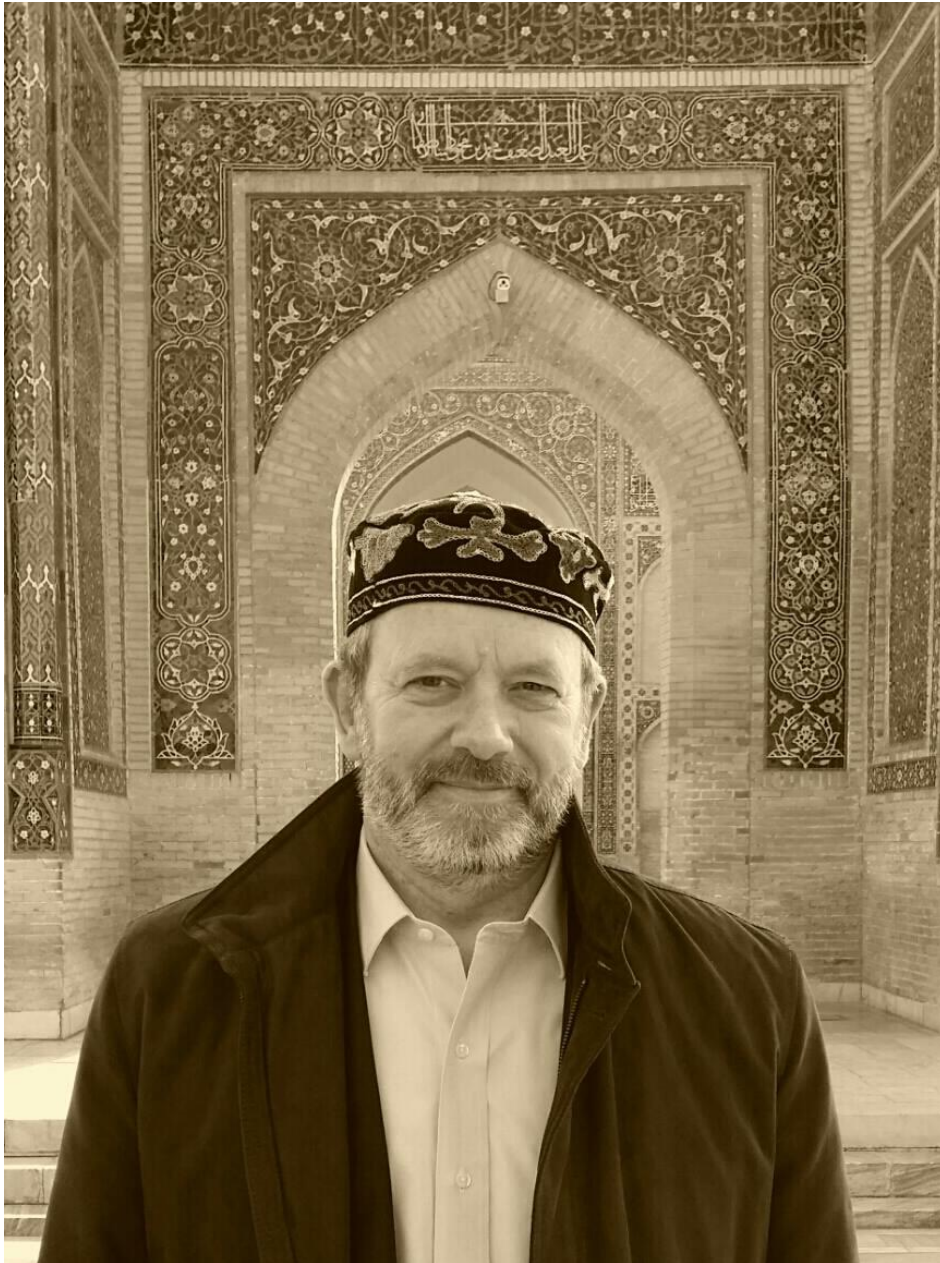


# Hepatology in resource-poor countries

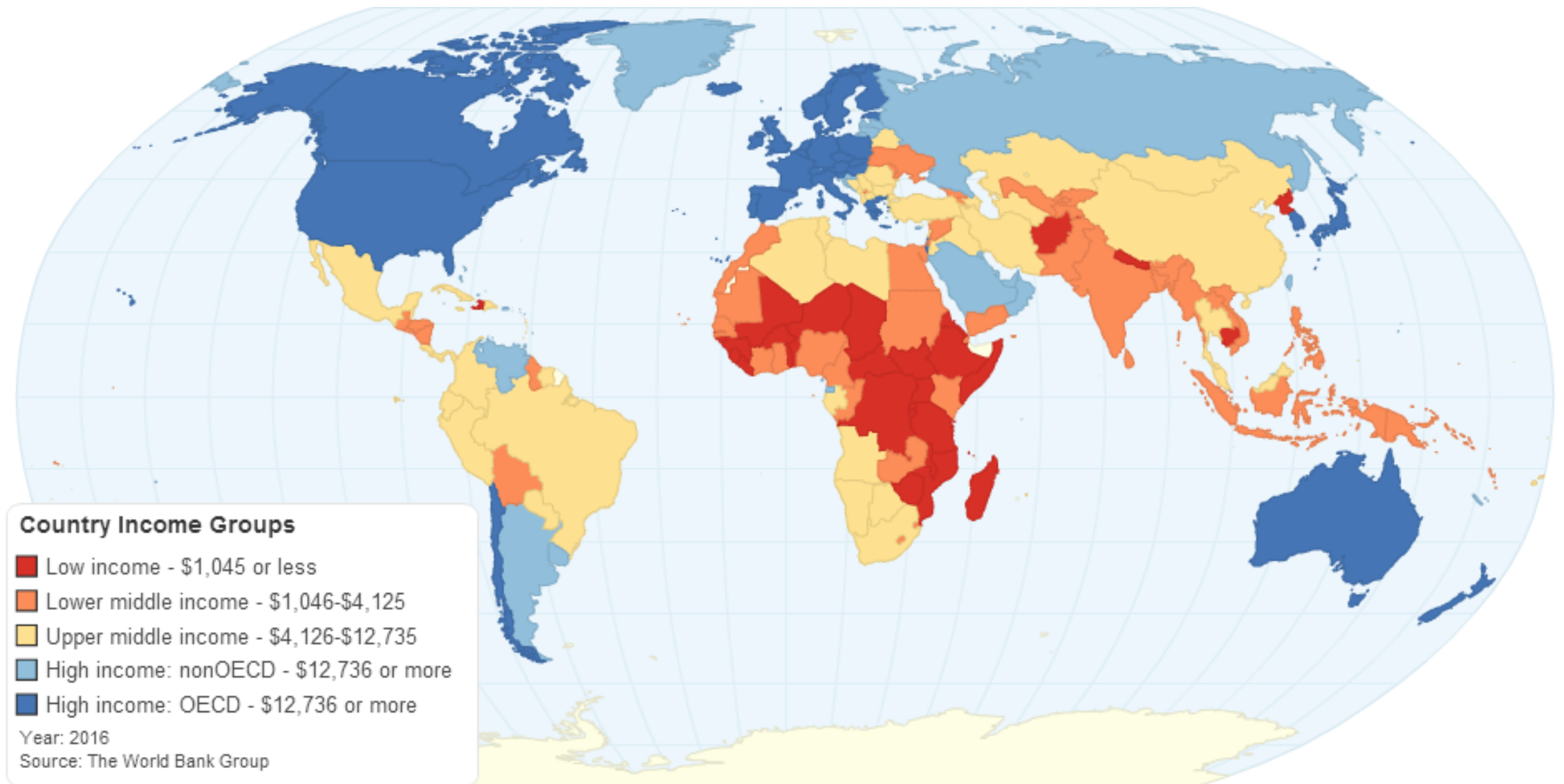


Samarqand, Timur mausoleum 2018

Francesco Negro  
*Hôpitaux Universitaires de Genève*

<b>Classification (The World Bank)</b>	<b>GNI per capita (Atlas method, 2014)</b>
<b>Low income</b>	<b>&lt; 1,045 USD</b>
<b>Low to middle income</b>	<b>1,045 – 4,125 USD</b>
<b>Middle income</b>	<b>1,045 – 12,736</b>
