Global burden of hepatitis B and C, and HIV co-infection

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Outline

- **Why we need global and national estimates of prevalence and burden for viral hepatitis?**
  - What is current status of national surveillance programmes?
  - What are consequences of poor data?
- **What are we aiming for?**
  - How can we learn from surveillance and estimation approaches used in HIV, TB and malaria?
- **What do we currently know or not know?** (HCV, HBV and HIV co-infection prevalence and burden)
  - Evolution of WHO and other estimates
  - Data Limitations and Challenges
- **How do we get to where we want to be?**
  - Next steps for WHO and countries

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Why do we need global and national estimates of prevalence and burden of viral hepatitis ?

- For use by country programme managers in strategic planning and allocation of resources
- To evaluate impact of prevention and control measures including vaccination and treatment scale-up
- Global advocacy for action – to inform and empower advocates and policymakers to accelerate progress
- For global reporting
- To inform modelling and assessment of the current and future disease burden and impact of treatment

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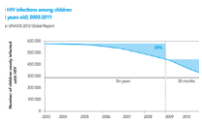
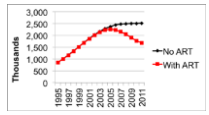
Estimates are also used to…..

Analyse trends over time



Estimate impact

Estimated no of AIDS related deaths over time with/without ART in LMICs

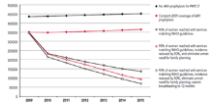


Measure population-level coverage

% of eligible people and pregnant women receiving ART in LMICs

Produce what-if scenarios

Estimated number of new child HIV infections, different scenarios, 25 high burden countries



Current status of national hepatitis surveillance programmes

- ***Aim***: To assess WHO Member States' response to hepatitis
- ***Response rate:*** 125 of 194 (64%)Member States
- Low levels of hepatitis surveillance in LMICs
- Different case definitions

Number of Member States reporting national surveillance systems for chronic viral hepatitis

Consequences of weak surveillance systems..

- Poor quality country-level data on burden of infection and disease outcomes
- Lack of data is a barrier to country-level dialogue and financial engagement
- Lack of reporting system to monitor implementation of treatment scale-up

What are we aiming for?

How can we learn from surveillance and estimation approaches used in HIV, TB and malaria?

Twelve key lessons from ART scale-up

I. Global funding initiatives
II. Reduction in drug costs through generic competition
III. Simplified drug regimens
IV. Innovative, simplified diagnostics
V. Simplified models of service delivery and testing
VI. Treatment guidelines
VII. Guiding principles of "Public health approach "+ "health equity"
VIII. The "leaky treatment cascade: Optimising adherence and retention
IX. Models for programme planning
X. Surveillance systems and monitoring tools
XI. Key role of community and engagement of PLHIV
XII. Research and trial networks in LMICs

Learning from approaches used to estimate disease burden in HIV, TB and malaria?

- Annual reports
  - HIV: 13th since 2002
  - TB: 18th since 1997
  - Malaria: 5th since 2008
- Based on data from 197 countries or 59 countries (malaria)

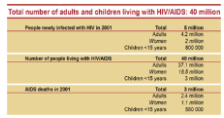
Data:

- Disease burden, incidence, deaths (adults/children)
- Trends in scale-up of interventions and impact on disease burden
  - *HIV*: no eligible/receiving ART/PMTCT
  - *TB*: no HIV tested, given IPT
  - *Malaria*: access to LLINs, RDTs, ACTs
- Progress towards global targets
- Drug (and insecticide) resistance
- International/domestic financing

We have come a long way….
18 WHO global TB control reports (1997– 2013)

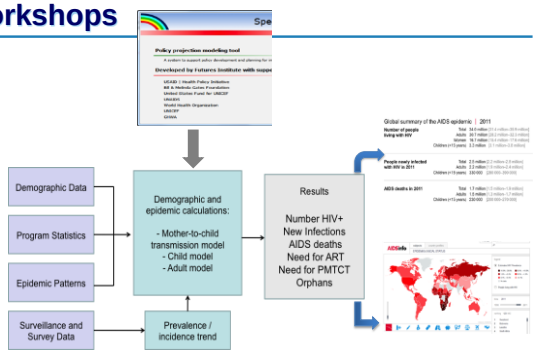
History and process of developing HIV estimates

