Hepatitis C virus infection in the Middle East and North Africa: A public health perspective

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June 14, 2015

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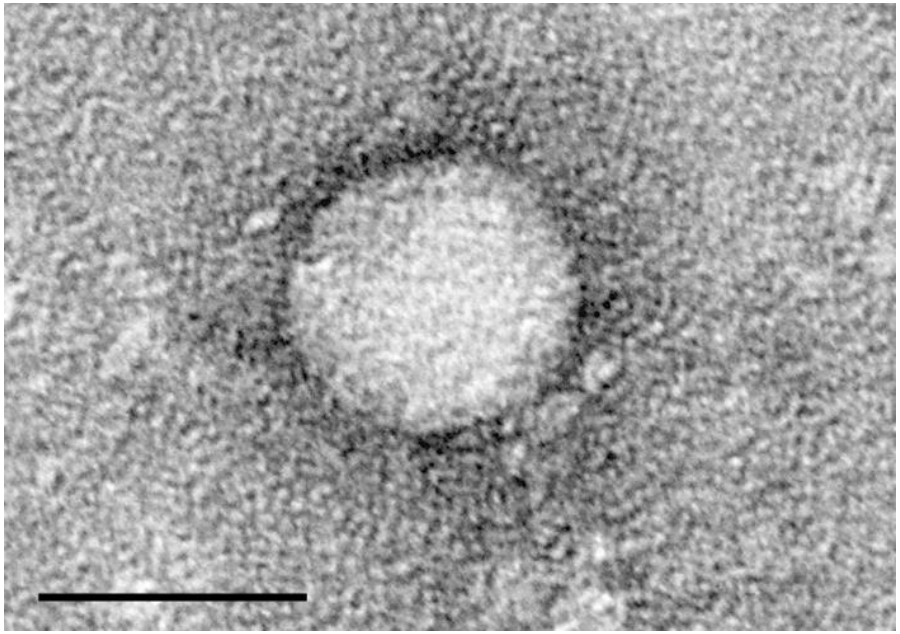
The discovery in 1989

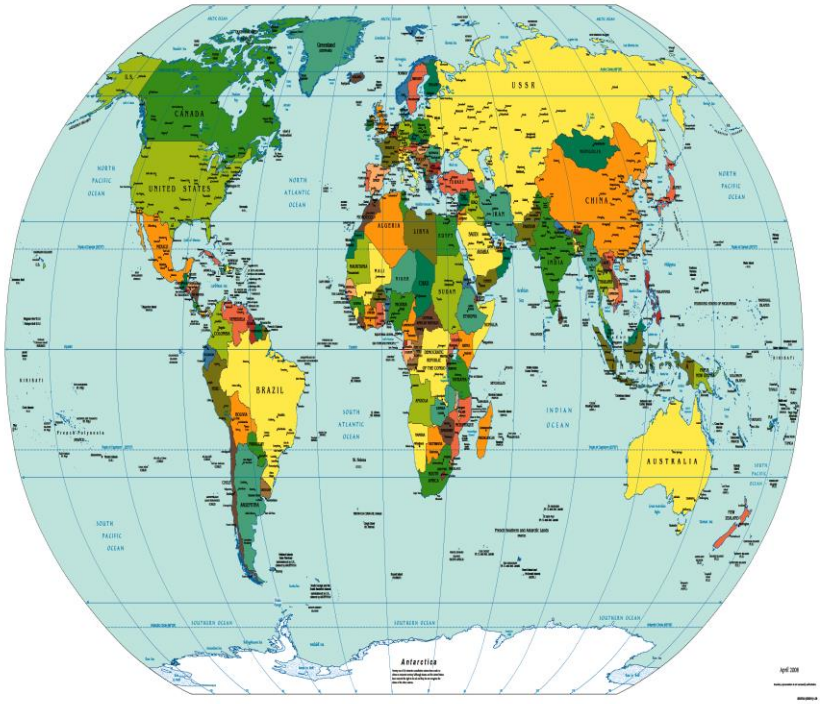
- A new virus, now called *hepatitis C virus*, was discovered



(Kuo et al, *Science* 1989) &
(Choo et al, *Science* 1989)

Global HCV prevalence

- Prevalence is about 0.1-3% across countries

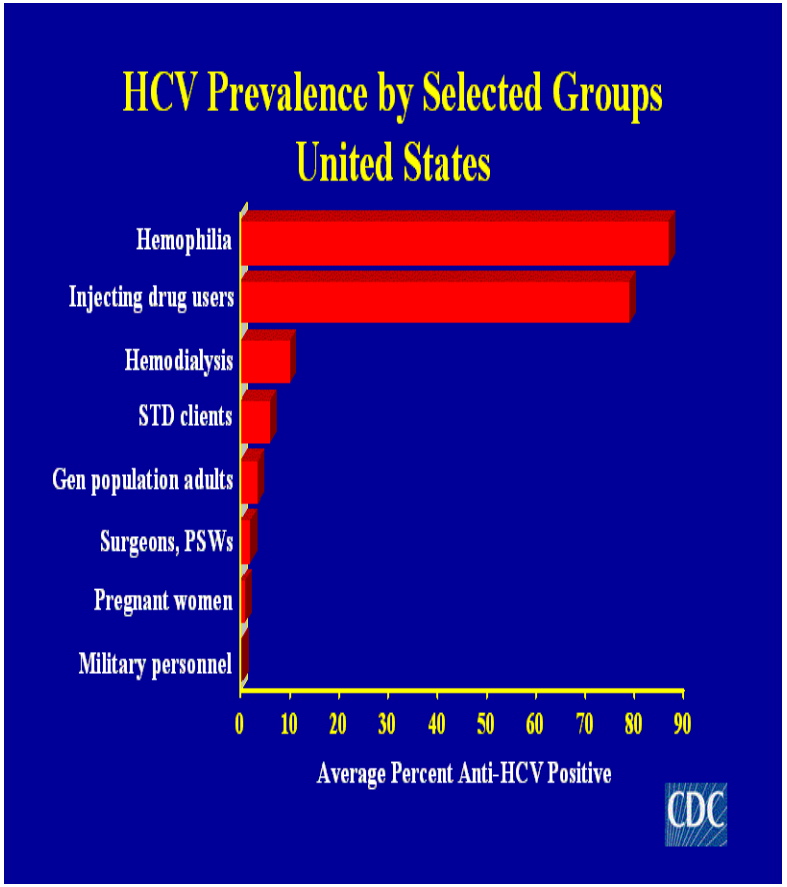


Hepatitis C virus transmission

HCV is mainly transmitted through parenteral exposures such as sharing of injections or blood transfusion

The epidemiology of a new infection

- Populations affected are those exposed to blood products
- High-risk groups include: dialysis patients, injecting drug users, and multi-transfused patients such as hemophiliacs and thalassemics



A surprising discovery

- Routine blood-donor screening in Riyadh, Saudi Arabia
- Among Egyptian blood donors, HCV prevalence was 19.2%
- Every other nationality is <2.5%

(Saeed et al, *Lancet*, 1991)