<b>Middle to upper income</b>	<b>4,125 – 12,736</b>
<b>High income</b>	<b>&gt; 12,736 USD</b>

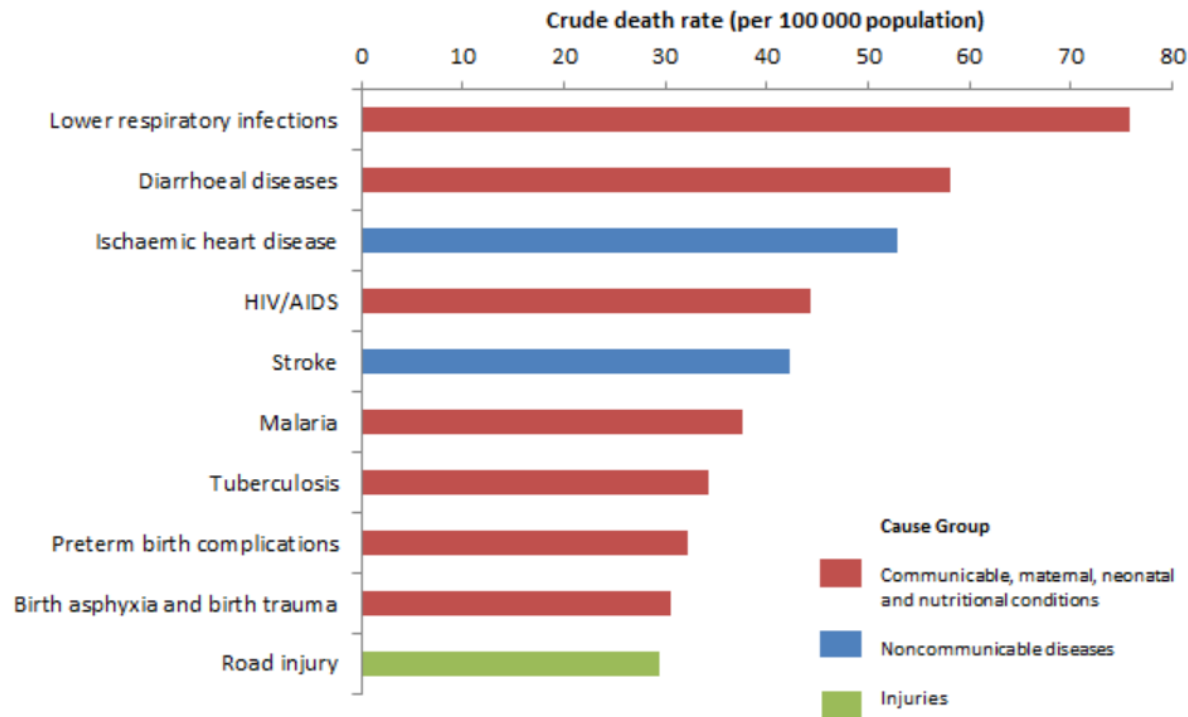
GDP measures the market value of all final goods and services produced in a given country  
GNI measures income generated by the country's citizens, regardless of the geographic location of income  
(incl. foreign aid, remittances from citizen living abroad, development assistance, capital inflow)



