR, reduce incidence	285,000	-95%
Increased treatment, SVR, without incidence reduction	1,250,000	-79%

Therapy:
Real-Life Results of the National Treatment Program in Egypt (November 2015)

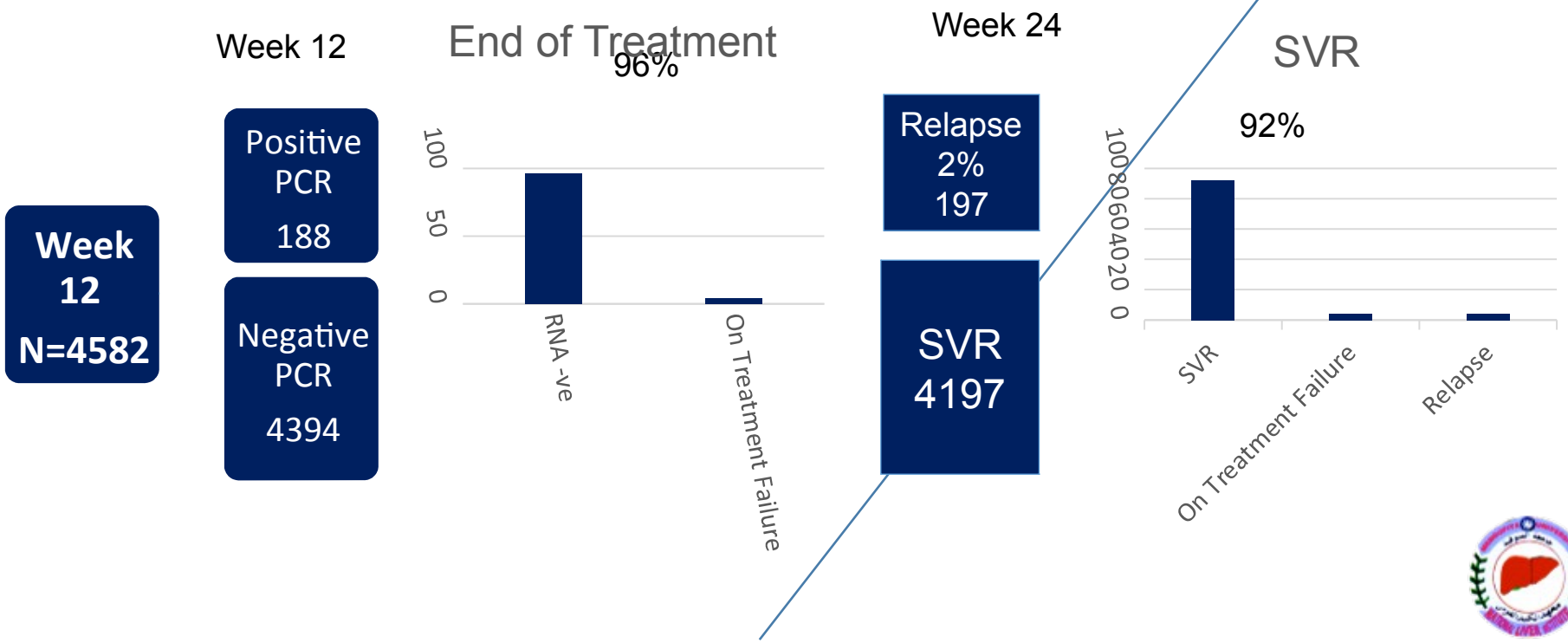
- Till November 2015, 185,000 patients have started treatment
- Data available at 12 weeks follow-up after end of therapy for 7209 patients with advanced fibrosis-cirrhosis (F3-F4)
- 4582 interferon eligible patients treated with SOF-PEG-RBV for 12 weeks (64%)
- 2627 interferon ineligible patients treated with SOF-RBV 24 weeks (36%))



Therapy:

Real-Life Results of the National Treatment Program in Egypt (November 2015)

