

Challenges in the elimination of hepatitis B

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Outline

- Challenges to reduce mortality
 - Diagnosing the undiagnosed
 - Addressing migrant health
 - Treatment
- Challenges to reduce incidence
 - Vaccination

Accelerating the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission

Graham S Cooke, Isabelle Andrieux-Meyer, Tanya L Applegate, Rifat Atun, Jessica R Burry, Hugo Cheinque Charles Gore, Max G Griswold, Saeed Hamid, Margaret E Hellard, JinLin Hou, Jess Howell, Jidong Jia, Nata Maud Lemoine, Olufunmilayo A Lesi, Liudmyla Maistat, Brian J McMahon, Homie Razavi, Teri Roberts, B C Wendy Spearman, Bridie E Taylor, David L Thomas, Imam Waked, John W Ward, Stefan Z Wiktor, on behalf of Hepatology Commissioners*

WHO region	WHO region						World	2020 target	2030 target
	African	Americas	E Med	Euro	SEA	W Pacific			
Population (million)	1000	989	654	914	1945	1867	7369		
Prevalence chronic HBV (%)	6.1%	0.7%	3.3%	1.6%	2%	6.2%	3.5%		
Prevalence chronic HCV (%)	1%	0.7%	2.3%	1.5%	0.5%	0.7%	1%		
Indicators									
Timely birth dose vaccine (%)	10%	72%	23%	39%	34%	84%	39%	50%	90%
Third dose HBV vaccine (%)	76%	89%	80%	81%	87%	90%	84%	90%	90%
Blood donations screened (%)	80%	98%	81%	99.9%	85%	98%	97%	95%	100%
Needle/syringe distribution (per 1000 people)	6	22	25	59	29	57	27	200	300
Needle/syringe reuse (%)					5.2%	3.2%	5%	0%	0%
Injection safety (%)					2.6%	2%	9%	30%	90%
Injection safety (injection safety)					8.7%	21.5%	20%	30%	90%
Injection safety (injection safety)					<1%*	10%*	5%*	5 million	80%
Injection safety (injection safety)					7.1%	4.8%	7.4%	3 million	80%
Cumulative incidence of HBV in under 5s (%)	3%	0.2%	1.6%	0.4%	0.7%	0.9%	1.3%	130%	190%
Incidence HCV (/100 000)	30.9	6.4	62.5	61.8	14.8	6	23.7	130%	190%

WHO region	WHO region					
	African	Americas	E Med	Euro	SEA	W Pacific
Population (million)	1000	989	654	914	1945	1867
Proportion of chronic HBV diagnosed (%)	0.3%	9.1%	1.8%	14%	2.6%	2%

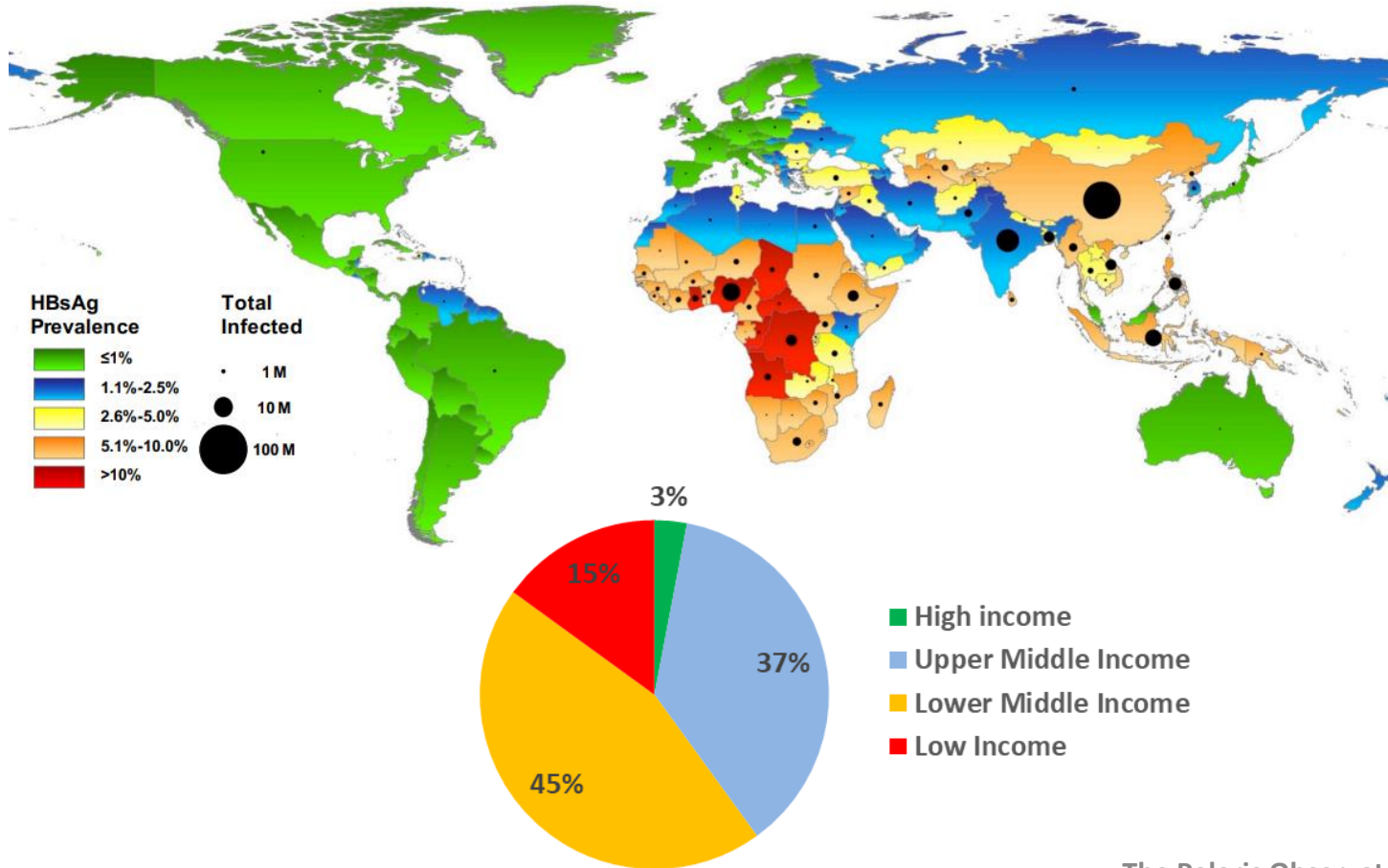
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Routine reporting from countries
 Estimates meeting standards defined by GATHER (gather-statement.org)
 Other estimates (including modelling)
 Extrapolation and inferences

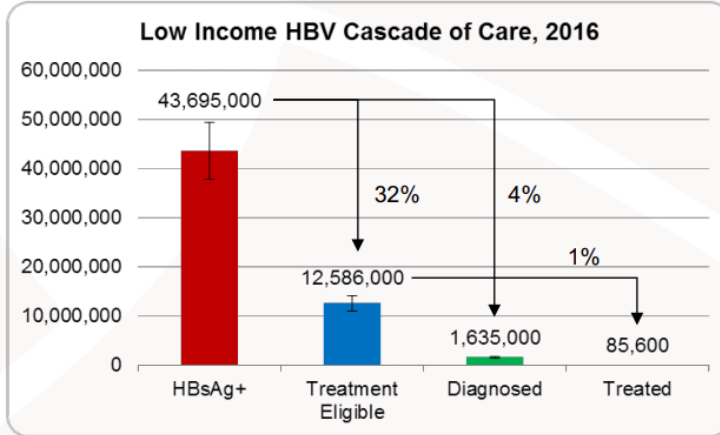
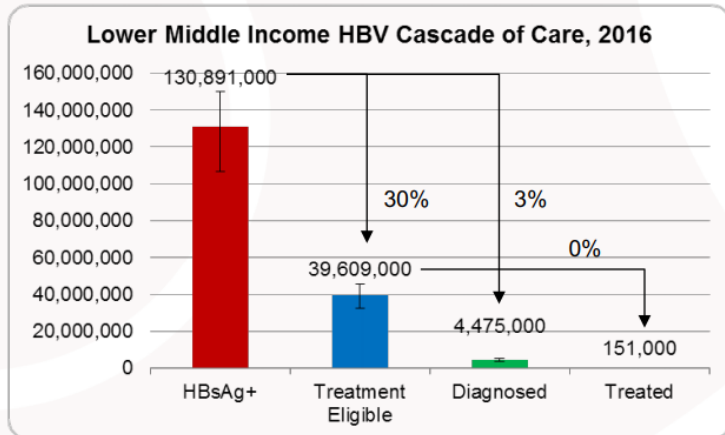
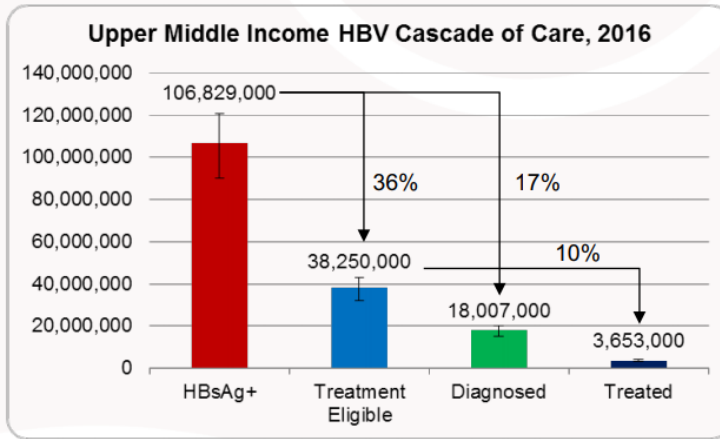
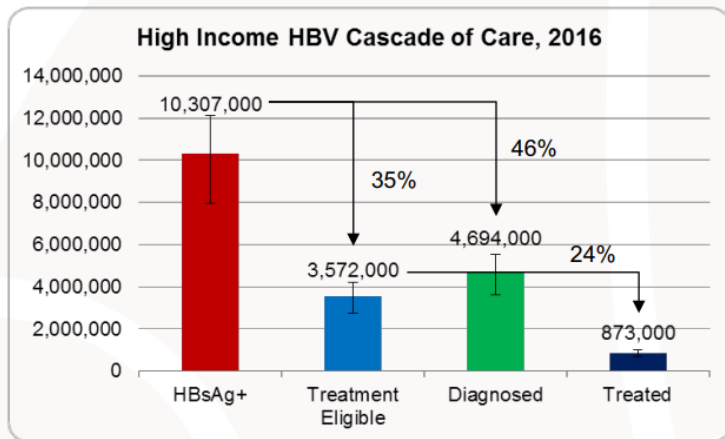
Figure 2: Baseline estimates (2015) of progress towards elimination targets