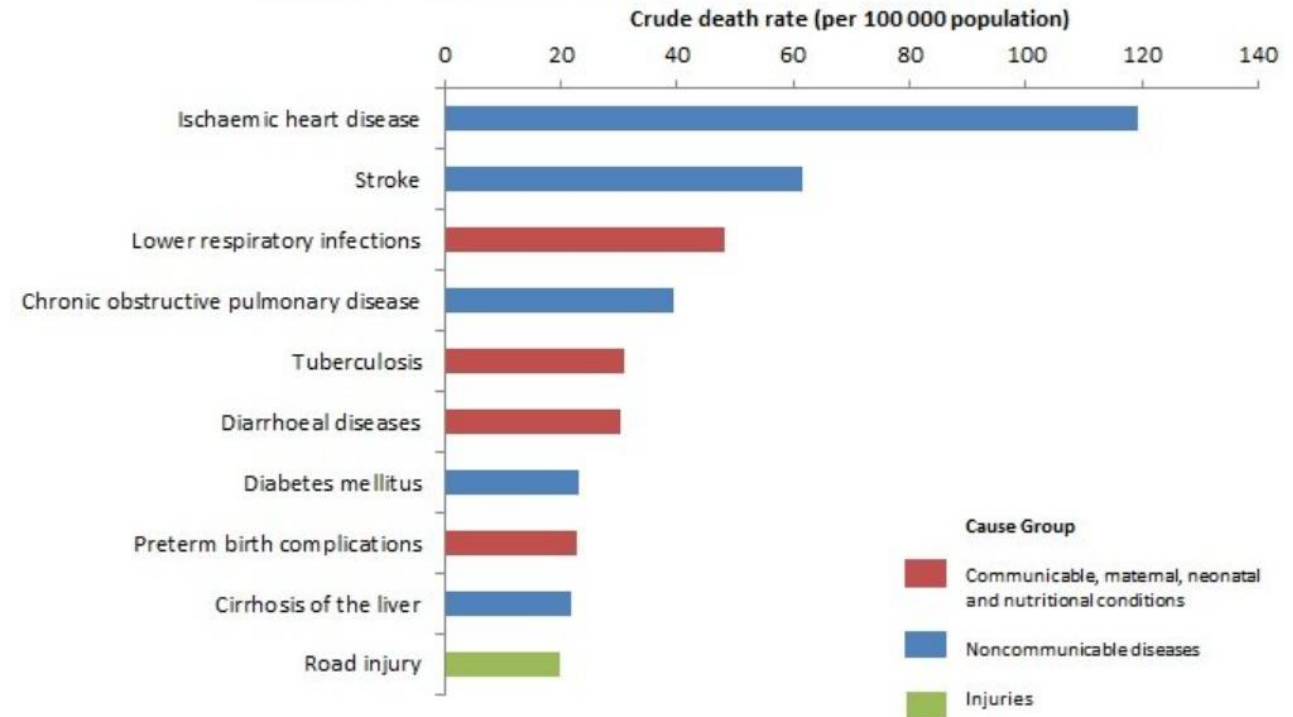
31 countries earn 1,045 USD or less of GNI per capita  
109 countries fall in the Middle Income definition (1,45 to 12,736 GNI per capita)

# What causes the most deaths in LIC / LMIC?

**Top 10 causes of deaths  
in low-income countries in 2016**



**Top 10 causes of deaths  
in lower-middle-income countries in 2016**

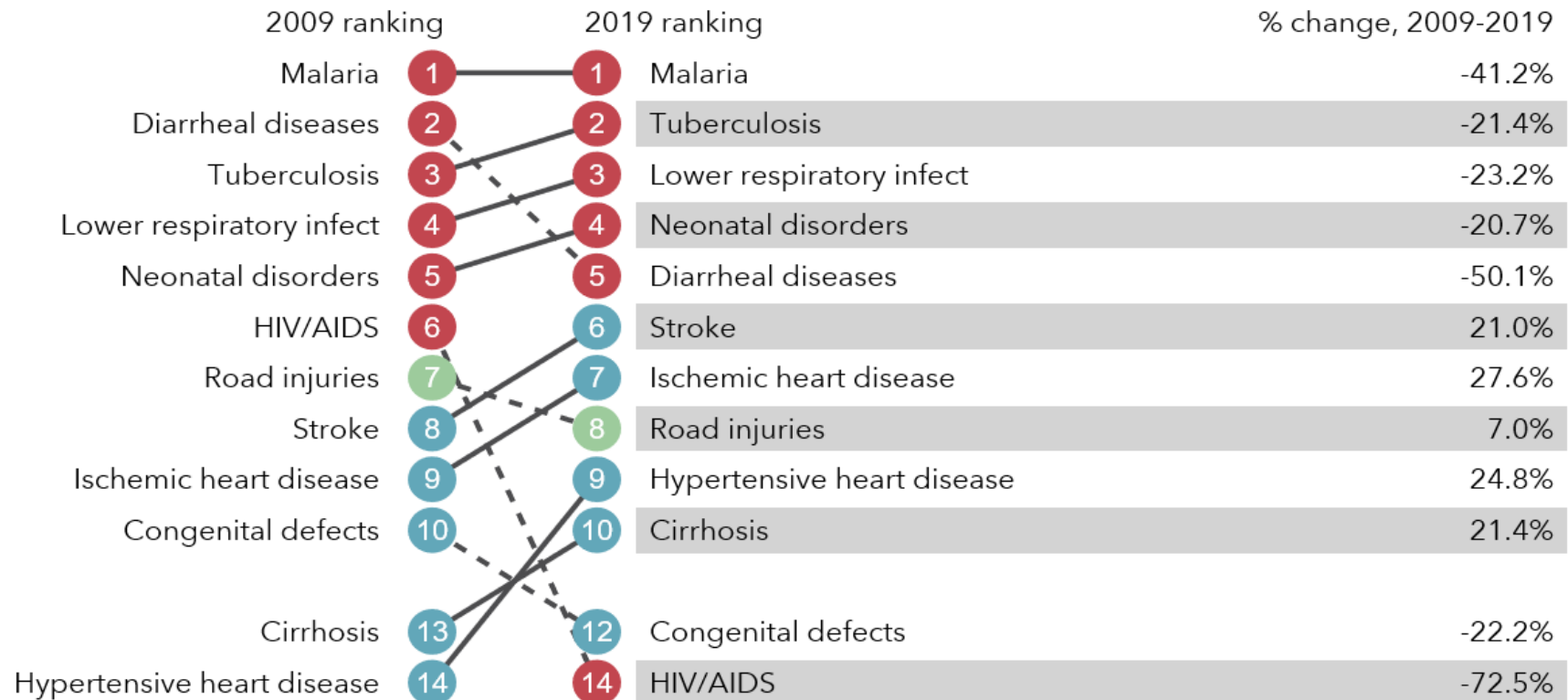


# What causes the most deaths in Low Income Countries?

(Democratic Republic of Congo, the most populous LIC in the world [101,780,263 in 2020],  
PPP GDP per capita = 843 USD)