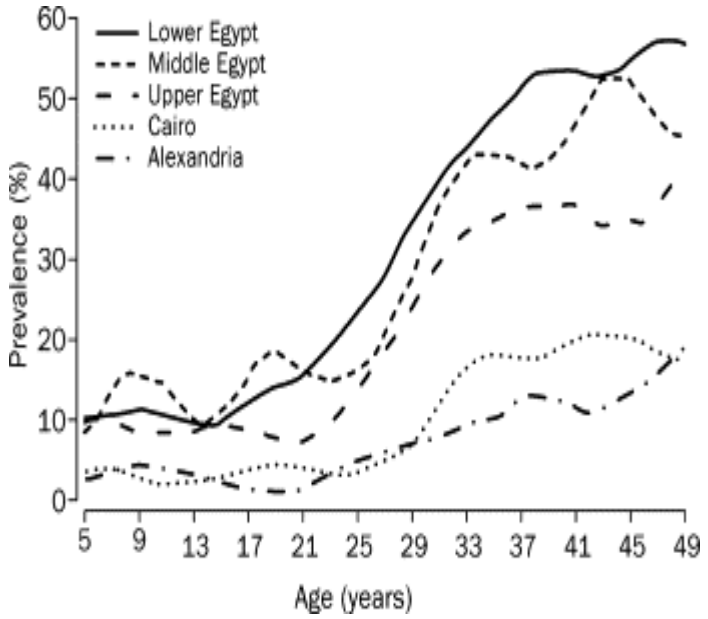
The first study in Egypt

- Among university student blood donors, HCV prevalence was 10.9%

(Kamel et al, *Lancet*, 1992)

HCV prevalence in Egypt

- Subsequent studies found prevalence levels as high as 50% among general population groups specially in the Nile Delta



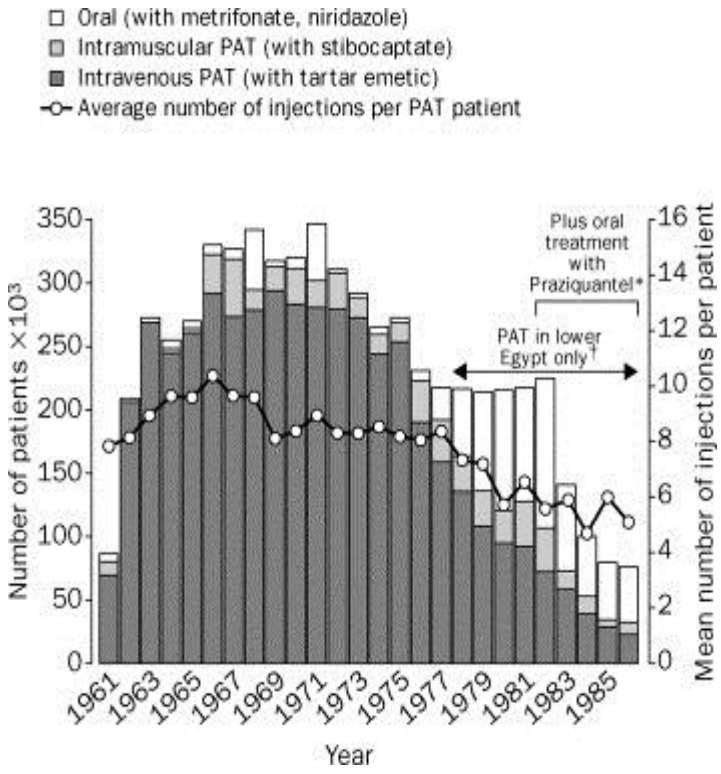
(Frank et al, *Lancet*, 2000)

Abdel Halim Hafez

Why Egypt?

A painful discovery

- *Frank et al* were able to link the HCV epidemic to the parenteral antischistosomal therapy (PAT) mass-treatment campaigns mainly from 1960 to 1985



(Frank et al, *Lancet*, 2000)

Sharing of non-sterilized injections

An observation by a WHO official

"***Patients are … lined up in queues for … injection*** *…* ***The skillful doctor began injecting at 9.20 am and completed 504 injections of men, women and children by 10.10 am*** *.*"

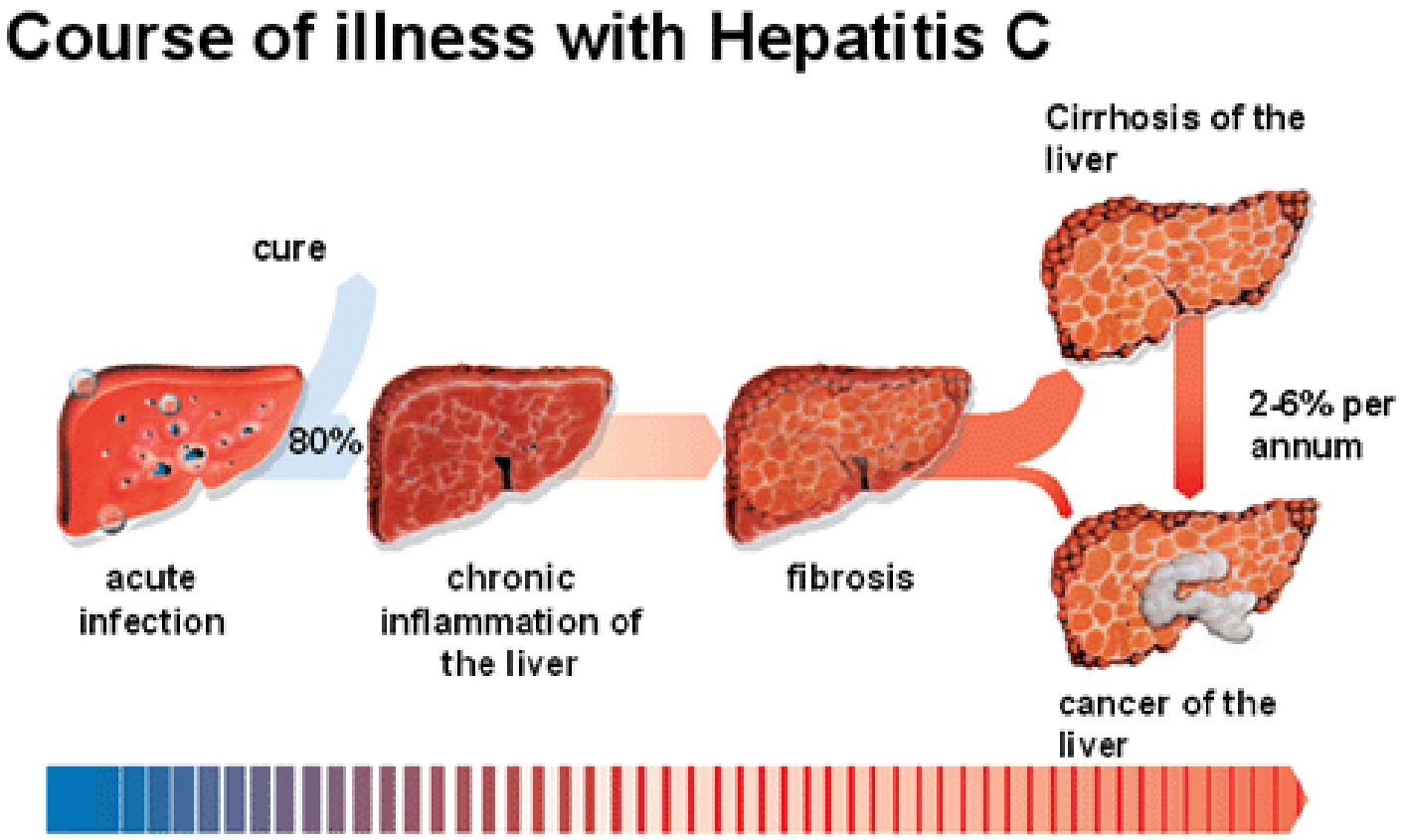
BG Maegraith, *WHO Report,* 1964

A first in the history book

"The world's largest iatrogenic transmission of blood-borne pathogens known to date"