Society (Reference)	Screening recommendations
<p>APASL (Sarin <i>et al</i>, Hepatol Int 2016)</p>	<p>High-risk groups, irrespective of prevalence and socioeconomic status</p>
<p>EASL (J Hepatol 2017)</p>	<p>No specific guidance, except among pregnant women</p>
<p>AASLD (Terrault <i>et al</i>, Hepatology 2018)</p>	<p>Persons born in regions with HBsAg prevalence of $\geq 2\%$ or US-born persons not vaccinated as an infant whose parents were born in regions with HBV endemicity $\geq 8\%$, pregnant women, people needing immunosuppressive medications including chemotherapy, blood donors, patients with end-stage renal disease, and other at-risk groups</p>
<p>WHO (www.who.org, 2015)</p>	<p>Universal screening in countries with HBsAg prevalence $\geq 2\%$, risk-based in other countries</p>
<p>ALEH (Gadano <i>et al</i>, Acta Gastroenterol Latinoam 2011)</p>	<p>No specific guidance</p>
<p>INASL (Arora <i>et al</i>, J Clin Exp Hepatol 2018)</p>	<p>No specific guidance</p>
<p>CSH/CMA/CSID (Hou <i>et al</i>, J Clin Transl Hepatol 2017)</p>	<p>No specific guidance</p>
<p>GHASSA (Wendy Spearman <i>et al</i>, Lancet Gastroenterol Hepatol 2017)</p>	<p>Risk-based and pregnant women</p>

In 2016, 60% of HBV infected persons were living in Low or Lower Middle Income countries



HBV Cascade of Care According to World Bank Lending Classification



The hurdles to diagnose HBV

- Lack of political will
- Lack of awareness, advocacy
- Lack of infrastructure
- Poor quality assays (no WHO prequalification)
- In LMIC, the cost of diagnostics can be higher than the cost of generic medicines