- Communicable, maternal, neonatal, and nutritional diseases
- Non-communicable diseases
- Injuries

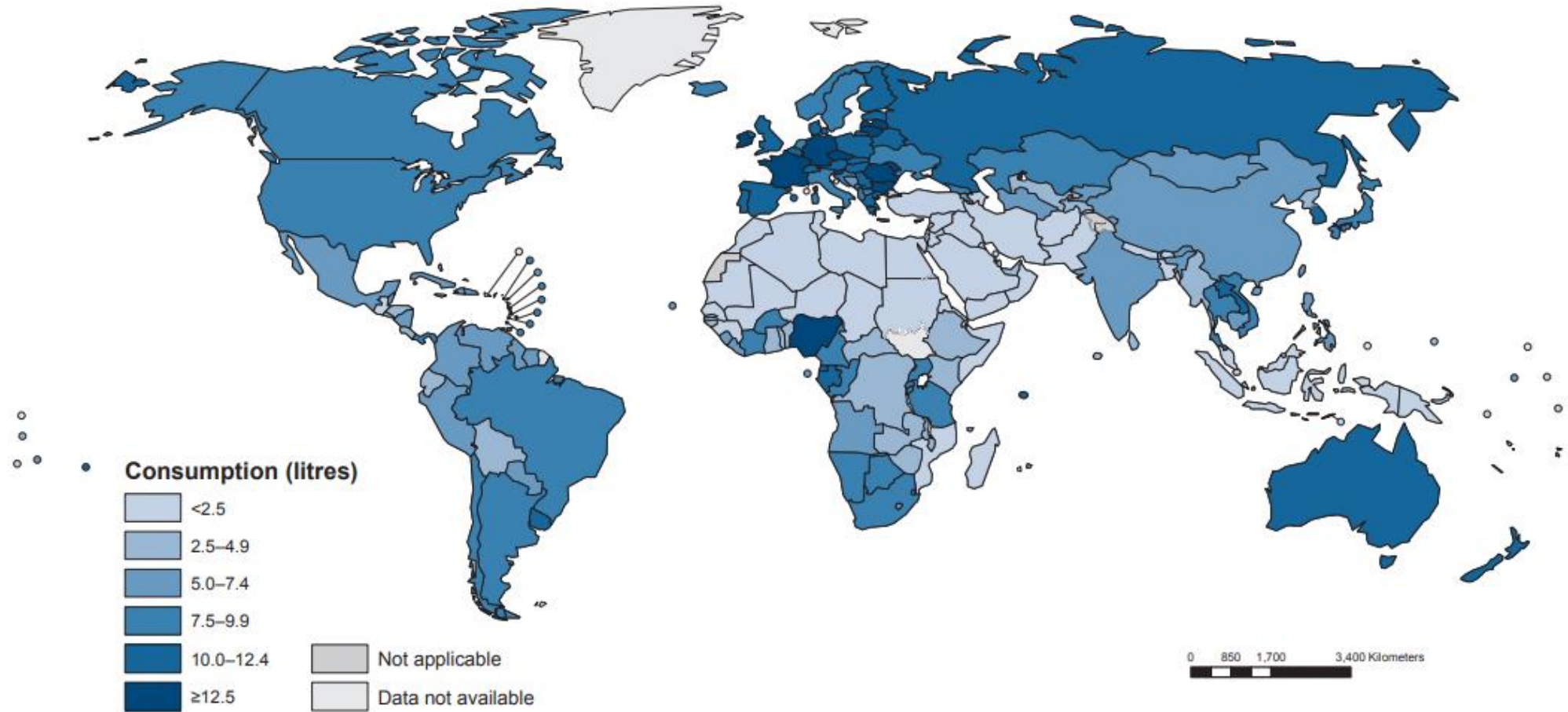


# Alcohol in LMIC



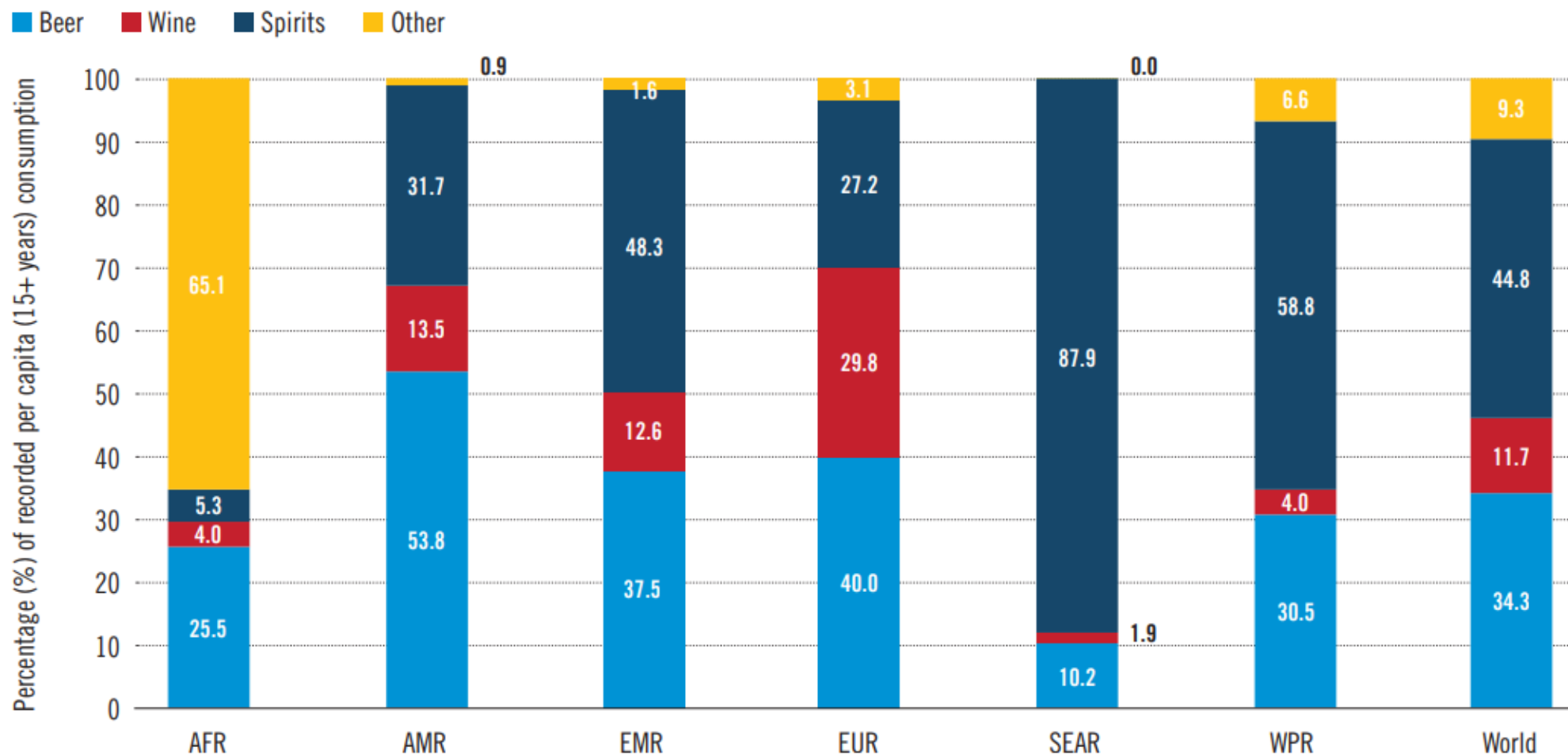
# Total alcohol per capita consumption, per year