Frank et al, *Lancet*, 2000

Hepatitis C virus disease progression

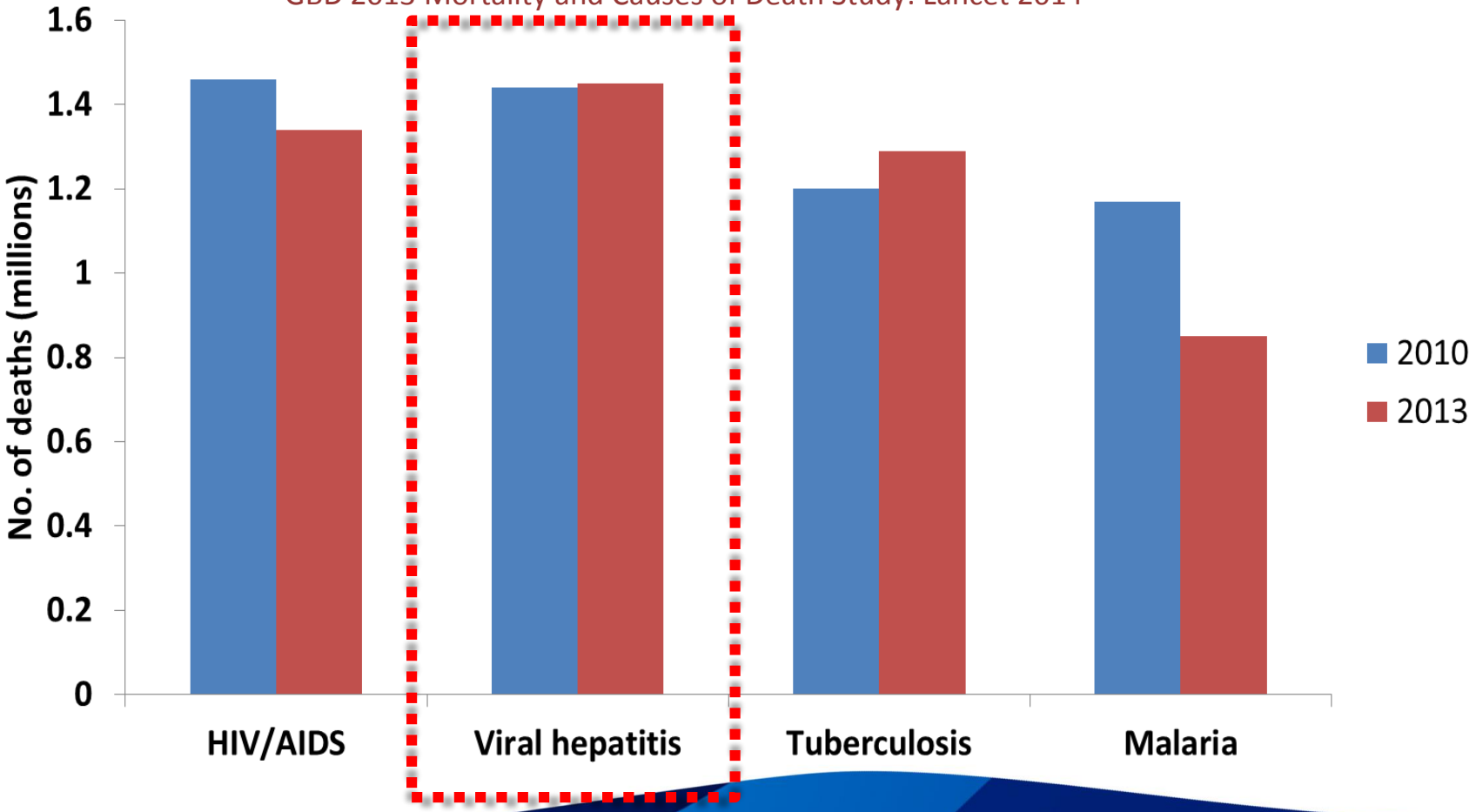


Hepatitis C virus disease progression

- Disease progression of chronic HCV infection:
  - **10%** per year progression rate from one fibrosis stage to the next
  - **10-20%** of chronically infected HCV individuals will develop cirrhosis within 20 years of infection
  - **1-3%** of chronically infected HCV individuals will develop liver cancer within 30 years of infection

Number of deaths/year from selected conditions, Global Burden of Disease Study 2010 and 2013

GBD 2013 Mortality and Causes of Death Study: Lancet 2014



Thanks to Dr Gottfried Hirnschall

World Health Organization

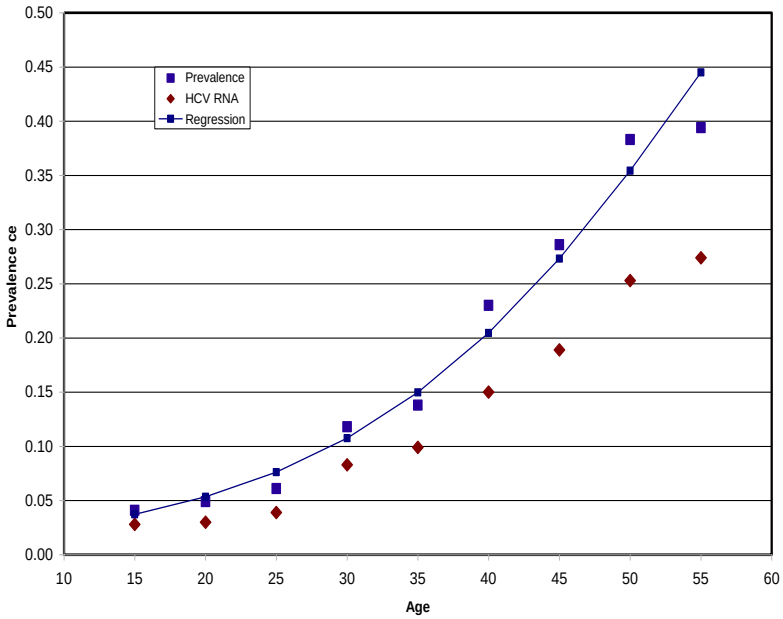
Coming back to Egypt

Questions to be answered

- Key questions:
  - To what extent is HCV transmission still ongoing?
  - What are the modes of exposures to HCV in Egypt today?