DISEASE AREAS



ANTIMICROBIAL
RESISTANCE



HEPATITIS C & HIV



MALARIA & FEVER



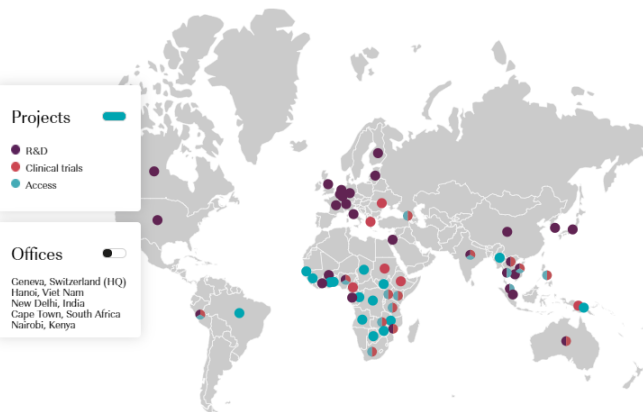
NEGLECTED
TROPICAL DISEASES



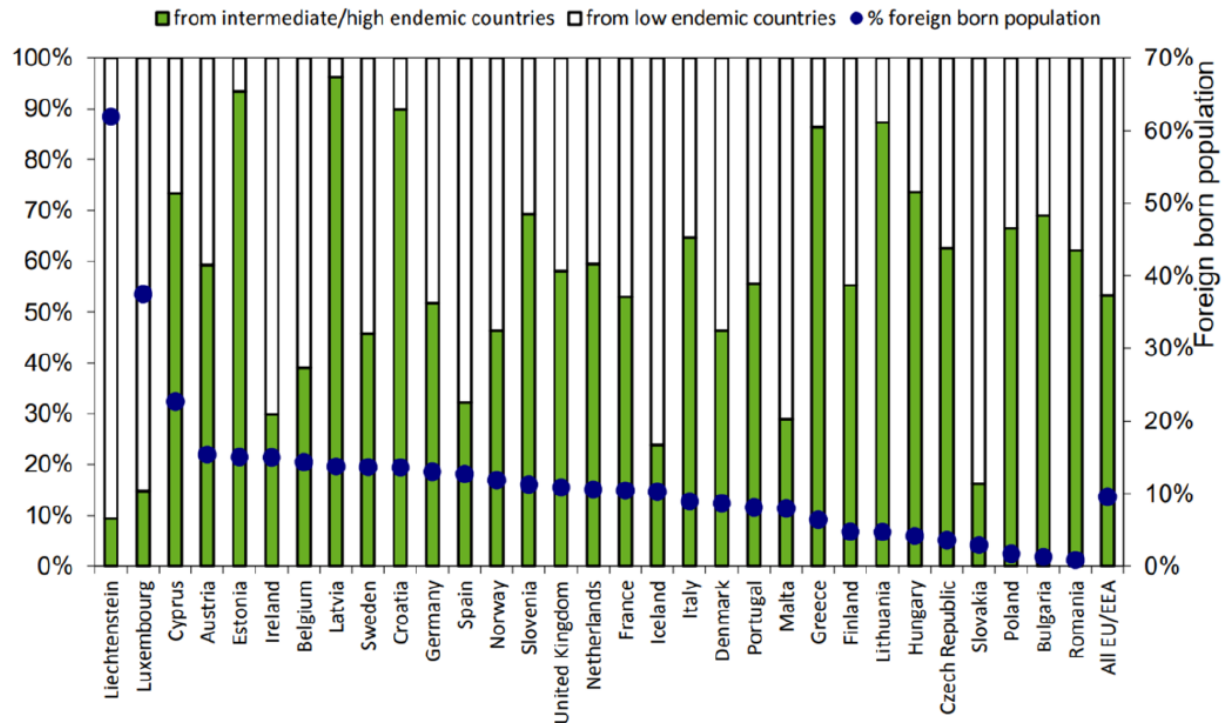
PANDEMIC
PREPAREDNESS



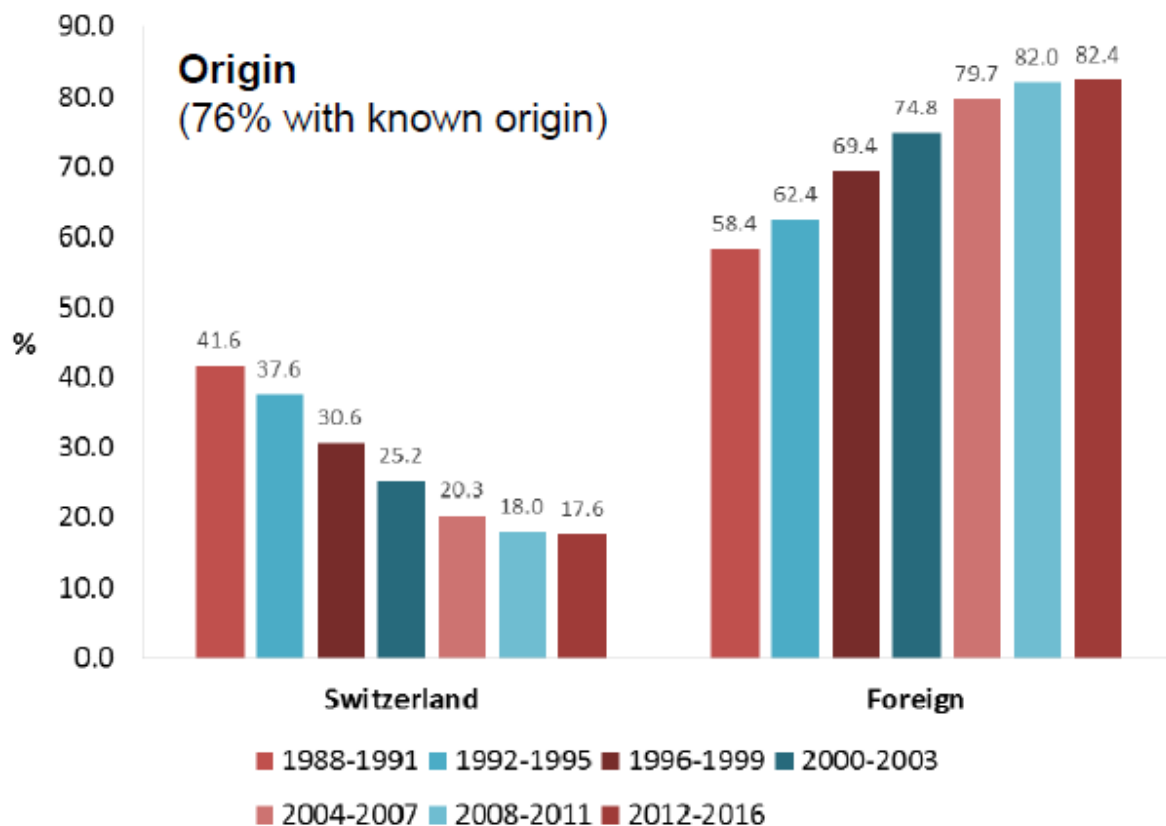
TUBERCULOSIS



Percentage of foreign-born population across the EU and proportion born in HBV endemic countries

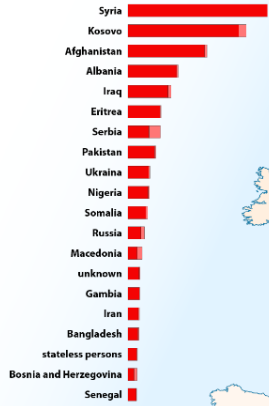


Percentage of foreign-born persons among HBV cases in Switzerland, 1988-2016



European Migrant Crisis 2015

Top Countries of Origin

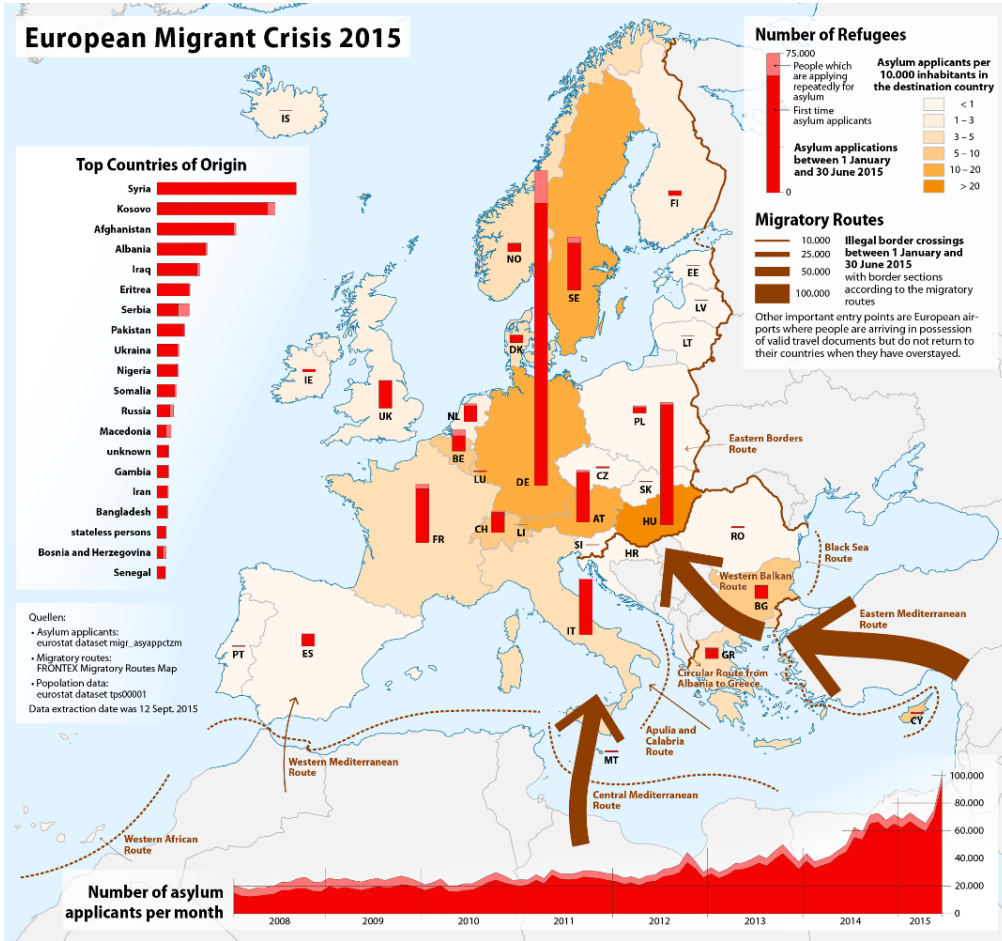
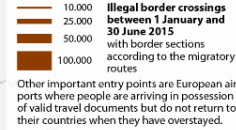


Quellen:
 • Asylum applicants: eurostat dataset migr_asypappctzm
 • Migratory routes: FRONTEX Migratory Routes Map
 • Population data: eurostat dataset tps00001
 Data extraction date was 12 Sept. 2015

Number of Refugees



Migratory Routes



Prevalence of HBsAg and immunity to HBV among immigrants

110 studies on 209,822 immigrants and refugees from intermediate or high HBV prevalence countries arriving in low prevalence countries

	HBsAg	Anti-HBs
Overall	7.2% (6.3 – 8.2)	39.7% (35.7 – 43.9)
East Asia/ Pacific	11.3% (10.3 – 12.4)	50.2% (45.8 – 54.6)
Sub-Saharan Africa		41.7% (37.6 – 45.9)
Eastern Europe/ Central Asia/ South Asia	5.8% (4.3 – 7.9)	NA
Latin America/ Caribbean/ Middle East/ North Africa	1.7% (1.1 – 2.7)	NA

Liver-related health issues among asylum seekers

- >80% of first-time asylum seekers in the EU-28 in 2017 were <35 years old

(source: EUROSTAT)

- Asylum seekers are in general healthy young males

SERRE-DELCOR *et al*, *Am J Trop Med Hyg* 2018;98:300-7

- Lower hospitalization rates for chronic medical conditions among migrants than non-migrants

TSITSAKIS *et al*, *Health policy* 2017;121:329-37

HOWEVER, asylum seekers are at risk of:

- Hepatitis A outbreaks due to overcrowding and poor sanitation in host facilities

MELHEM *et al*, *Eur J Epidemiol* 2016;31:711-4; MELLOU *et al*, *Euro Surveill* 2017;22:30448

MICHAELIS *et al*, *Emerg Microbes Infect* 2017;6:e26

- Sexual abuse and sexually-transmitted infections

DE SCHRIJVER *et al*, *Int J Environ Res Public Health* 2018;15:E1979; OLIVEIRA *et al*, *Global Health* 2018;14:48

CASTAGNA *et al*, 2018;132:1197-204; PANNETIER *et al*, *Lancet Public Health* 2018;3:e16-e23

- Social marginalization, mental health issues and substance abuse

QURESHI *et al*, *Am J Addict* 2014;23:337-42; ANAGNOSTOPOULOS *et al*, *Int J Soc Psychiatry* 2017;63:352-8

Barriers to health screening in migrants

- Lack of staff training and support
- Lack of professionalism
- Poor management
- Funding schemes, communication difficulties
- Cultural inadequacy
- Insufficient patient involvement in delivery and testing
- User-unfriendly settings

Liver Disease and Migrant Health

The current system of providing healthcare to asylum seekers and migrants is failing, resulting in unnecessary prevalence of liver disease, infection with hepatitis viruses and alcohol abuse.



In 2017, six hundred and fifty thousand first-time asylum seekers applied for international protection in the Member States of the EU.