(15+ years, litres of pure alcohol, 2016)



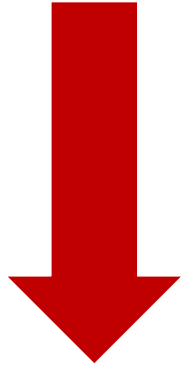
## Percentage of alcohol per capita consumption of different types of beverages, by WHO region, 2016

(other: fermented beverages made of rice, palm, sorghum, banana, millet, maize)





# HIC



More frequent consumption  
of smaller quantities of wine,  
mostly on a daily basis

# LMIC

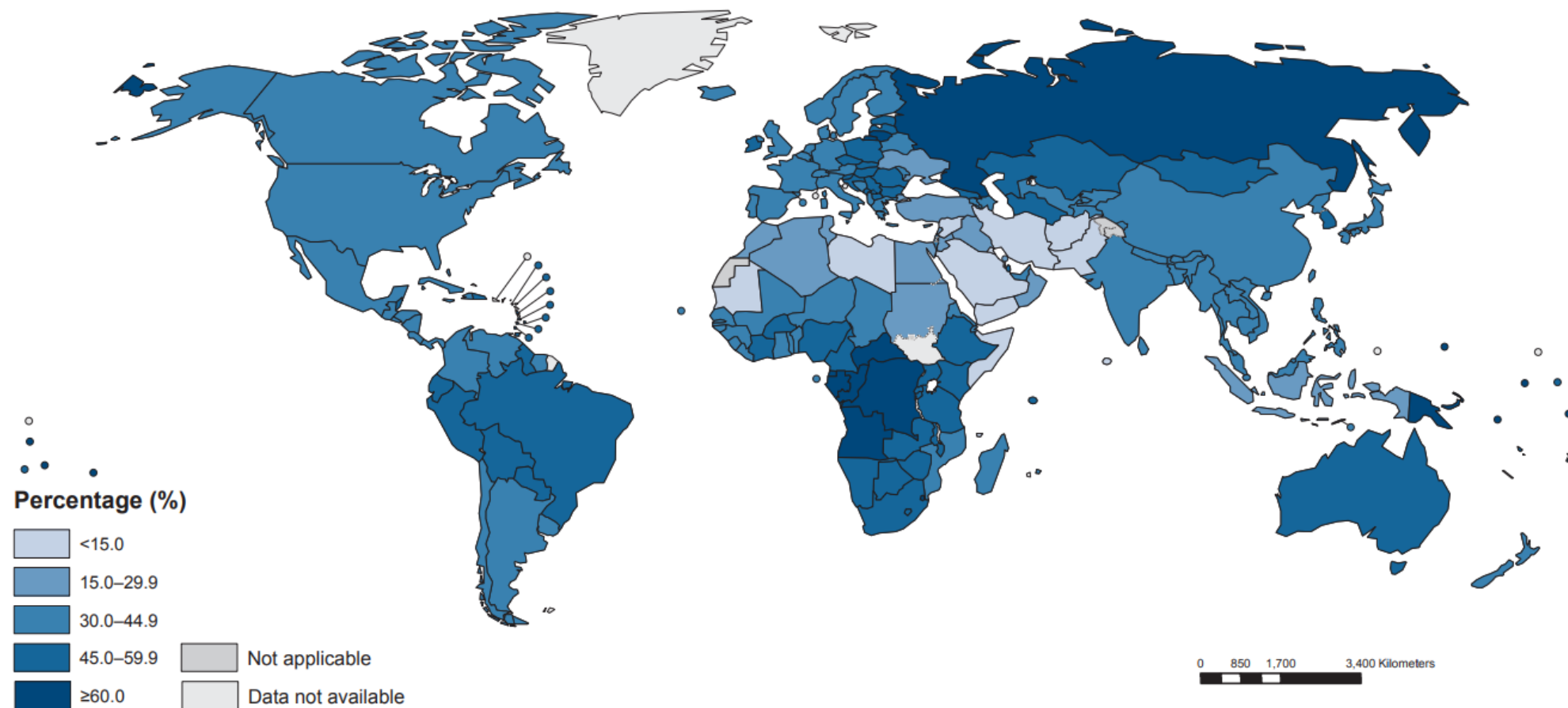


Adults more likely to engage  
in the riskiest pattern of drinking  
(infrequent consumption  
of large quantities of spirits)