- Late 1990s regional and global estimates of people living with HIV calculated in Geneva
- Since 2003 estimates developed through country-led process
  - **Country-led process**: UNAIDS and partners support workshops every 2 years attended by country teams to train on software
  - Country teams use country data to produce national estimates
  - Consensus on inputs by national programme managers and on results by stakeholders



HIV Estimates Workshop Schedule: March-May 2013
Sub-Saharan Africa
13-15 & 18-20 March (Johannesburg, South Africa)
10-12 & 15-17 May (Dakar, Senegal) [French]
Asia
22-26 April & 29 April-3 May (Bangkok, Thailand)
Middle East and North Africa
13-15 May (Egypt)
Eastern Europe & Central Asia
20-23 May (Tashkent, Uzbekistan) [Russian]
South & Central America
15-17 & 22-24 May (Panama City, Panama) [Spanish]
Caribbean
21- 23 May (Port of Spain, Trinidad & Tobago)

Process of deriving HIV estimates at workshops



To access data: http://www.unaids.org/en/dataanalysis/datatools/aidsinfo/
or www.aidsinfoonline.org

Models and estimates have improved over time

- Improved surveillance by countries
  - Increasing no. of nationally-representative household surveys (Calibrates HIV prevalence from antenatal clinics)
- Improved assumptions based on evolving research
- Improved curve fitting models
  - From 4 parameter model to model that allows variation in force of infection over time
- Changes made based on recommendations of *UNAIDS Reference Group on Estimates, Modelling and Projections*
  - Methods published in peer-reviewed journals
  - Incorporated into software on a regular basis

What do we know now (and not know)?
(HBV, HCV and co-infection prevalence and burden)

- Evolution of WHO and other estimates
- Data Limitations and other challenges

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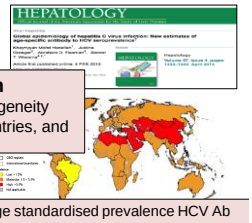
WHO sponsored systematic reviews and hepatitis prevalence and burden estimates

HBsAg

- Age- sex and region-specific prevalence
- 1990 and 2005, 21 GBD regions
- 396 studies
- (3.7%) 240 million HBsAg pos in 2005
- Significant decrease in prevalence temporally related to HBV immunization

HCV Ab



- Age standardised prevalence HCV Ab
- 1990 and 2005, 21 GBD regions
- 232 studies
- (2.8%; UI 2.6-3.1) > 185 million HCV Ab in 2005
- Significant increase in prevalence from 2.3% to 2.8%

Limitation
Did not capture heterogeneity across and within countries, and sub-populations

Seroprevalence of HCV and estimated numbers of persons infected

Region	Prevalence (%)	Estimated number of people infected
Asia Pacific	1.4	>2.4 million
Central Asia	3.8	>2.9 million
East Asia	3.7	>50 million
South Asia	3.4	>50 million
South-East Asia	2.0	>11 million
Australasia	2.7	>0.6 million
Caribbean	2.1	>0.7 million
Central Europe	2.4	>2.9 million
Eastern Europe	2.9	>6.2 million
Western Europe	2.4	>10 million

Source: Hannafiah et al. Hepatology 2013

High prevalence does not always equate to high burden

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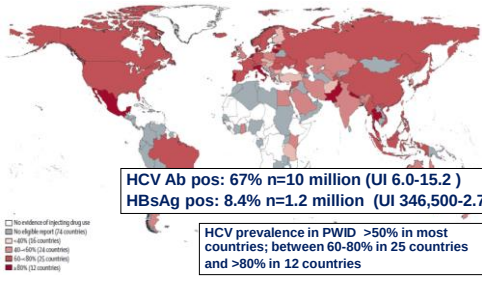
Prevalence of HCV among PWID in 77 countries (82% of global PWID pop)



HCV Ab pos: 67% n=10 million (UI 6.0-15.2)
HBsAg pos: 8.4% n=1.2 million (UI 346,500-2.7)

HCV prevalence in PWID >50% in most countries; between 60-80% in 25 countries and >80% in 12 countries

Nelson et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet, 378 (9791), 2011.