An estimate of incidence among the living Egyptian cohort

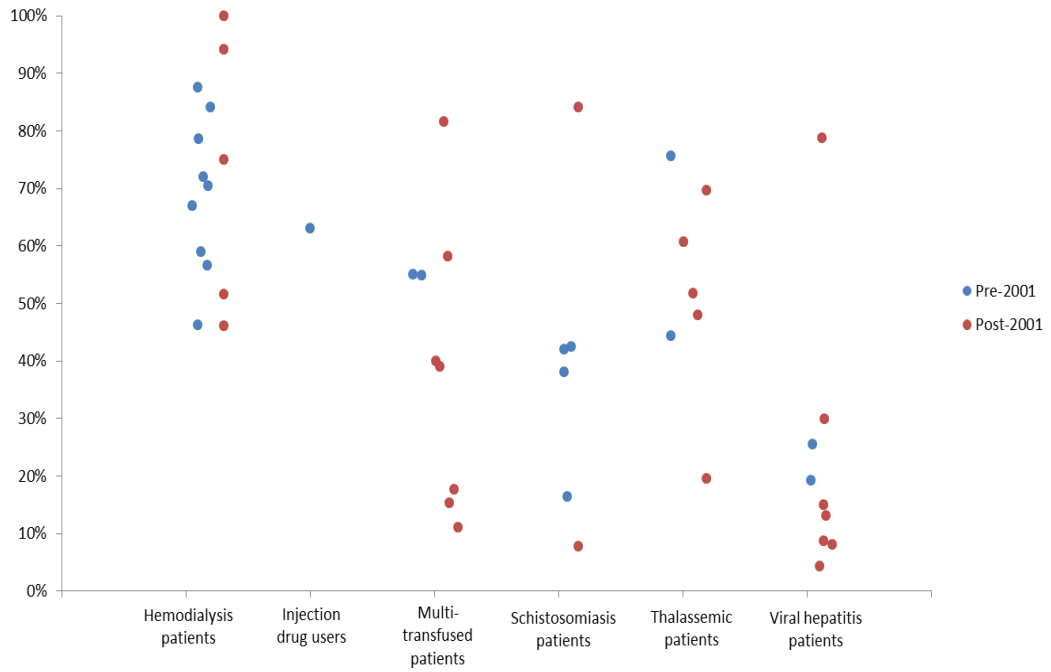
- The incidence levels are suggestive of endemic and intense ongoing HCV transmission



(Miller and Abu-Raddad, *PNAS*, 2010)

Systematic review and data synthesis of HCV data

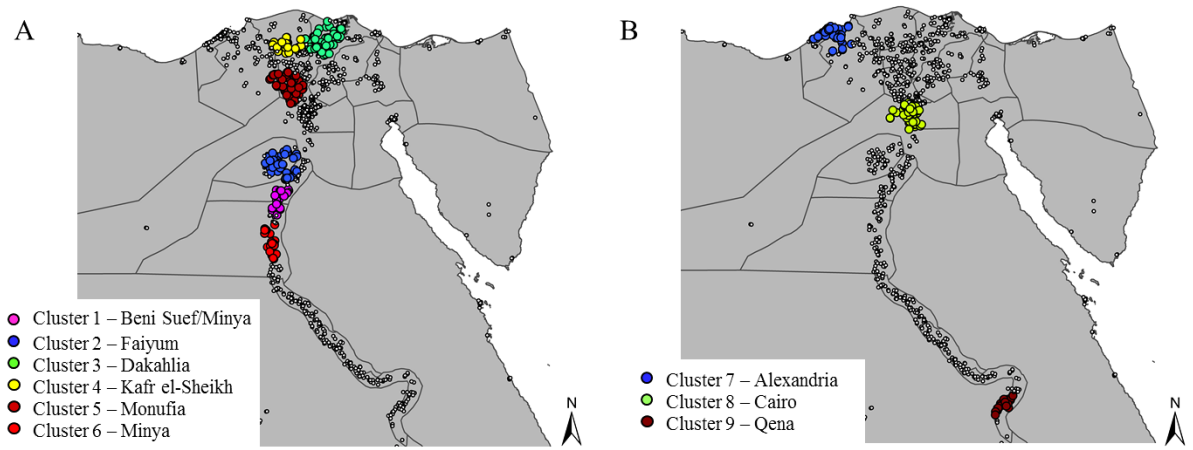
- Ongoing transmission in medical settings



(Mohamoud et al, *BMC Infectious Diseases*, 2013)

Clustering of HCV infection in Egypt

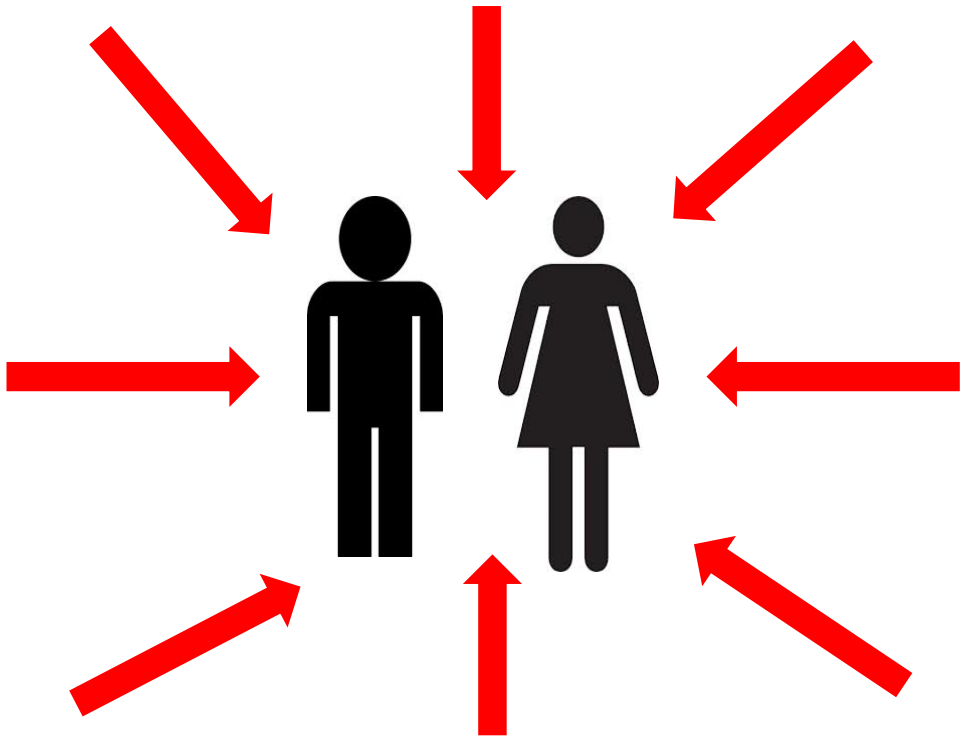
Clusters with high (A) and low (B) HCV prevalence



(Cuadros et al, *Hepatology*, 2014)

Multiple modes of exposure

- Multiple modes of HCV exposure appear to be present and mainly linked to medical care



HCV infection in other countries in the Middle East and North Africa (MENA)?

MENA HCV Epidemiology Synthesis Project

Aims of HCV Synthesis Project:

1. To describe analytically HCV epidemiology across MENA

2. To estimate the national population-level HCV prevalence in each MENA country

3. To estimate the number of HCV infected individuals in each MENA country

MENA sub-regions

HCV incidence

HCV incidence among clinical high risk populations- Fertile Crescent

Table 1. Studies reporting hepatitis C virus (HCV) incidence in countries of the Fertile Crescent region.