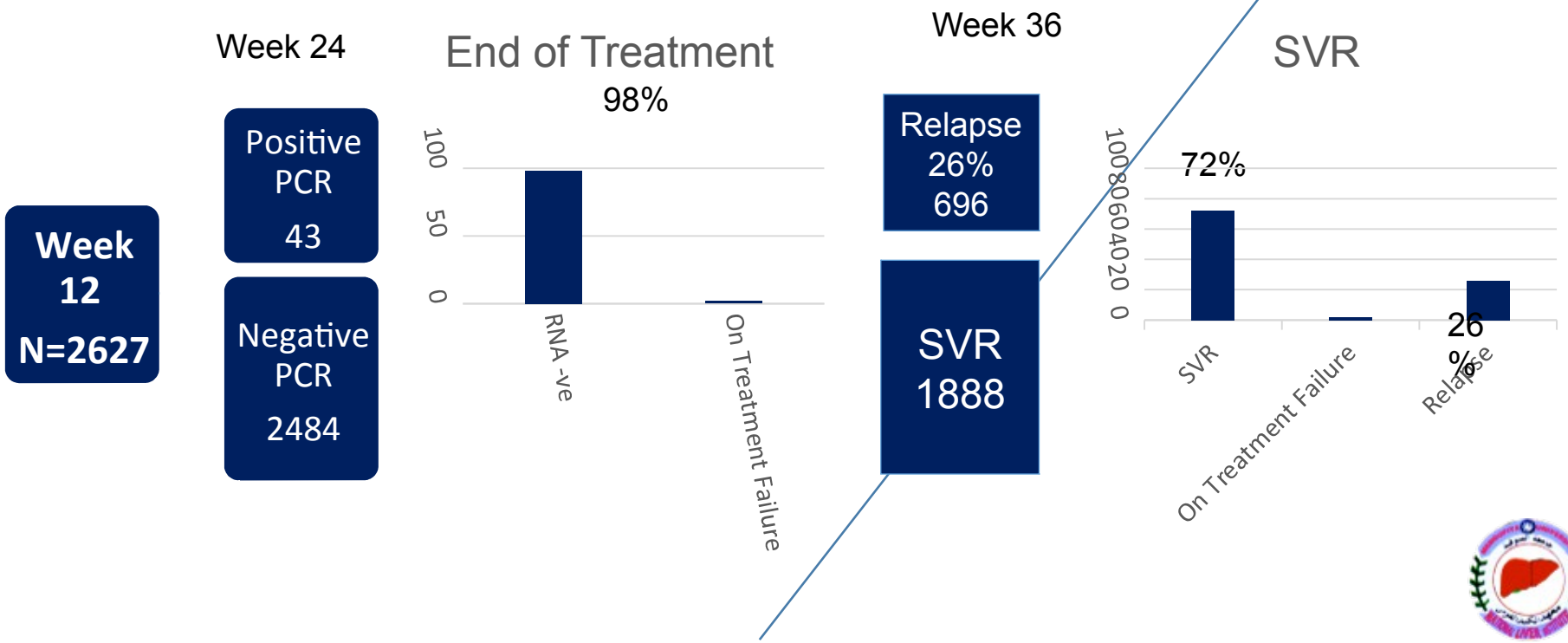
Triple therapy (SOF-PEG-RBV 12 wks)



Therapy:

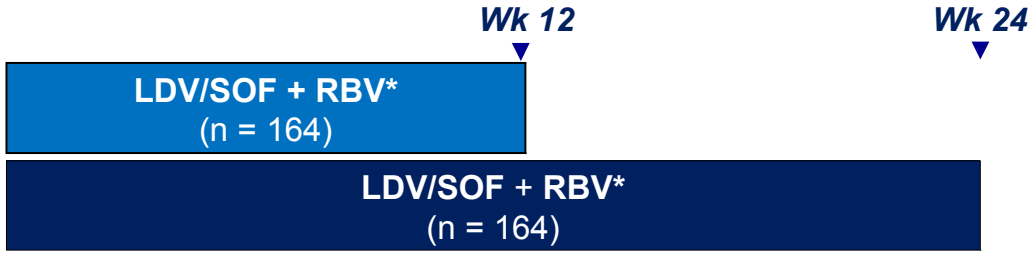
Real-Life Results of the National Treatment Program in Egypt (November 2015)