Other WHO hepatitis related estimates

Blood safety

Hepatitis C virus prevalence/reactivity in blood donations as reported in the WHO Global Database on Blood Safety 2008

Immunization

Number of countries having introduced HepB vaccine* and global infant HepB3 coverage, 1989-2012

Injection safety

Evolution of the Global Use of Unsafe Medical Injections, 2000–2010

Jacques Pépin*, Claire Nour Abou Chakra, Eric Pépin, Vincent Nault

nt J STD AIDS. 2004 Jan;15(1):7-16.
The global burden of disease attributable to contaminated injections given in health care settings.

Injecting drug use, UNODC Report 2014

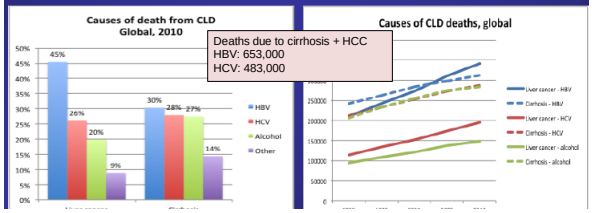
Nos of PWID; Prevalence of HIV, HBsAg and HCV in PWID by country and region

Country-specific modelling of HCV epidemic and impact of treatment in 16 countries

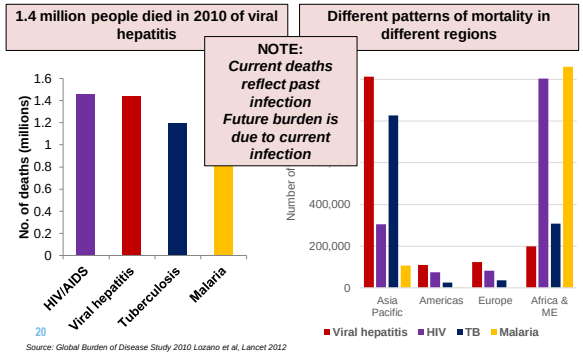
- Aim to develop consensus estimates on size of HCV population based on:
  - Systematic review of best available published and unpublished data
  - Face to face meetings with input from expert panel.
- Focus on high income countries (exception of Egypt, Brazil and Turkey)
  - convenience sample
  - If no country data available use of data from countries with similar health care practice and risk factors
- Used modeling to estimate the number of infections in 2013 and disease burden in the future.

Global Burden of Disease, 2010 Deaths – Cirrhosis and Liver Cancer

- 750,000 liver cancer deaths and 1.03 million cirrhosis deaths
- Total deaths increased from 1.25 to 1.75 million per year
- An increasing proportion due to liver cancer
- HBV associated with 45% of liver cancer & 30% of cirrhosis
- HCV and alcohol each cause approximately 25% of deaths



Estimated annual deaths from selected causes globally and by region,



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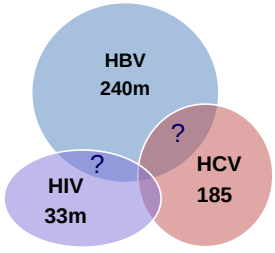
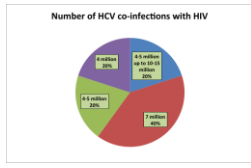
Source: Global Burden of Disease Study 2010 Lozano et al, Lancet 2012

The biggest problem - its the data…

- **Big gaps**
  - **Limited scope:** Few studies from developing/transitional countries
  - **Selective in geographic coverage:**
    - Regional data often based on one country eg. India or Thailand in S/SE Asian region; Nigeria and S. Africa in SSA.
    - Only one city/region of country
  - Limited data on co-infection
- **Unrepresentative samples**
  - Samples poorly representative of gen population, or representative of only one part of population (eg. pregnant women, blood donors)
  - Undersampling of high prevalence groups eg. homeless, prisoners that have higher HCV prevalence.
- **Use of inaccurate diagnostic tests:** 1st and 2nd generation HCV antibody assays with false positives