Citation	Year of data collection	Study site	Population	Study design	Sample size at recruitment	Lost to follow-up	HCV sero-conversion risk (relative to total sample size)	Duration of follow-up
Jordan								
Batieha, 07 [37]	2003	Dialysis units/ National	Hemodialysis patients	Ret. cohort	1300	NA	9.2%	12 months
Iraq								
Al-Rubaie, 11 [38]	2009	Hospital	Hemodialysis patients	Pros. cohort	57	0	40.3%	12 months
Al-Jadiry, 08 [40]	2007	Hospital	Pediatric patients with acute lymphoblastic leukemia	Pros. cohort	123	0	3.2%	30 months (median)
Al-Kubaisy, 00 [42]		Hospital	Newborns to HCV infected women	Pros. cohort	26	0	0%	6 months
Al-Ali, 14 [39]	2006-07	Hospital	Pediatric cancer patients on chemotherapy	Pros. cohort	85	22	3.2%	12 months
Al-Ani, 11 [41]	2007-09	Hospital	Healthy children	Pros. cohort	60	0	0%	6 months
Al-Ani, 11 [41]	2007-09	Hospital	Pediatric patients with leukemia on chemotherapy	Pros. cohort	29	0	3.5%	6 months
Al-Ani, 11 [41]	2007-09	Hospital	Pediatric patients with leukemia who have had their baseline screening prior to chemotherapy	Pros. cohort	27	0	0%	6 months

*Abbreviations: Pros: prospective, Ret: retrospective.

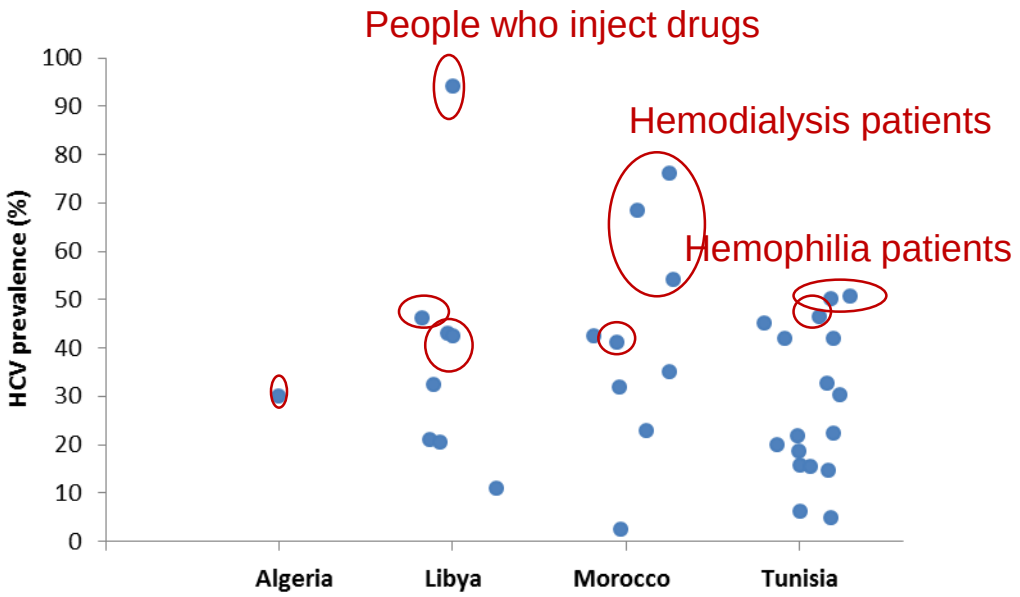
(Chemaitelly et al, *under review*)

HCV prevalence

HCV prevalence among populations at high risk- Arab Maghreb

- High HCV prevalence indicating transmission in clinical settings and among PWID
- Including:
  - Hemodialysis patients
  - Hemophilia patients
  - Thalassemia patients
  - Multi-transfused patients
  - People who inject drugs

- Range of HCV prevalence:
  - Algeria: 30% (1 study)
  - Libya: 0-94.2% (9 studies)
  - Mauritania: No data
  - Morocco: 2.3-76% (9 studies)
  - Tunisia: 4.7-50.5% (17 studies)

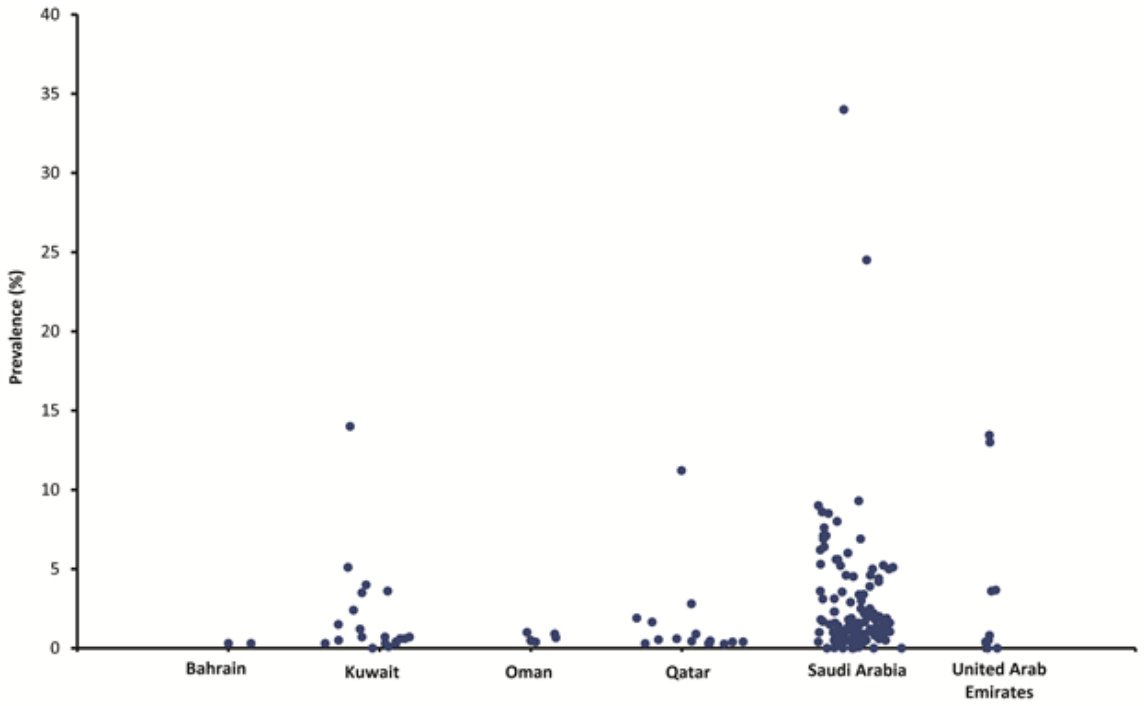


(Fadlalla et al, *PLoS One*, 2015)

HCV prevalence among the general population- Arabian Gulf

- Low HCV prevalence for the majority of measures.
- Including:
  - Blood donors
  - Pregnant women
  - Children
  - Outpatient clinics' attendees
  - Other general population

- Range of HCV prevalence:
  - Bahrain: 0.3% (2 studies)
  - Kingdom of Saudi Arabia: 0%-34% (269 studies)
  - Kuwait: 0.1%-14.0% (29 studies)
  - Oman: 0.4%-0.9% (2 studies)
  - Qatar: 0.3%-11.2% (4 studies)
  - UAE: 0%-3.6%(7 studies)

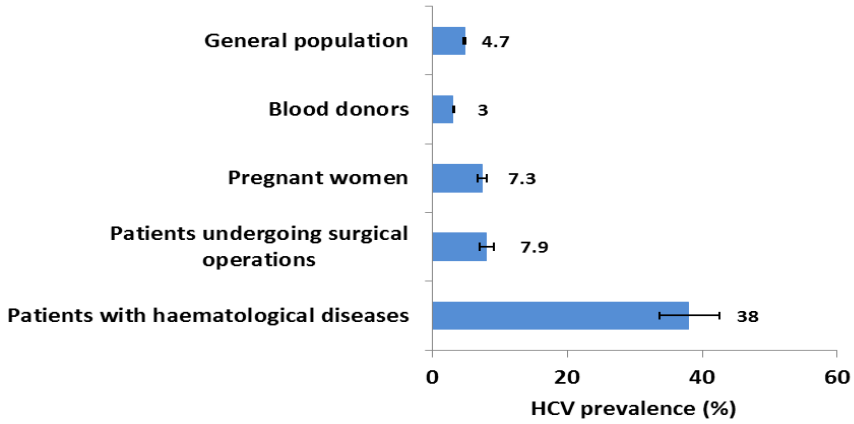


(Mohamoud et al, *ongoing work)*

HCV in Pakistan

National population-based survey

- HCV prevalence measured at 4.8%



Qureshi, H., et al., *Prevalence of hepatitis B and C viral infections in Pakistan: findings of a national survey appealing for effective prevention and control measures.* East Mediterr Health J, 2010. **16 Suppl**: p. S15-23.