# Hazardous, harmful or dependent alcohol drinking in LMIC

Country	Proportion (adult population)	Reference
Tanzania	28%	Francis JM, <i>et al.</i> PLoS One 2015
Namibia	40%	Seth P, <i>et al.</i> PLoS One 2015
Ethiopia	31%	Teferra S, <i>et al.</i> BMC Public Health 2016
Uganda	21%	Kullgren G, <i>et al.</i> Afr J Psychiatry 2009
India	22%	Ghosh S, <i>et al.</i> J Heal Popul Nutr 2012

# Prevalence of heavy episodic drinking among current drinkers (15+ years, 2016)





## Consommation d'alcool : Les Gabonais, champions d'Afrique !



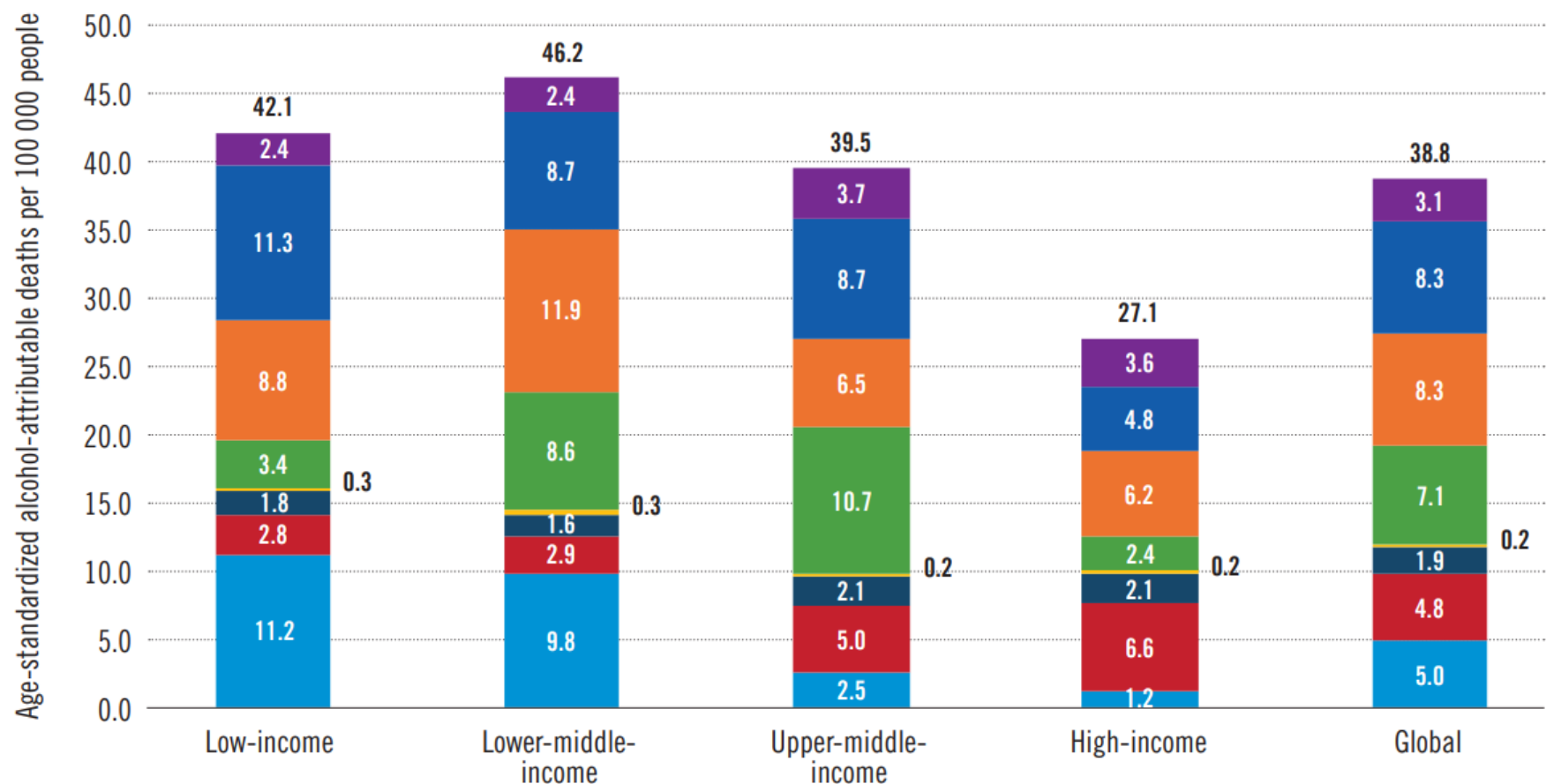