Burden of HIV, HBV and HCV infection and co-infection





Variability in estimates of HIV-HCV coinfection cited in literature

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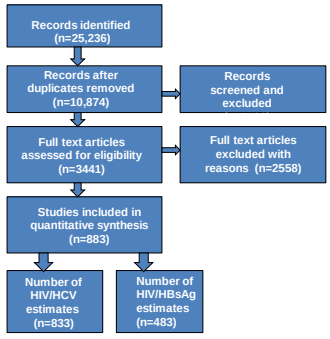
Global Systematic review of prevalence of HIV/HBsAg and HIV/HCV Ab co-infection

- Based on prevalence studies in:
  - HIV+ persons stratified by risk group (where available) OR
  - Gen pop surveys reporting HIV/HCV or HBV co-infection
- **Key features**
  - Databases searched: *Medline/Embase, Cinahl, Global Health, Popline, Web of Science, Cochrane, AWI, IMSEAR, WPRIM, IMEMR, LILACS.*
  - Non-English language
  - Unpublished country serosurveys identified via WHO regional offices
  - Survey conducted 2002 – 2013
  - Sample size > 50 HIV + cases
  - Excluded studies if populn recruited on basis of HCV Ab



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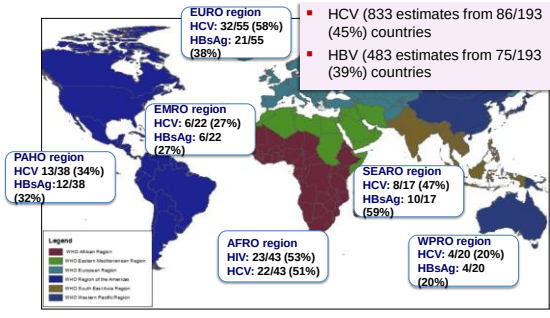
Availability of country data by WHO regions



- HCV (833 estimates from 86/193 (45%) countries
- HBV (483 estimates from 75/193 (39%) countries

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Available data (no. studies) by population

Population	HCV n	HBV n
Gen popn: household, blood donors, pregnant women	29	29
PWID: >75% PWID + PLHIV	120	25
MSM: +PLHIV	78	32
PLHIV-Hetero:	67	70
Mixed	185	158
Other: prisoners, STI, homeless etc	175	160
Children	9	8

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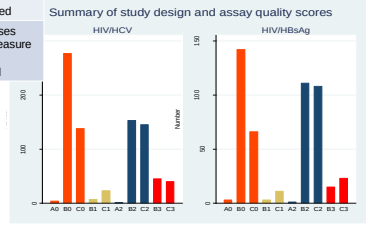
Study Quality rating

Study design	
A	Multi-site study with large sample (>1500 HIV cases) - study design appropriate for measuring prevalence - age, sex and HIV risk categories reported
B	>1 site study with I>200 HIV cases - study design not specifically designed to measure prevalence - some HIV risk categories reported
C	Single site study with <200 HIV cases - study design not designed to measure prevalence - few HIV risk categories reported

Assay quality	
0	Assay type not specified
1	1st generation HCVAb or HBsAg rapid test: No confirmatory test
2	2nd/3rd generation HCVAb or HBsAg rapid test: No confirmatory test
3	2nd/3rd generation HCVAb or HBsAg rapid test: + Confirmatory test



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Summary of HCV-HIV prevalence 314 estimates 5 populations and 11 regions

	Mid-point co-infection prevalence (Interquartile range) **Number of studies**				
	Gen pop	**PWID**	**MSM**	**Hetero**	**Pregnant**
East Africa	1.3% (0-4.9) **5**	71 % (42-99) **2**	20%(1-38) **2**	4% (3-9) **10**	0.6% (0.1-5) **3**
Cental and West Africa	5 % (2-12) **9**		8% **1**	8% (4-12.4) **19**	10.1 (5-16) **4**
South Africa			2% **1**	0.5% (0-1) **3**	
Latin America	7% (0.8-16.1) **3**	82% (52-88) **4**	4% (0-16) **6**	11% (8-15) **2**	10% (5-18) **4**
North America		84 (41-89) **25**	13 (8-15) **16**	12 (9-25) **9**	4% **1**
South East Asia	5% (3-29) **7**	90 (86-97) **18**	6% (5-8) **5**	5% (1.5-7) **5**	
Eastern Europe and Central Asia		82% (68-95) **8**			
Europe	6% (0.3-30) **3**	82% (53-91) **41**	8% (4-17) **40**	11% (4-23) **11**	3% **1**
East Med	1% **1**	81% (74-89) **7**			
East Asia		96% (80-98) **15**	4% (2-9) **3**	51% (6-89) **7**	
Western Pacific			9% (7-10) **4**		