Umar, M., et al., *Hepatitis C in Pakistan: a review of available data.* Hepat Mon, 2010. **10**(3): p. 205-14.

Documented modes of HCV exposure in MENA

Exposures to HCV in medical settings

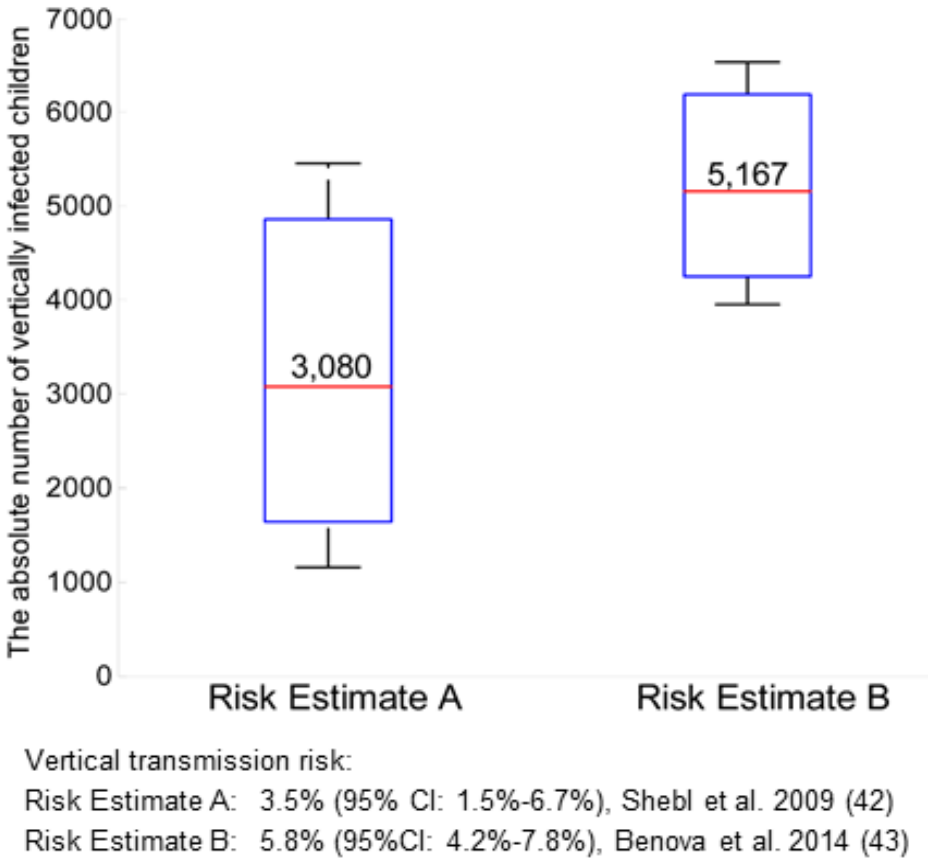
- Medical settings exposures:
  - Hemodialysis
  - Blood transfusions
  - Invasive clinical procedures
  - Hospitalization
  - Injections
  - Dental work
  - Women during child birth/miscarriage

Exposures to HCV in communities

- Community and informal health-provider related exposures:
  - Cupping (*hijama*)
  - Cautery
  - Tattooing
  - Shaving at barber shops
  - Circumcision (for females)
  - Injections administered by non-healthcare professionals

Mother to child transmission

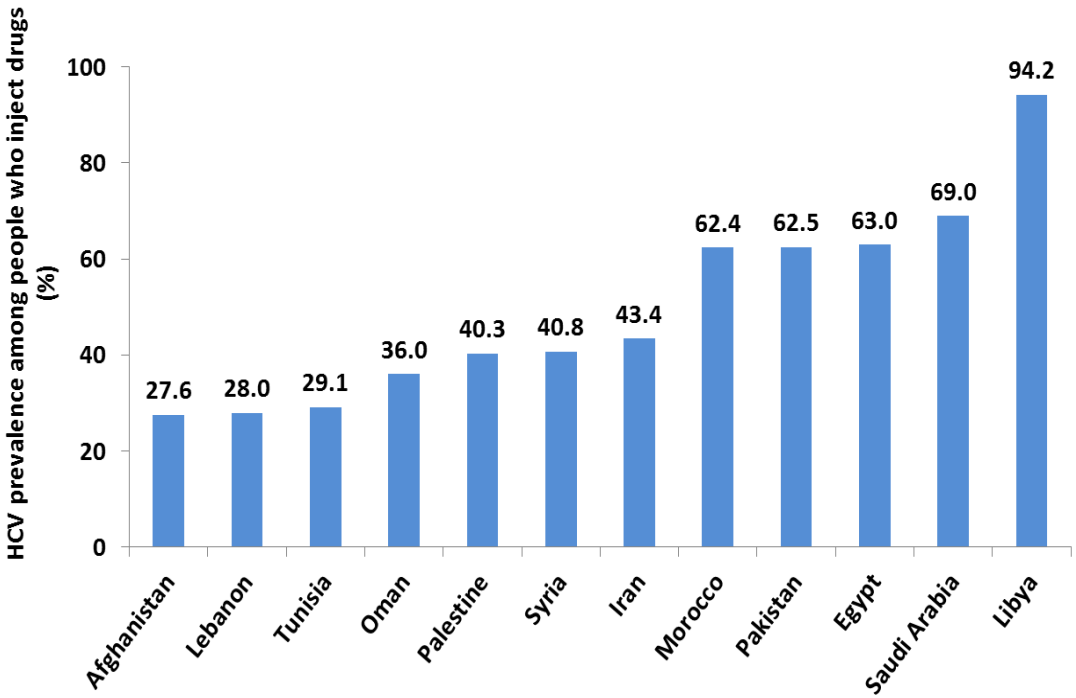
- Mother to child transmission is a significant contributor to HCV incidence in Egypt
- Contribution could be also significant in Pakistan
- This mode of transmission seems limited in other countries



(Benova et al, *Hepatology*, 2015)