La Rédaction

28/11/2019

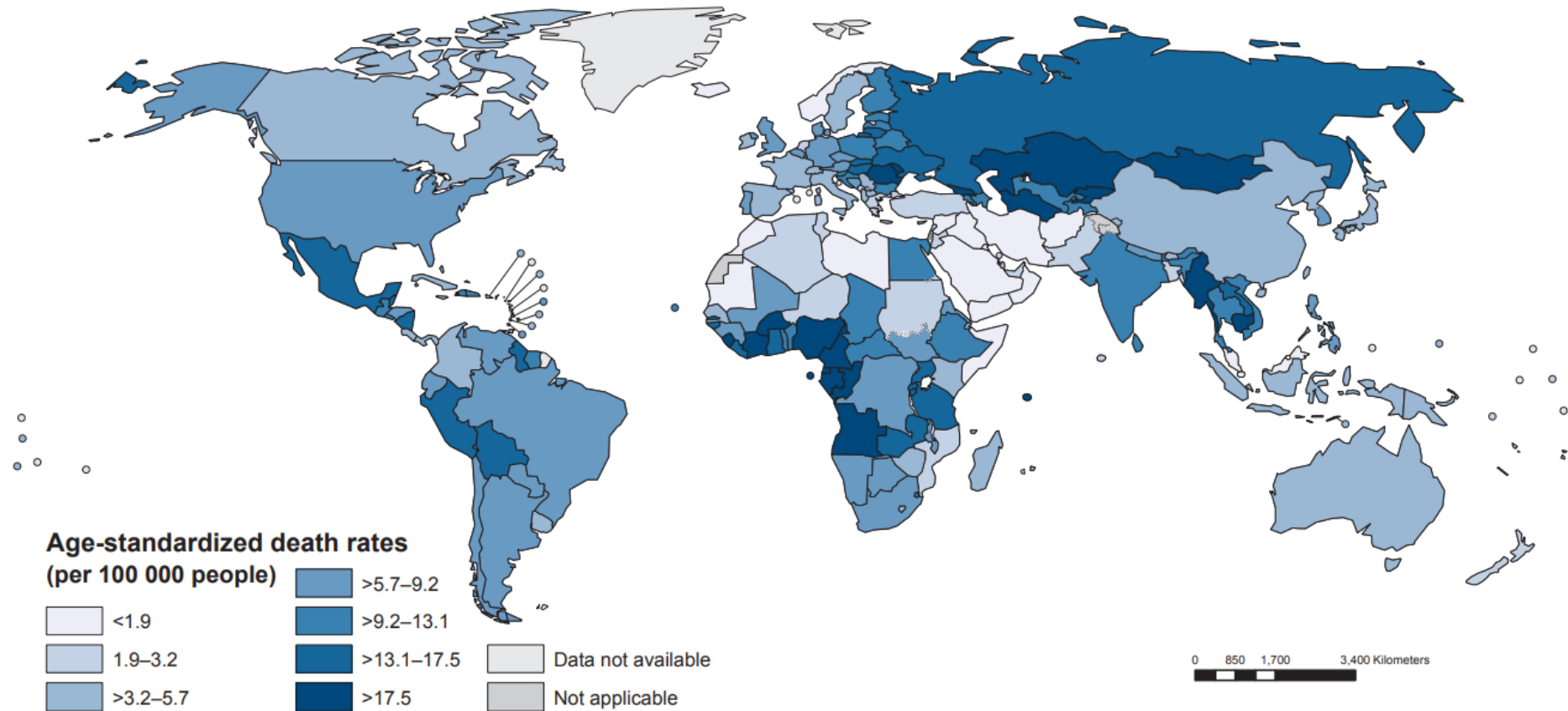


# Alcohol attributable deaths, by income group (2016)

■ Infectious diseases   
 ■ Malignant neoplasms   
 ■ Alcohol use disorders   
 ■ Epilepsy   
 ■ Cardiovascular diseases and diabetes  
■ Digestive diseases   
■ Unintentional injuries   
■ Intentional injuries

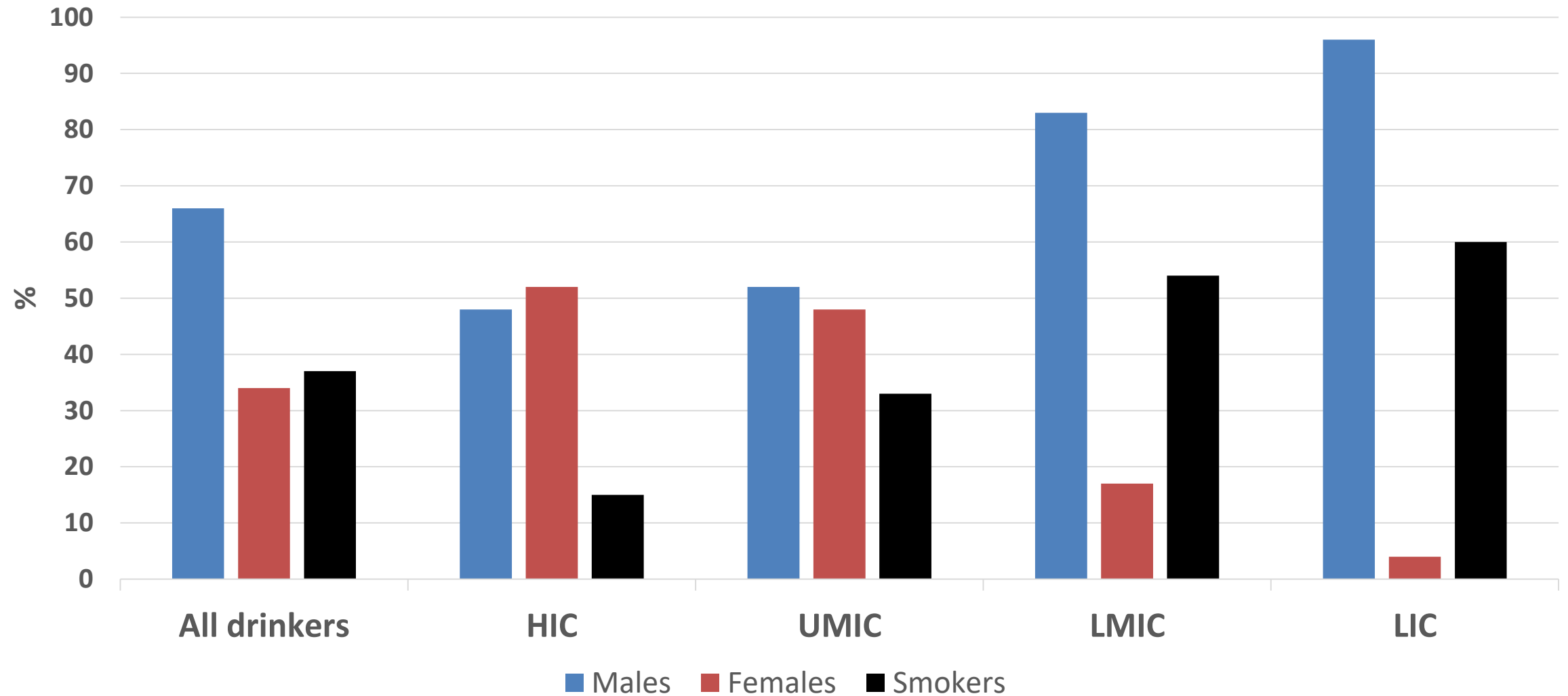


# Age-standardized alcohol-attributable digestive disease death rates (cirrhosis – excluding HCC – and pancreatitis, 2016)