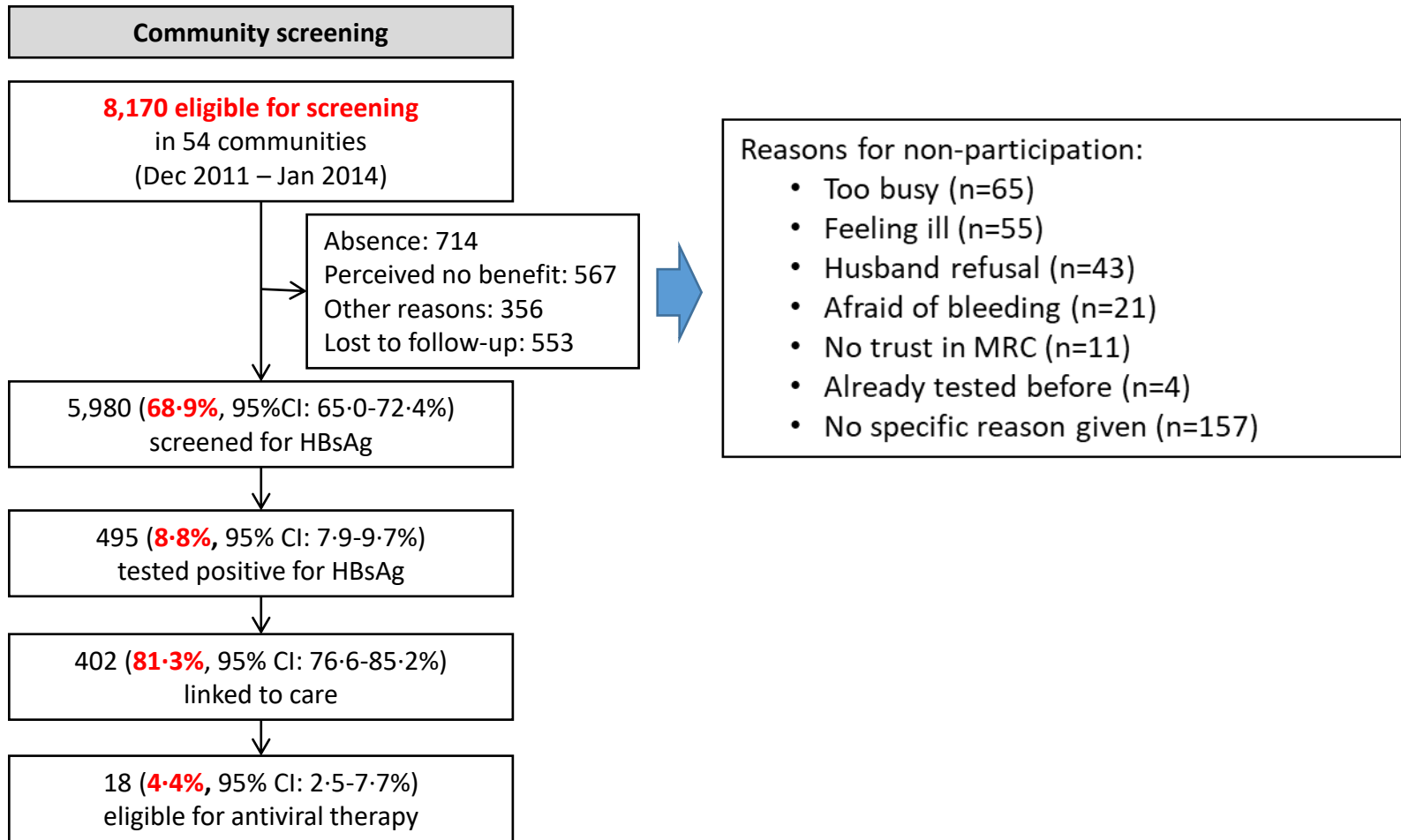


Over 80% of the first-time asylum seekers in the EU-28 in 2017 were less than 35 years old. Nearly one third were under 18 years old. Three quarters of applicants aged between 14 and 35 were male.

European governments should adopt a public health and human rights-based approach to migrant health. Asylum seekers and irregular migrants must have knowledge of their rights in health related matters and be granted access to affordable and timely healthcare treatment in patient-friendly, non-discriminatory settings.

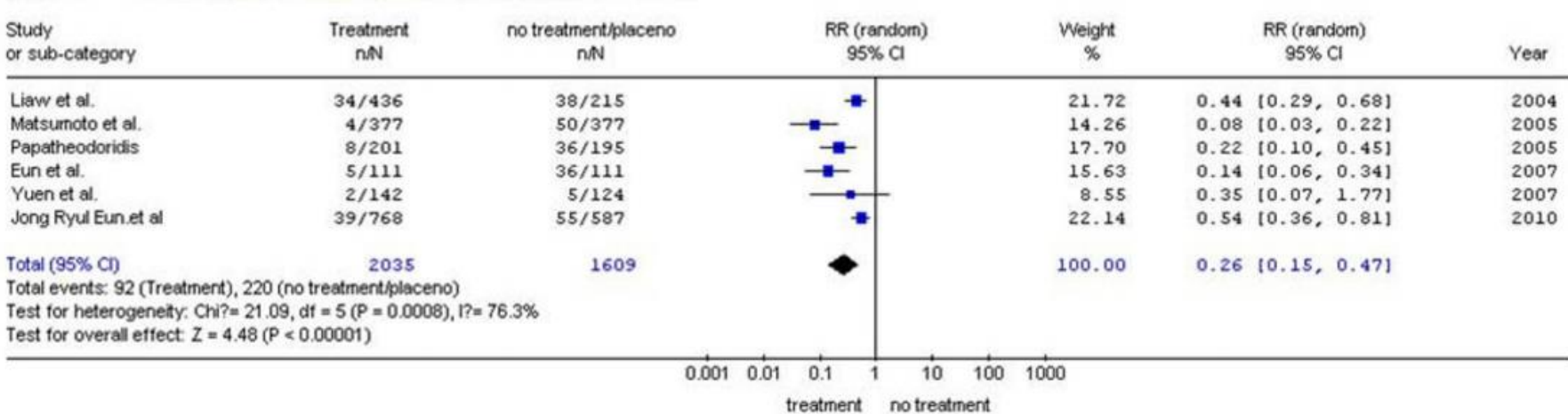
Acceptability and feasibility of a screen-and-treat programme for hepatitis B virus infection in The Gambia: the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) study

Maud Lemoine, Yusuke Shimakawa*, Ramou Njie*, Makie Taal, Gibril Ndow, Isabelle Chemin, Sumantra Ghosh, Harr F Njai†, Adam Jeng, Amina Sow, Coumba Toure-Kane, Souleymane Mboup, Penda Suso, Saydiba Tamba, Abdullah Jatta, Louise Sarr, Aboubacar Kambi, William Stanger, Shevanthi Nayagam, Jessica Howell, Liliane Mpabanzi, Ousman Nyan, Tumani Corrah, Hilton Whittle, Simon D Taylor-Robinson, Umberto D'Alessandro, Maimuna Mendy, Mark R Thursz, on behalf of the PROLIFICA investigators*