Exposure to HCV among people who inject drugs

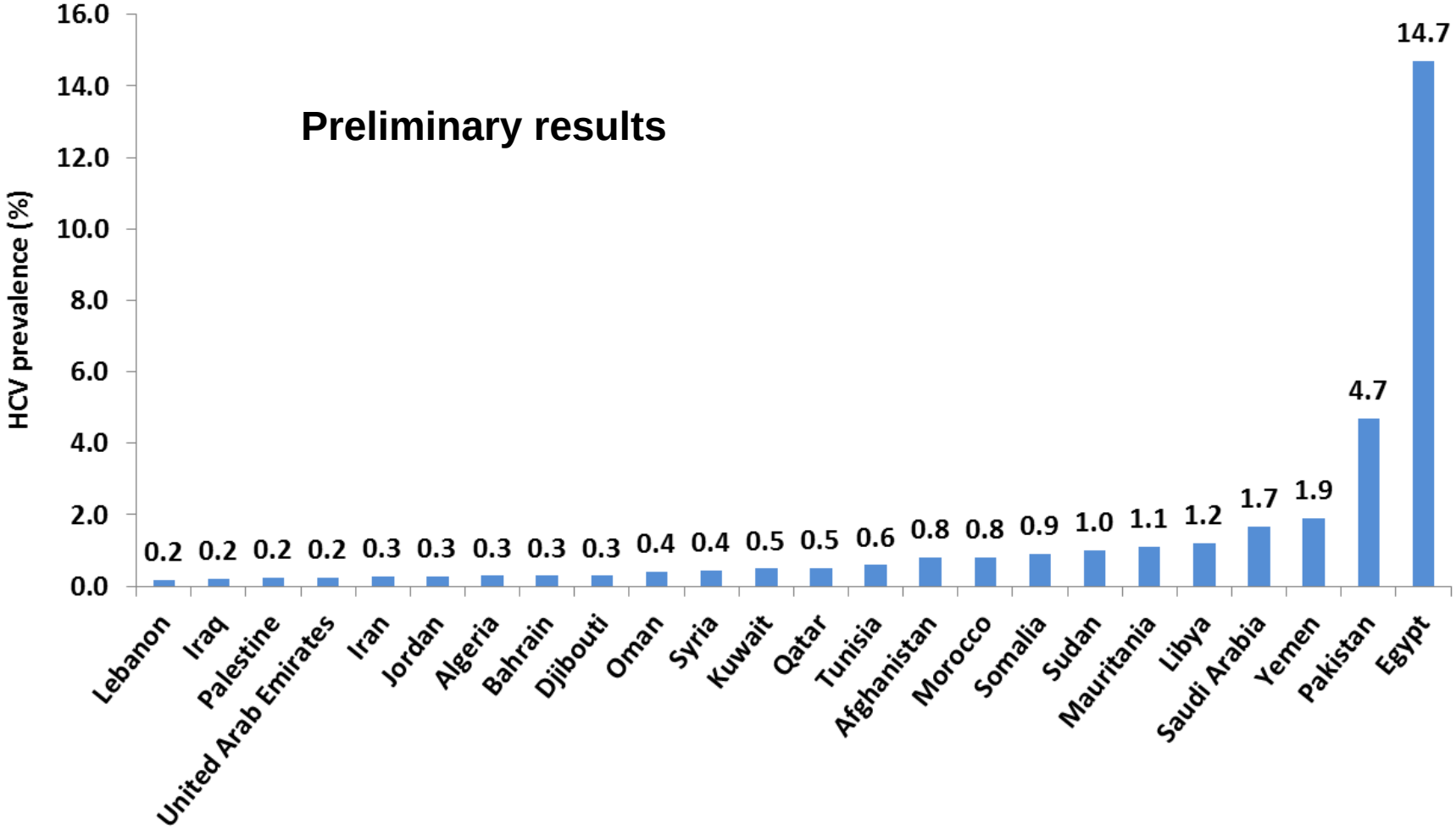
- Evidence for sharing of needles/syringes as a risk factor for HCV exposure
- As expected, HCV prevalence is high among PWID across MENA countries



(Mumtaz et al, *PLoS Med, 2014)*

Estimates for HCV prevalence and number of HCV infections in MENA

National population-level estimates of HCV prevalence



Number of HCV antibody positive persons in MENA: **Preliminary estimates for the 15-59 years age group**

Egypt
7.56 million

Pakistan
4.92 million

Horn of Africa
0.53 million

Arabian Gulf
0.46 million

The number of HCV antibody positive individuals in MENA is ~ **14.2 million**

Iran and Afghanistan
0.28 million

Fertile Crescent
0.11 million

Arab Maghreb
0.34 million

Number of HCV chronically infected persons in MENA: **Preliminary estimates for the 15-59 years age group**

Egypt	Pakistan	Horn of Africa	Arabian Gulf
5.07 million	3.30 million	0.36 million	0.30 million

The number of HCV chronically infected individuals with HCV in MENA is ~ **9.52 million**

Iran and Afghanistan	Fertile Crescent	Arab Maghreb
0.19 million	0.07 million	0.23 million

A brave new world…

Breakthrough in HCV treatment: Direct-acting antivirals (DAAs)

- Release of a new drug Sovaldi (Sofosbuvir) by Gilead in 2013
- Oral well-tolerated treatment
- Treatment duration: 12 weeks
- Efficacy: >90%
- Extremely expensive drug
  - $1000 per pill
  - $84,000 per 12-week treatment course

Sovaldi sales reached $10.3 billion by the end of 2014, which makes it the best-selling drug in the world in its first year on the market.

Breakthrough in HCV treatment: Direct-acting antivirals (DAAs)

- *Daklinza (daclatasvir), Viekira Pak (combination), and Harvoni (combination of* ledipasvir and sofosbuvir*)*
- Rapidly developing pipeline
- Recognized as one of the most impressive success stories in modern medicine
- Access to treatment is the main obstacle; Saudi Arabia pays currently $101,460 per treatment course

HCV treatment dilemma

We have highly efficacious drugs, but they are unaffordable for the vast majority of humanity

Breakthrough in access to treatment

- 99% discount for Egypt; < $1000 per treatment course
- Pakistan obtained a similar discount recently
- Generics are being produced with as little as $750 per treatment course
- Production costs may go down to as little as $101
- Patents are not likely to be granted by national bodies in MENA