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Summary of HBsAg-HIV from 170 estimates in 5 populations and 11 regions

	Gen pop	PWID	MSM	Hetero	Pregnant
	Mid-point co-infection prevalence (Interquartile range) **Number of studies**				
East Africa	8% (6-11) **10**		9% **1**	6.5%(5-10) **10**	4% (2-5) 2
West, Central Africa	11% (6-15) **11**		22% **1**	12% (8-20.5) **32**	9% (0-13) **3**
South Africa			6.5% **1**	7% (5-20) **7**	5% (3-6) **2**
Latin America	1% (0.6-2) **3**	27% **1**	9% (6-11) **5**	3% (2-7) **4**	0.5% (0.5-1.8) **3**
North America		7% **1**	5% (5-6) **2**	17% **1**	
South East Asia	2% (1-2) **2**	18% (10-20) **10**	15% (10-19) **6**	9% (0-15) **10**	
Eastern Europe and CAR					
Europe		4% (3-7) **3**	5% (4-6) **9**	7% (2-11) **2**	
East Med	10% **1**	8% (4-44) **6**			
East Asia		9.5% (2.5-37) **4**	12% (10-13.5) **4**	5% (4-6%) **4**	
Western Pacific			4% (3-5) **6**		

How do we get to where we want to be?

- Next steps for WHO and countries

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New World Health Assembly Hepatitis Resolution (May 2014)

WHO mandated to:

- Provide technical support to Member States to:
  - Develop national viral hepatitis strategies and plans
  - Improve surveillance systems
- Develop systems to:
  - Set global targets and indicators
  - Monitor and report global progress
  - Estimate burden of disease and associated impact
- Develop guidance to:
  - Prevent, diagnose, care for and treat hepatitis
  - Integrate hepatitis into existing health programs

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What is WHO response? Global Hepatitis Framework

Axis 1: Awareness raising: Partnerships, resource mobilization and communication

Axis 2: Evidence-Based Policy and Data for action

Axis 3: Prevention of virus transmission

Axis 4: Screening, care and treatment

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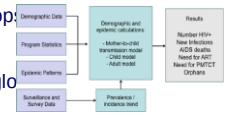
Axis 2: WHO priorities and activities

- ☑ Publish global prevalence and burden estimates for viral hepatitis
- ☑ Develop guidelines for hepatitis surveillance in low- and middle-income countries and conduct regional adaptation workshops
- Conduct country hepatitis burden-of-disease and national planning workshops
- Develop a monitoring and reporting framework for assessing country and glo hepatitis response; Predictive model
- Establish modelling reference group

	HCV	HBsAg
Infected	170-185 million (130-150m active)	240 million
Deaths per year	(483,000) 500,000	(653,000) 700,000



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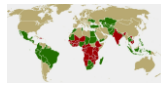
Challenges and next steps for countries

- Priority is to improve coverage and quality of primary data collection for prevalence and disease outcomes:-
  - vital registration systems
  - Representative, population-based and risk group seroprevalence surveys
  - Potential to "piggy-back" onto DHS
  - Use of accurate diagnostic tests



- Transparency of estimates and models; publicly available
- Evidence gaps:
  - Acute HBV and HCV; No. of persons in need HCV/HBV treatment; MTCT; Drug resistance; Advanced liver disease
  - Data in children and adolescents

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Acknowledgements

Systematic Review Team

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Hande Harmanci

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Txema Calleja

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World Hepatitis Day 28th July 2014

#thinkhepatitis

- **WHO World Hepatitis Day 2014 page live in Arabic, Chinese, English, French, Spanish and Russian**
- **18 July: WHD14 promotional banner across WHO website**
- **23 July: WHO HQ participating in Geneva and Melbourne news conferences**
- **25 July: WHO webpages updated with WHD14 stories, features and reports**
- **28 July: WHD14 global social media outreach on twitter, facebook**

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