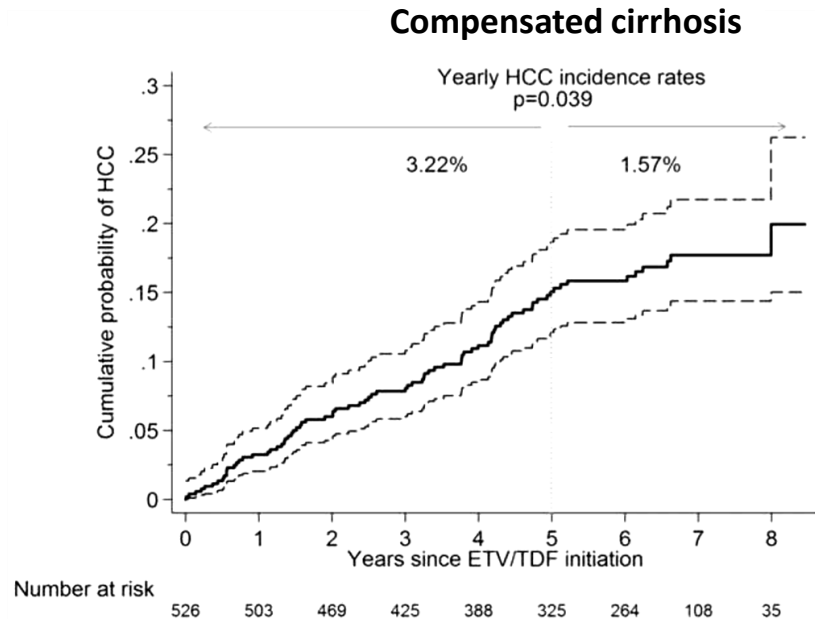
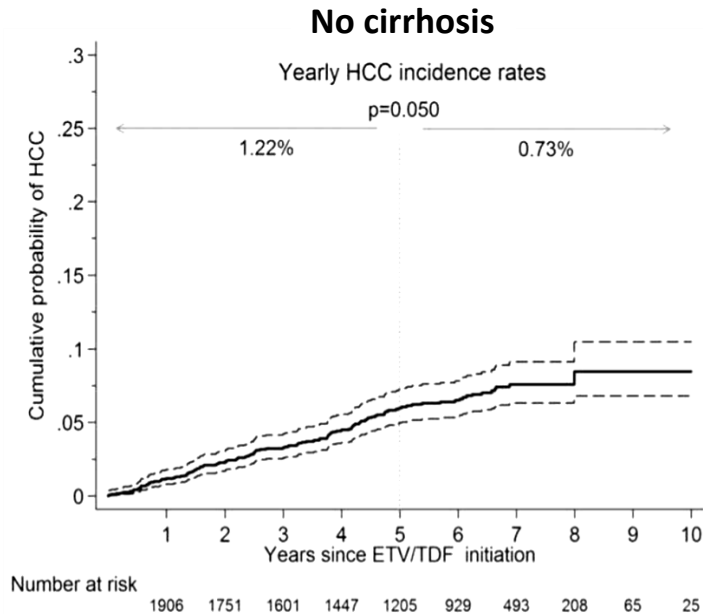
Nucleos(t)ide analogues reduce the incidence of decompensated cirrhosis, HCC or HBV-related death compared to placebo

A meta-analysis



Risk of HCC in chronic hepatitis B treated with ETV or TDF

European multicenter cohort; n=1,951 adult Caucasian chronic hepatitis B patients without HCC at baseline, treated with ETV or TDF

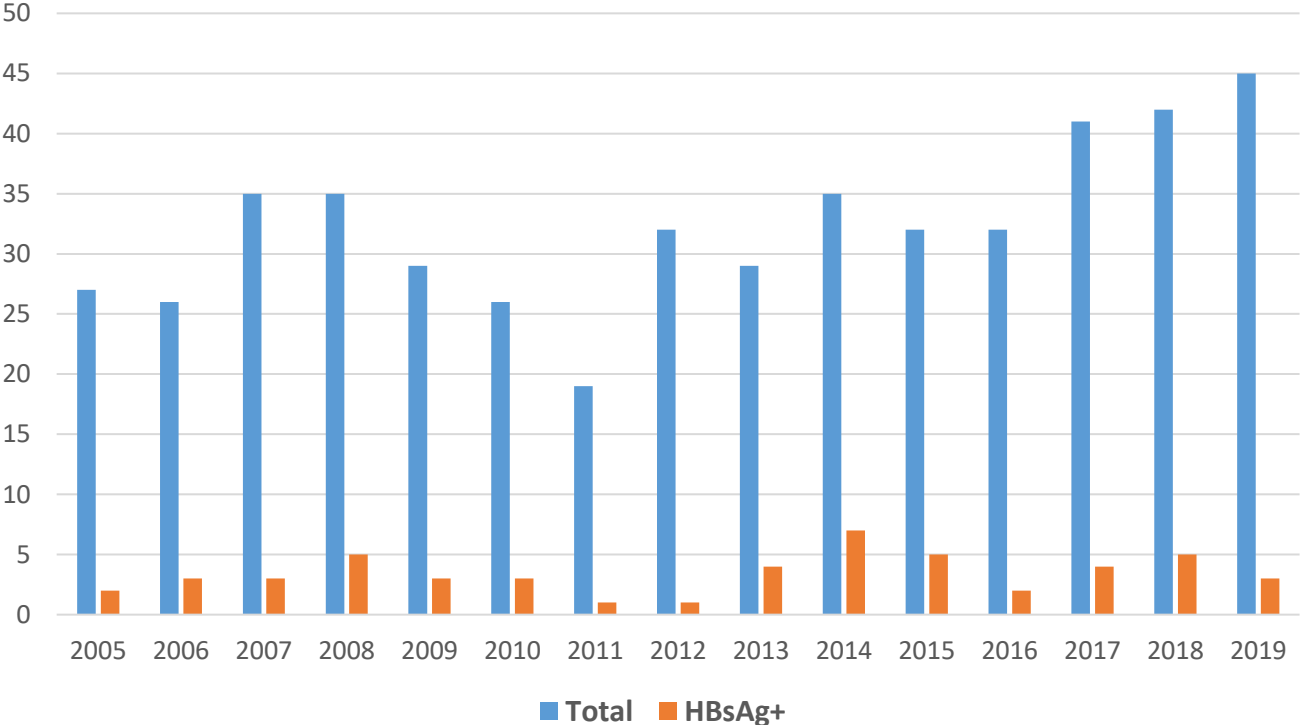


Factors independently associated with HCC after 5 years of therapy:

Age >50, thrombocytopenia (basal and after 5 years of therapy), Fibroscan ≥ 12 kPa after 5 years of therapy

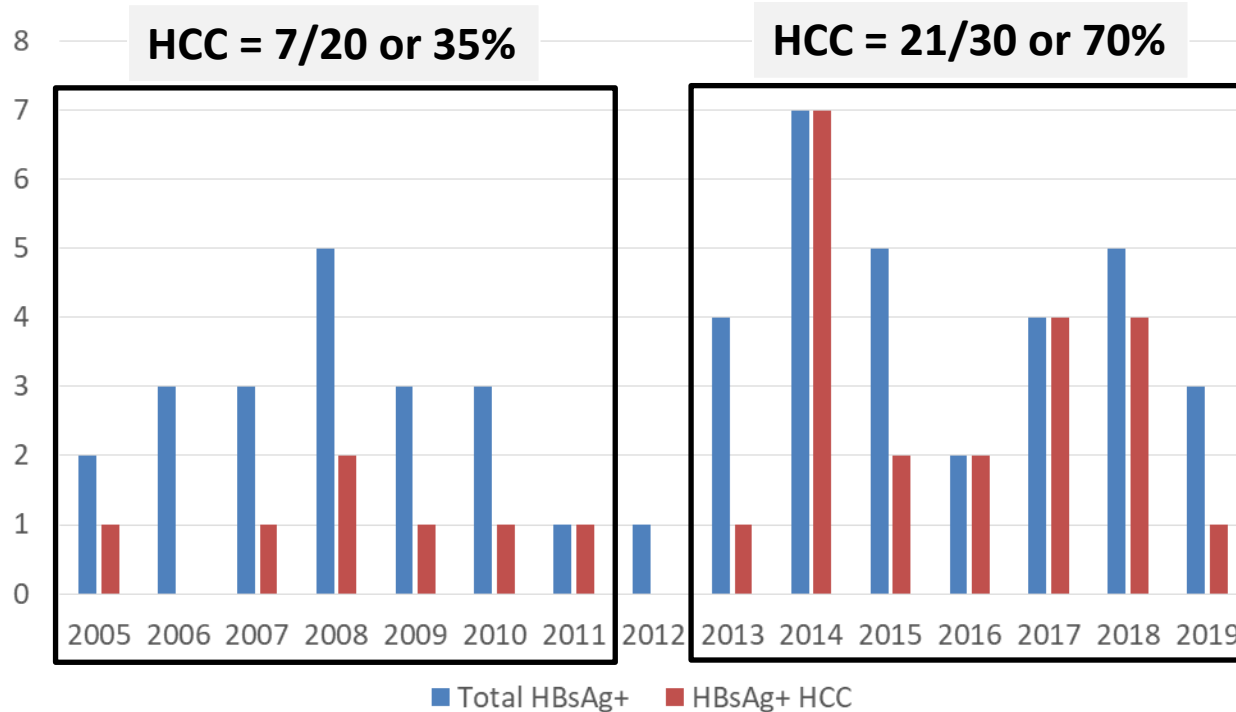
Adult Liver Transplants in Geneva, 2005-2019

HBsAg-positive (n=51) vs. total (n=485)