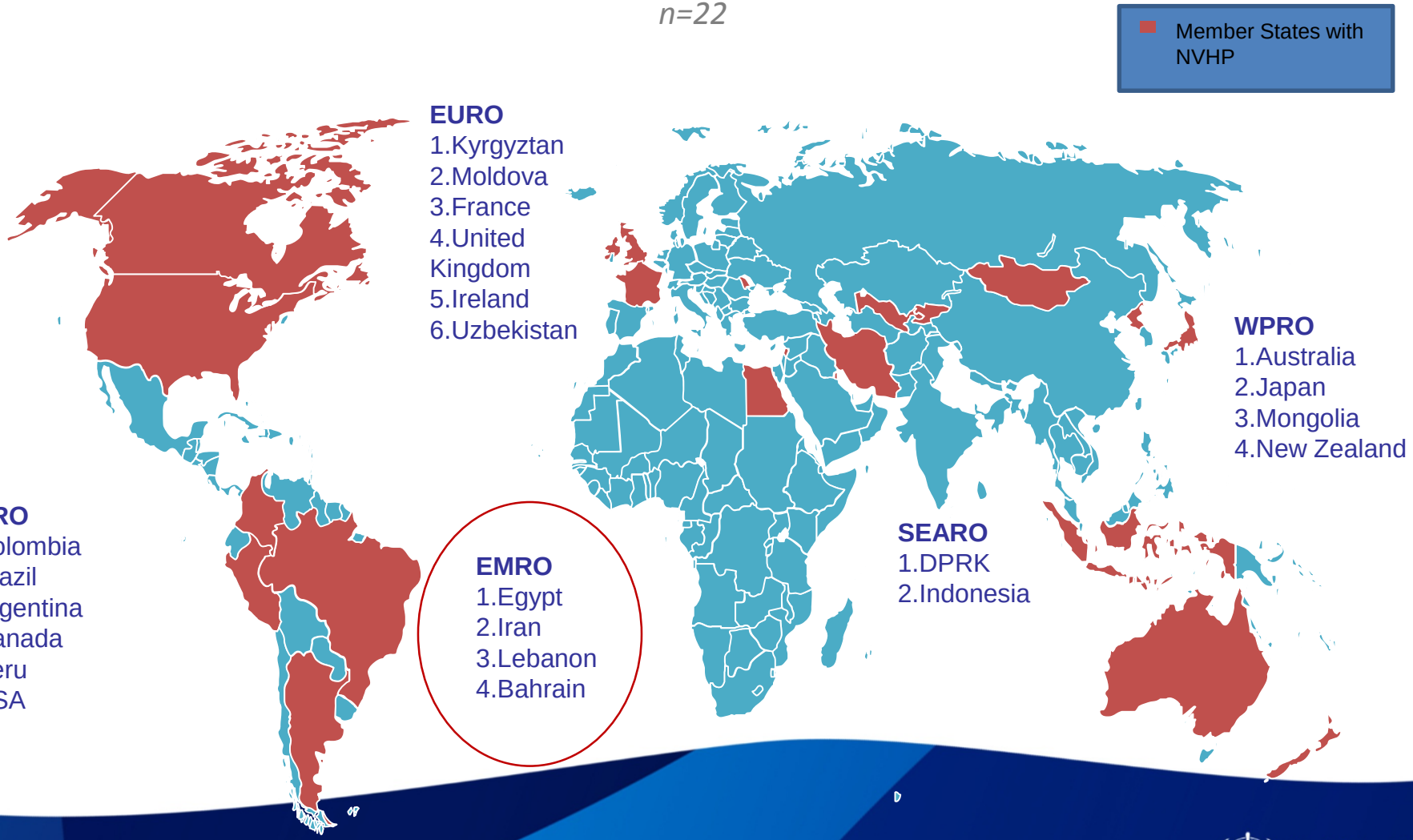
The path forward…

Policy and Strategies

- The first *Global Health Sector Strategy on Viral Hepatitis* is being drafted
- Development of *National Strategic Plans for Viral Hepatitis* and possibly a *Viral Hepatitis Programs* for each country

Countries with National Viral Hepatitis Plans (NVHP, Oct 2014)

n=22

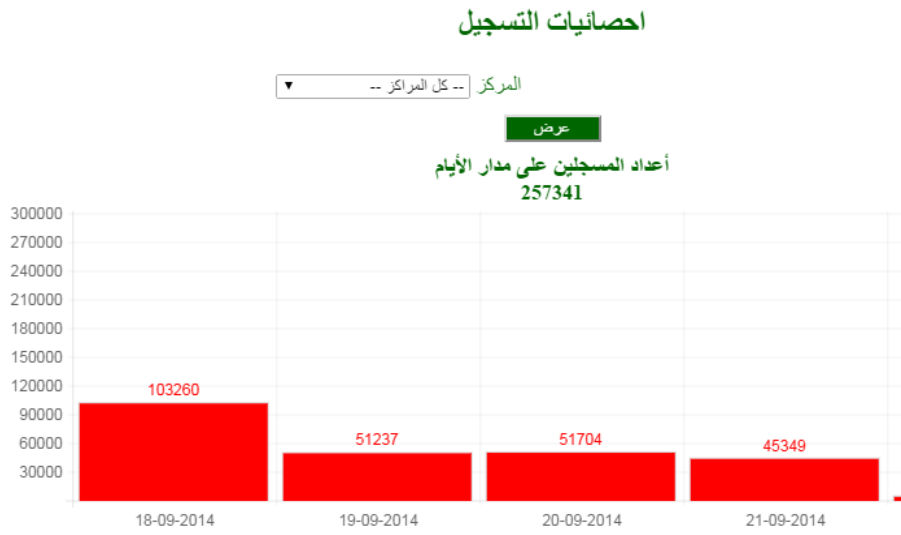


Thanks to Dr Gottfried Hirnschall

World Health Organization

Programmatic interventions: HCV Screening, testing and treatment

- HCV screening, testing, and treatment program
- Egypt National HCV treatment program:
  - One of the largest in the world
  - Over 400,000 treated
  - 835,291 registered in the new treatment program in just few months
- Birth cohort screening is a possibility
- Screening and treatment are cost-effective



Thanks to Dr Manal El-Sayed

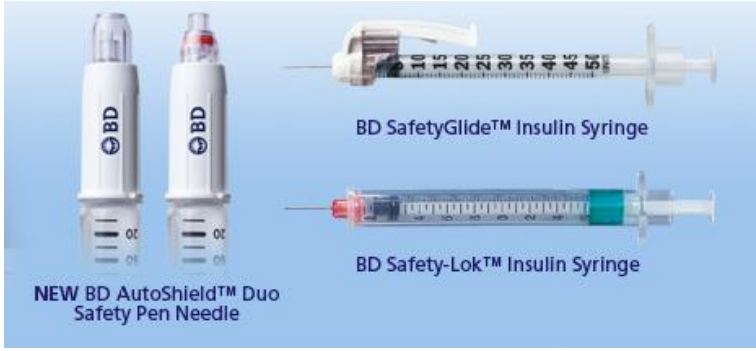
Programmatic interventions: Blood safety

- Blood screening for hepatitis C virus by PCR
- Only about 25% of blood units are screened by PCR in Egypt; the rest by ELISA of unknown quality

World Blood Donor Day

Programmatic interventions: Injection safety

- New WHO injection safety guidelines and policy (2015)
  - Shift to "smart" syringes by 2020
- Average number of injections per person/year in MENA is 4.3; the highest in the world
  - In Egypt it is 6.8
- Pilot program for "smart" syringes including Egypt



Programmatic interventions: Harm reduction for PWID

- Harm reduction expansion in the region
  - Needle/syringe exchange programs
  - Drug dependence treatment
- 626,000 people who inject drugs (PWID) in MENA
- Iran is a world leader in harm reduction

Programmatic interventions: Improved infection control

- Infection control is a major challenge that is not easy to overcome in settings of limited resources

Conclusions

- Overall, HCV prevalence in the population at large in most MENA countries is **about 1-3%,** comparable to most countries globally, with the notable exceptions of Egypt and Pakistan.

- **Healthcare-related exposures** and **injecting drug use** are the major drivers of HCV incidence.

- New or improved strategies need to be implemented for
  - **HCV screening, testing, and treatment**
  - **Blood safety**
  - **Injection safety**
  - **Harm reduction for PWID**
  - **Infection control**

- HCV elimination is now feasible, and possibly as early as 2030.

Acknowledgement

MENA HCV Epidemiology Synthesis Project was made possible by NPRP grant number 04-924-3-251 from the Qatar National Research Fund (a member of Qatar Foundation). Additional support was provided by the Biostatistics, Epidemiology, and Biomathematics Research Core at Weill Cornell Medical College in Qatar.

الصندوق القطري لرعاية البحث العلمي
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