Dual therapy (SOF-RBV 24 wks)



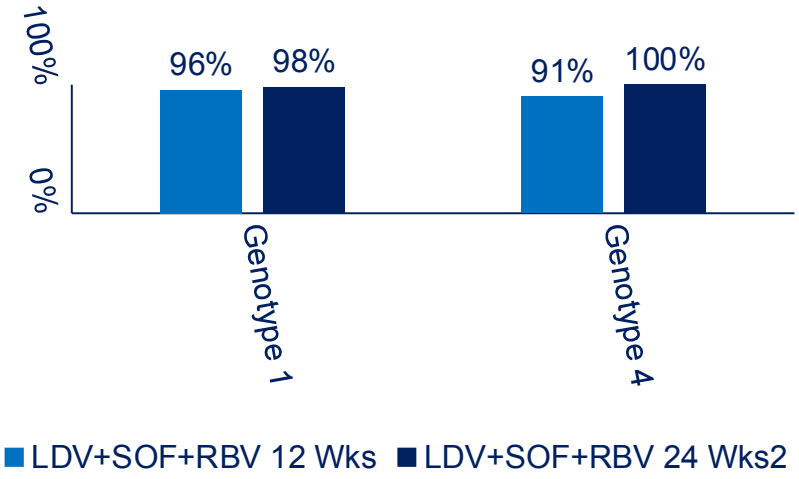
SOLAR-2 Interim Results: LDV/SOF + RBV in Decompensated Cirrhosis or Transplant

GT1 or 4 HCV with decompensated cirrhosis or recurrent HCV after liver transplantation (N = 328)

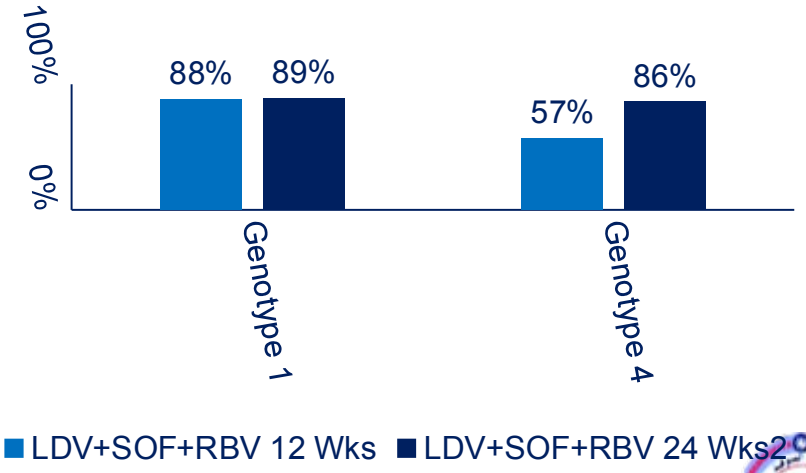


*RBV dose: weight-based (1000 mg/day if < 75 kg; 1200 mg/day if ≥ 75 kg) for METAVIR F0-F3 and CTP A cirrhosis; 600 mg/day with subsequent dose escalation for CTP B/C cirrhosis. LDV/SOF 90/400 mg QD.

F0-F3 and Child A Post-Transplant



Child B and C Pre and Post Transplant



Manns M, et al. EASL 2015. Abstract G02.

Current Disease Burden

Disease Burden in Egypt	Number
Chronic hepatitis	5,200,000
Compensated cirrhosis	630,000
Decompensated cirrhosis	138,000

- Even with 90% response rate in patients without cirrhosis, 500,000 patients will fail treatment
- In 750,000 patients with cirrhosis in whom SVR rate with best treatment in clinical trial setting is ~75%-80%, expected SVR in real-life setting ~70%, and 250,000 will not respond
- Effective re-treatment options for patients who fail DAA combinations are needed

Razavi H, et al. J Viral Hepat. 2014;Suppl 1:34-59. Waked I et al. Arab J Gastro. 2014; doi:10.1016/j.ajg.2014.04.003

Do you think HCV-G4 will be globally eradicated?

- Yes, By
  - 5 years?
  - 10 years?
  - 20 years?
- Never?

شُكراً

Thank You