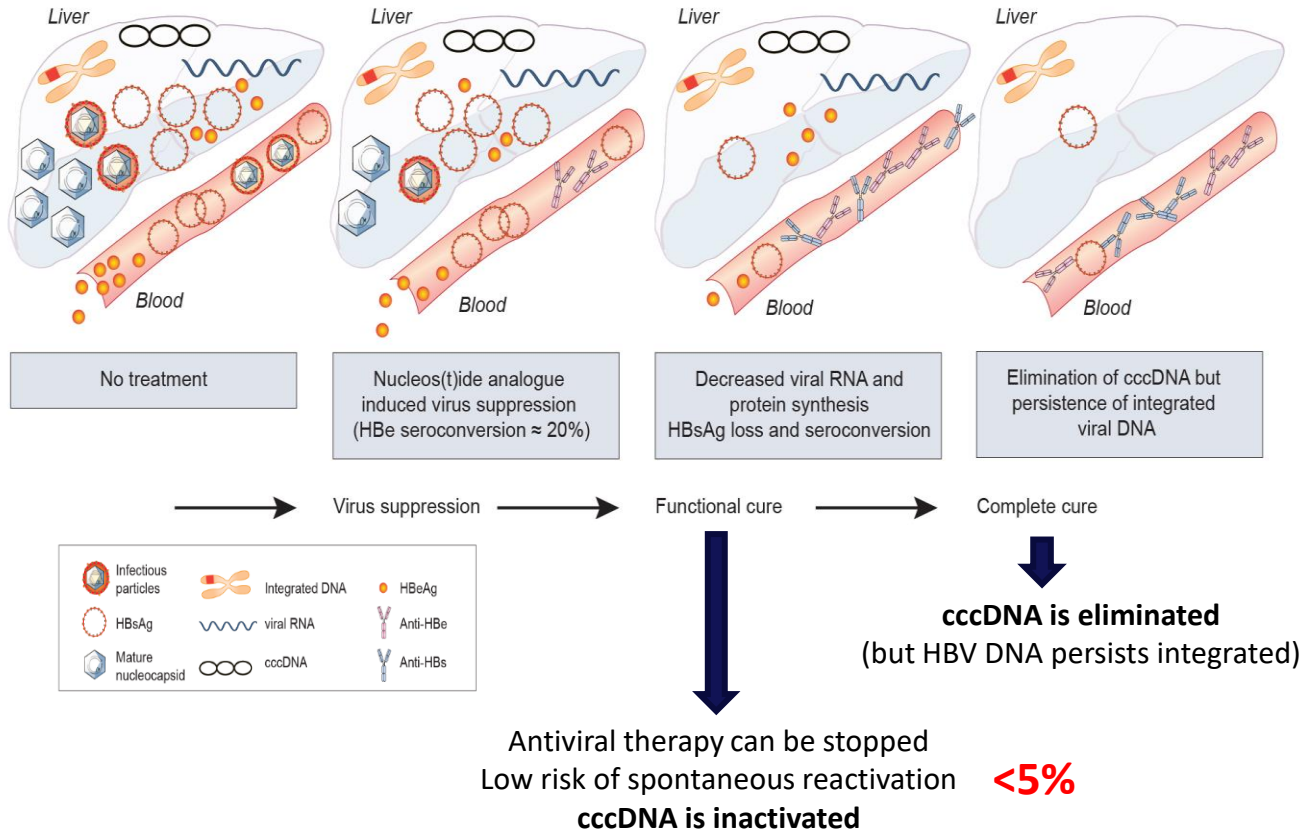


Adult Liver Transplants in Geneva, 2005-2019 (n=485)

HCC over total HBsAg+ (n=51)

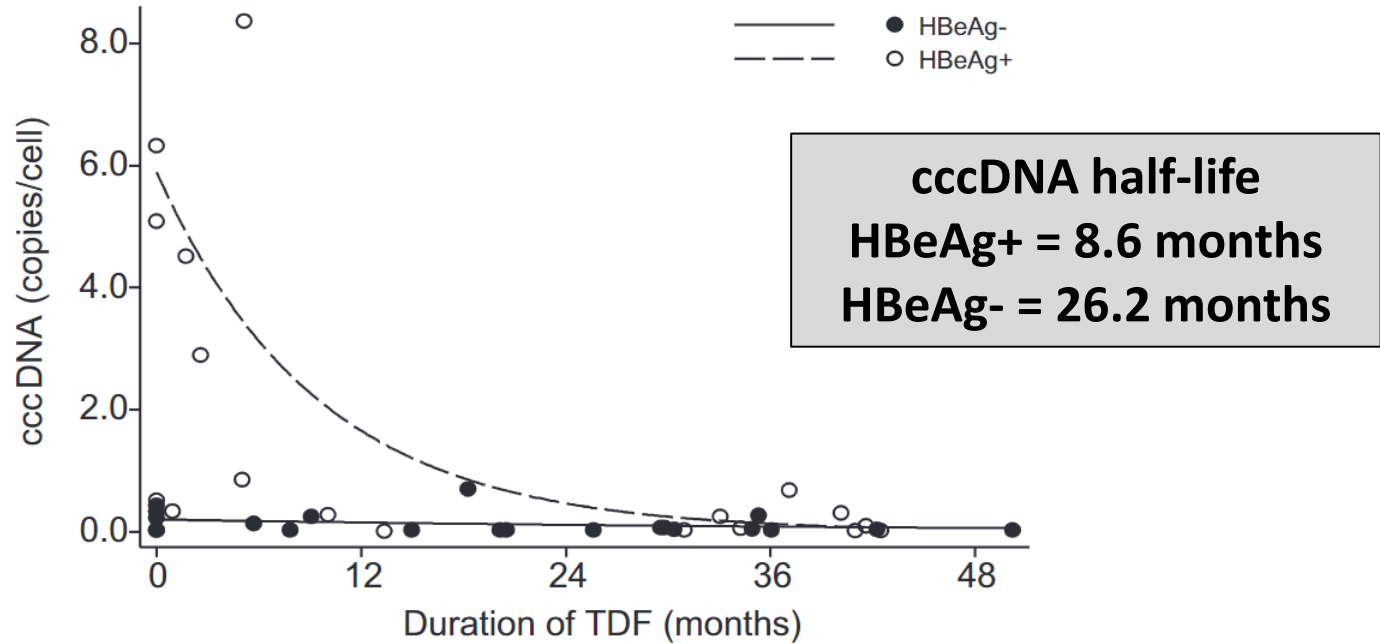


With current technologies, a complete HBV cure is unlikely

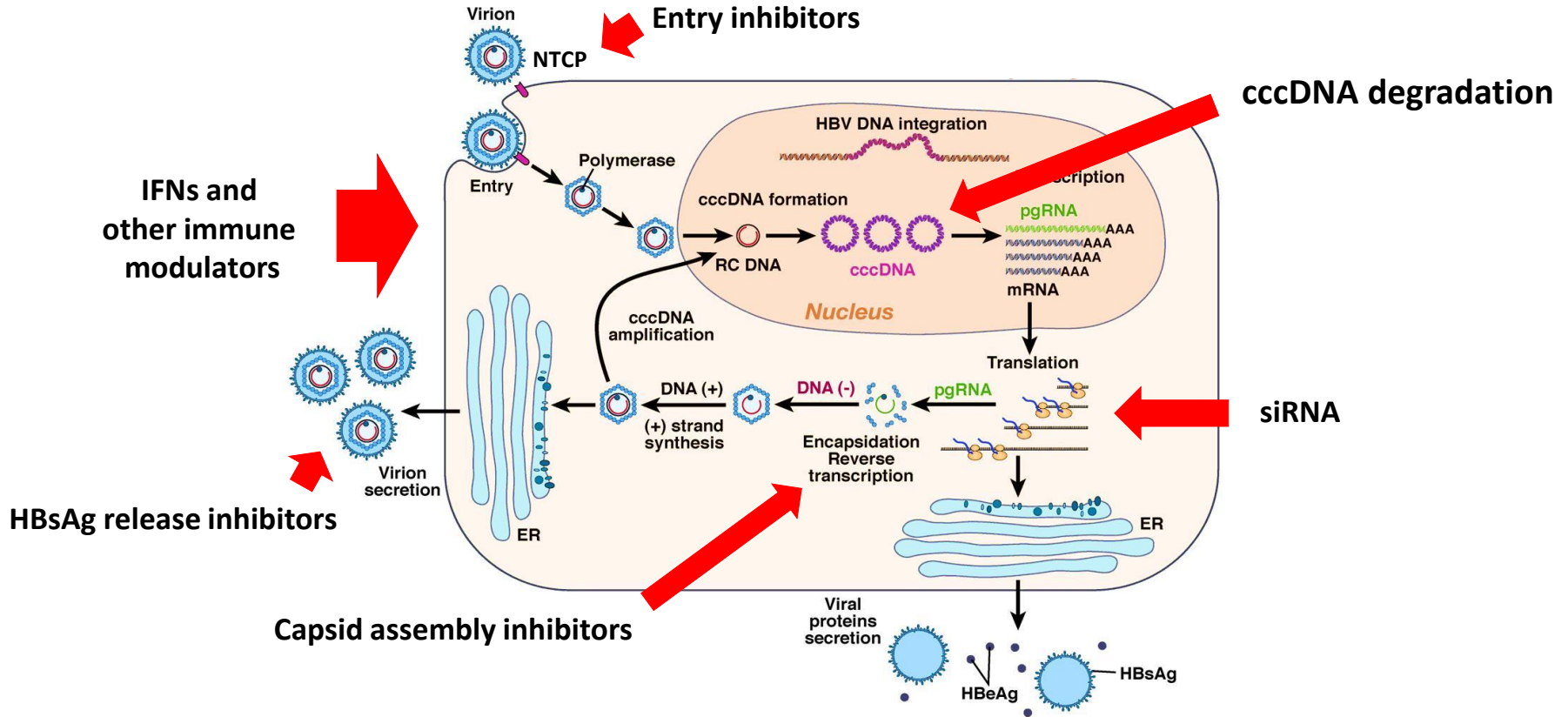


HBV cccDNA decay during TDF therapy of HIV/HBV coinfecting patients

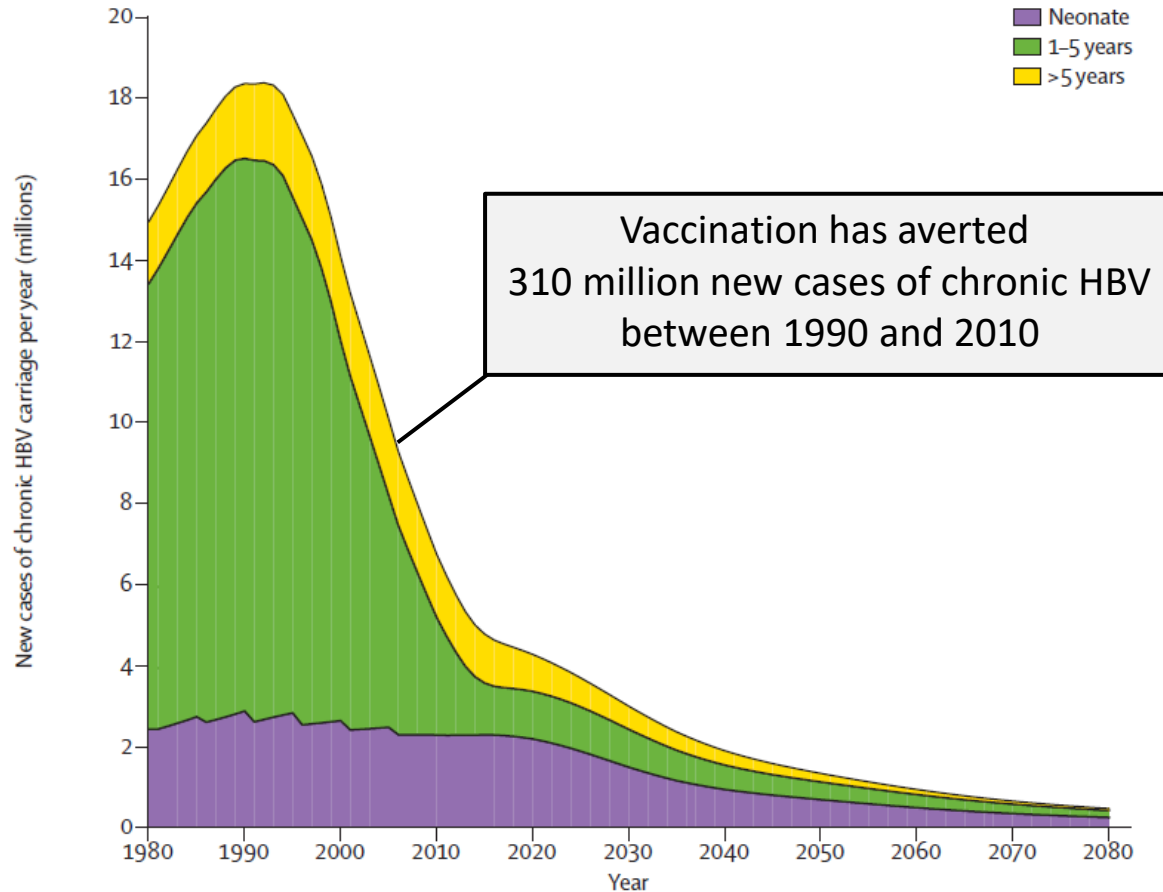
(n=27, FU 29.6 months [IQR = 15.0–36.1])



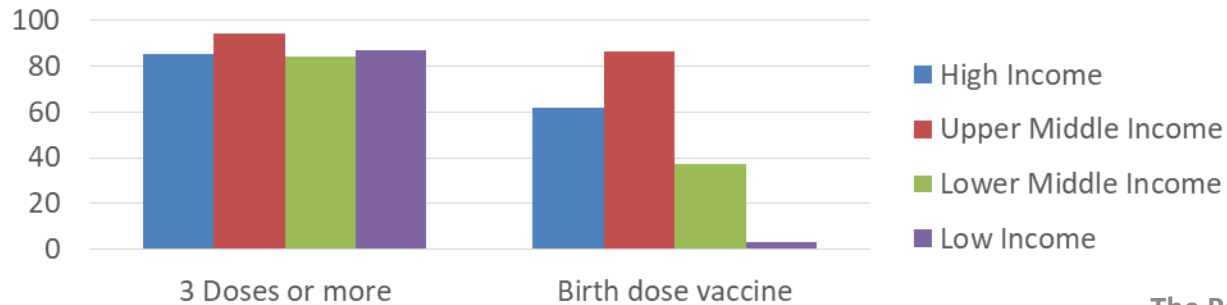
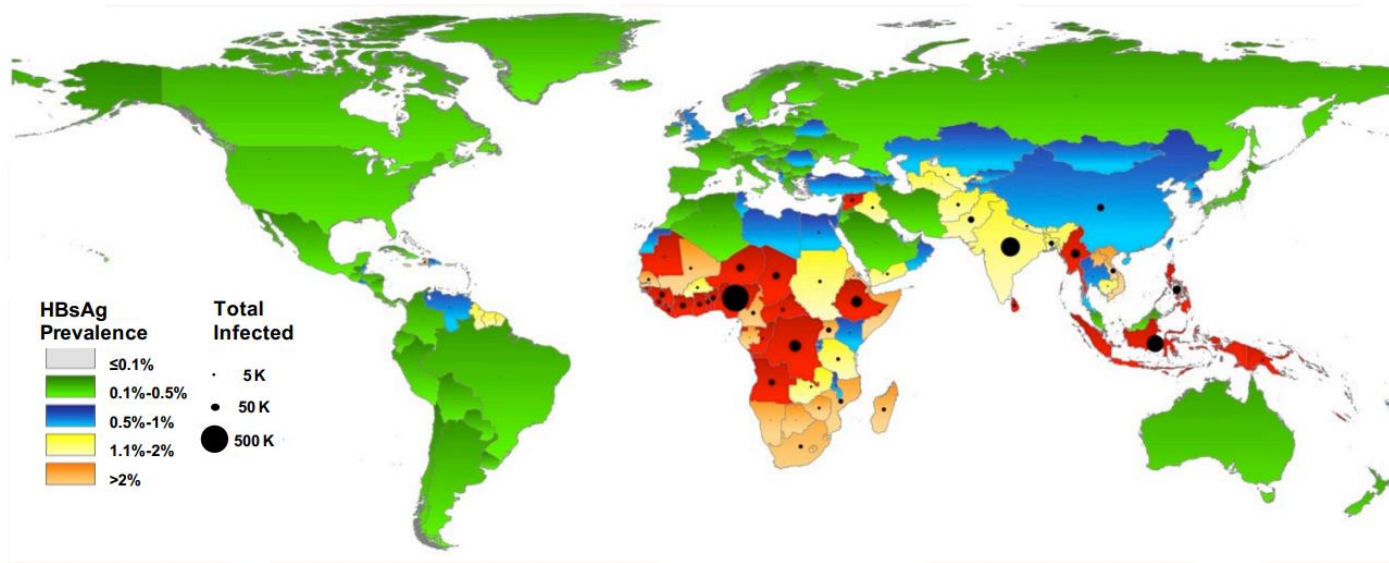
The HBV replication cycle: scope for new treatment targets



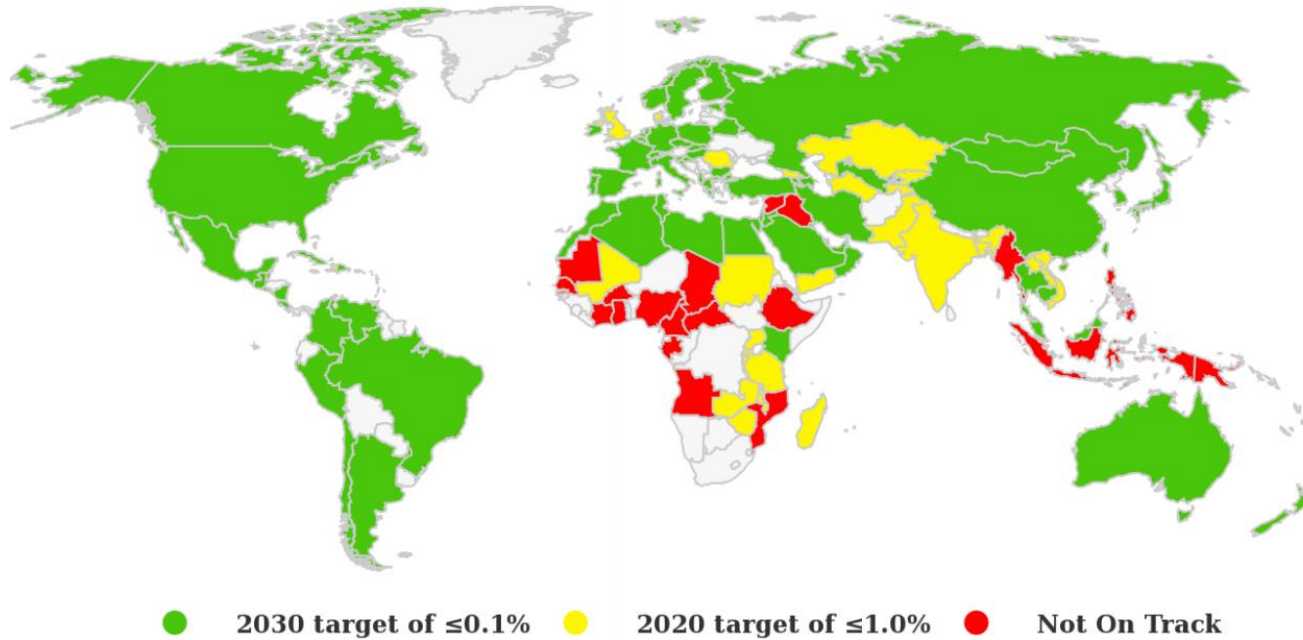
The global HBV vaccination campaign is a success story



In 2016, 1.8 million (1.6-2.2 million) 5-year-old children were HBsAg+



HBV 5-year old HBsAg prevalence elimination targets



Twenty countries are NOT on track to reach the 2030 and 2020 targets for HBV prevalence among 5-year-old children



[< BACK TO OUR ALLIANCE](#)

About our Alliance

**Gavi, the Vaccine Alliance,
helps vaccinate almost
half the world's children
against deadly and
debilitating infectious
diseases**



Antenatal and delivery care in the WHO AFRO Region coverage and impact on maternal mortality

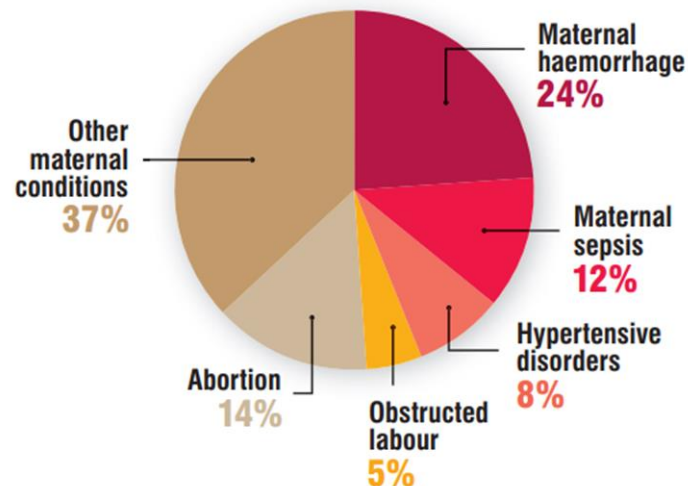
Antenatal and delivery care coverage

Region/subregions	Antenatal care coverage (%) 2000–2007		Delivery care coverage (%) 2000–2007	
	Attended clinic at least once	Attended clinic at least four times	Skilled attendant present at birth	Delivered at health institution
Sub-Saharan Africa	72	42	47	40
Eastern and Southern Africa	72	40	40	33
West and Central Africa	71	44	49	46
Middle East and North Africa	72	–	81	71
South Asia	68	34	41	35
East Asia and the Pacific	89	66	87	73
Latin America and the Caribbean	94	83	85	86
CEE/CIS*	90	–	94	89

* Central and Eastern Europe and the Commonwealth of Independent States

Source: UNICEF. *Progress for Children*, New York; 2007.

Causes of maternal death in the African Region (WHO, 2008)



In the WHO AFRO Region, every minute a woman dies in labour or suffers lifetime complications from pregnancy and delivery

How the Anti-Vaxxers Are Winning

By PETER J. HOTEZ FEB. 8, 2017



Getty Images



public health gains. The first blow will be [measles](#) outbreaks in America.

Measles is one of the most lethal of all human single person infections. A single person infected with measles can infect more than a dozen people, typically infecting those who have not received their measles vaccine. Such high levels of transmission mean that when the percentage of the community who have

[measles vaccine](#) falls below 90 percent to 95 percent, major outbreaks, as in the 1950s when four million Americans were infected and 450 died. Worldwide, measles still kills a million children each year.



Opinion | OP-ED CONTRIBUTOR

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Getty Images



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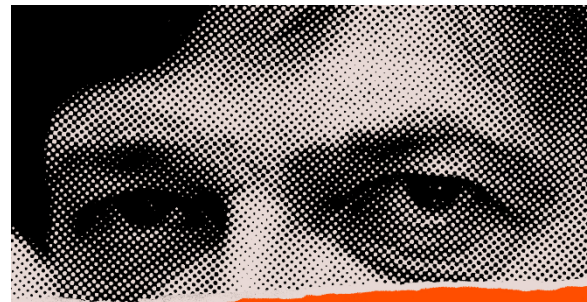


MEASLES OUTBREAK

WHY PARENTS REFUSE TO VACCINATE

CNN

PT 8:39 PM



THE DOCTOR WHO FOOLED THE WORLD

Andrew Wakefield's war on vaccines

BRIAN DEER

SCRIBE

Pourquoi la France est "extrêmement anti-vaccin" : interview croisée de deux experts

par [Xavier Demagny](#) [@](#), [Louis-Valentin Lopez](#) publié le 17 novembre 2020 à 8h00



Avec près de la moitié de la population hostile à l'idée de se faire vacciner contre la Covid-19, la France est l'un des pays qui compte le plus d'anti-vaccin. Interview croisée de Antoine Bristielle, professeur agrégé de sciences sociales, et Rudy Reichstadt, directeur de Conspiracy Watch sur le profil des anti-vax.



Rudy Reichstadt, à gauche, est directeur de Conspiracy Watch et Antoine Bristielle, à droite, est professeur agrégé de sciences sociales. © France Inter



"L'anti-vaccination est une 'maladie' de pays riches et développés"

Vaccine hesitancy: an emergent issue

- Vaccine hesitancy reported among 20-30% of parents

MIKO D, *et al.* *Medicina* 2019;55:pii: E282

SANTIBANEZ TA, *et al.* *Pediatrics* 2020 Nov 9 [Epub ahead of print]

OLSON O, *et al.* *Vaccines (Basel)* 2020;8:E590

- Vaccine coverage decreasing among children of rich strata also in LMIC

CATA-PRETA BO, *et al.* *Am J Prev Med* 2020:S0749-3797(20)30395-0

- Vaccine propensity is affected by perceived risk of mortality (vs. risk of morbidity), older age, male sex, availability/convenience of services, ideology, religious affiliations, income



Air pollution and climate change
Noncommunicable diseases
Global influenza pandemic
Fragile and vulnerable settings
(drought, famine, conflict, population displacement, weak health services)
Antimicrobial resistance
Ebola and other high-threat pathogens
Weak primary health care
Vaccine hesitancy
Dengue
HIV

Universal vaccination of children: a difficult decision for parents

- Freedom of choice vs. collective responsibility (i.e. those who refuse vaccination still profit from others being vaccinated)
- Choices may be affected by personal specificities/medical conditions (for example, the child of a parent with multiple sclerosis)
- Role of the 'anticipated regret' (people feel less guilty if they **have not** intervened and a problem occurs, than if they **do** intervene and a problem occurs)
- It is difficult for parents to accept that their child may grow as a possible risk-taking teenager/young adult (e.g. IVDU, or high-risk sex)

The conundrum of expert-lay interaction on science

- Do rigorous science
- Improve access to data for general practitioners
- Improve long-term pharmacovigilance (medicines, vaccines)
- Ask the collaboration of media (including social media) to translate science into understandable language
- Teach communication skills (e.g. to explain the risk-to-benefit ratio) and emotional intelligence
- Address cognitive biases to combat fake news
- Shift from Public Understanding of Science (PUS) to Public Engagemnt of Science and Technology (PEST)