## Alcohol drinkers features, by income region



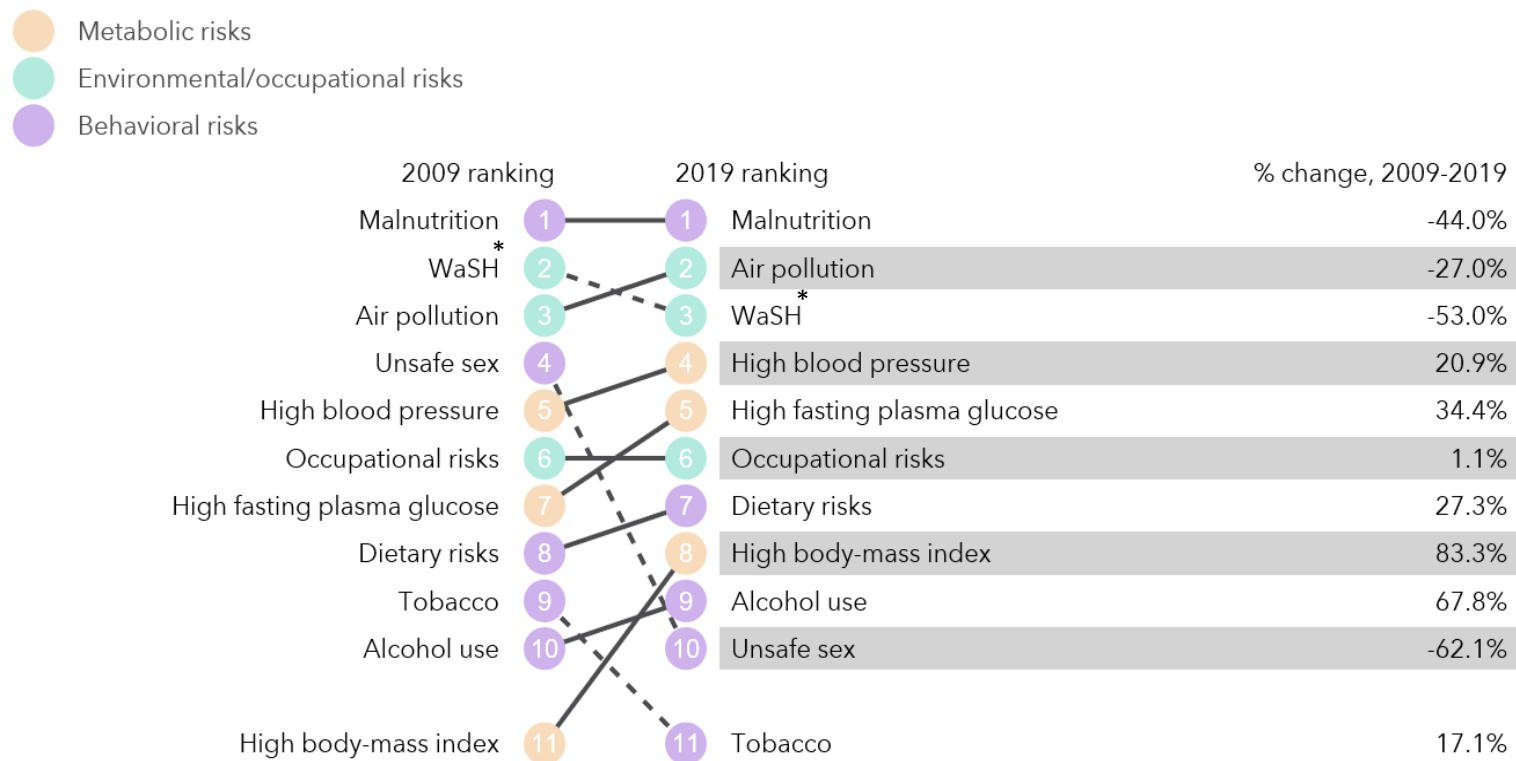
## **Alcohol causes a disproportionate amount of harm among persons of lower socioeconomic status**

- Alcohol-attributable mortality and age-adjusted burden of alcohol attributable DALYs are highest in low- and lower-middle-income countries
- Socioeconomic status impacts volume, patterns and context in which alcohol is consumed
- In LIC and LMIC, alcohol consumption clusters with other risk factors affecting similar diseases – such as smoking, obesity and sedentary lifestyle
- Inadequate policy measures

# MAFLD in LMIC

# What risk factors drive the most death and disability combined in Low Income Countries?

(Democratic Republic of Congo, the most populous LIC in the world [101,780,263 in 2020], PPP GDP per capita = 843 USD)



Top 10 risks contributing to total number of DALYs in 2019 and percent change 2009–2019, all ages combined  
See related publication: [https://doi.org/10.1016/S0140-6736\(20\)30752-2](https://doi.org/10.1016/S0140-6736(20)30752-2)

\*WaSH: Water, Sanitation and Hygiene

# Selected findings from the NAFLD Global Policy Study (n=83)

Data from a 17-item-questionnaire covering five categories on NAFLD:  
(1) policies; (2) guidelines; (3) awareness/participation; (4) data and monitoring; and (5) management.

Region	Population**	Strategy	Guideline	Registry	Lifestyle programs
East Asia & Pacific (n=11)	2,004	0/11 (0%)	3/11 (27%)	1/11 (9%)	3/10* (30%)
Europe & Central Asia (n=40)	708	0/40 (0%)	15/40 (38%)	3/40 (8%)	13/38* (34%)
Latin America & Caribbean (n=8)	466	0/8 (0%)	5/8 (63%)	1/8 (13%)	2/7* (29%)
Middle East & North Africa (n=9)	288	0/9 (0%)	1/9 (11%)	1/9 (11%)	5/8* (63%)
North America (n=1)	37	0/1 (0%)	0/1 (0%)	0/1 (0%)	1/1 (100%)
South Asia (n=5)	1,776	0/5 (0%)	2/5 (40%)	1/5 (20%)	5/5 (100%)
Sub-Saharan Africa (n=9)	549	0/9 (0%)	0/9 (0%)	0/9 (0%)	3/9 (33%)
Total (n=83)	5,828	0/83 (0%)	26/83 (31%)	7/83 (8%)	32/78* (41%)
*Denominator for each variable adjusted to remove countries responding with “don’t know”. **Population of contributing countries (millions). NAFLD, non-alcoholic fatty liver disease.					

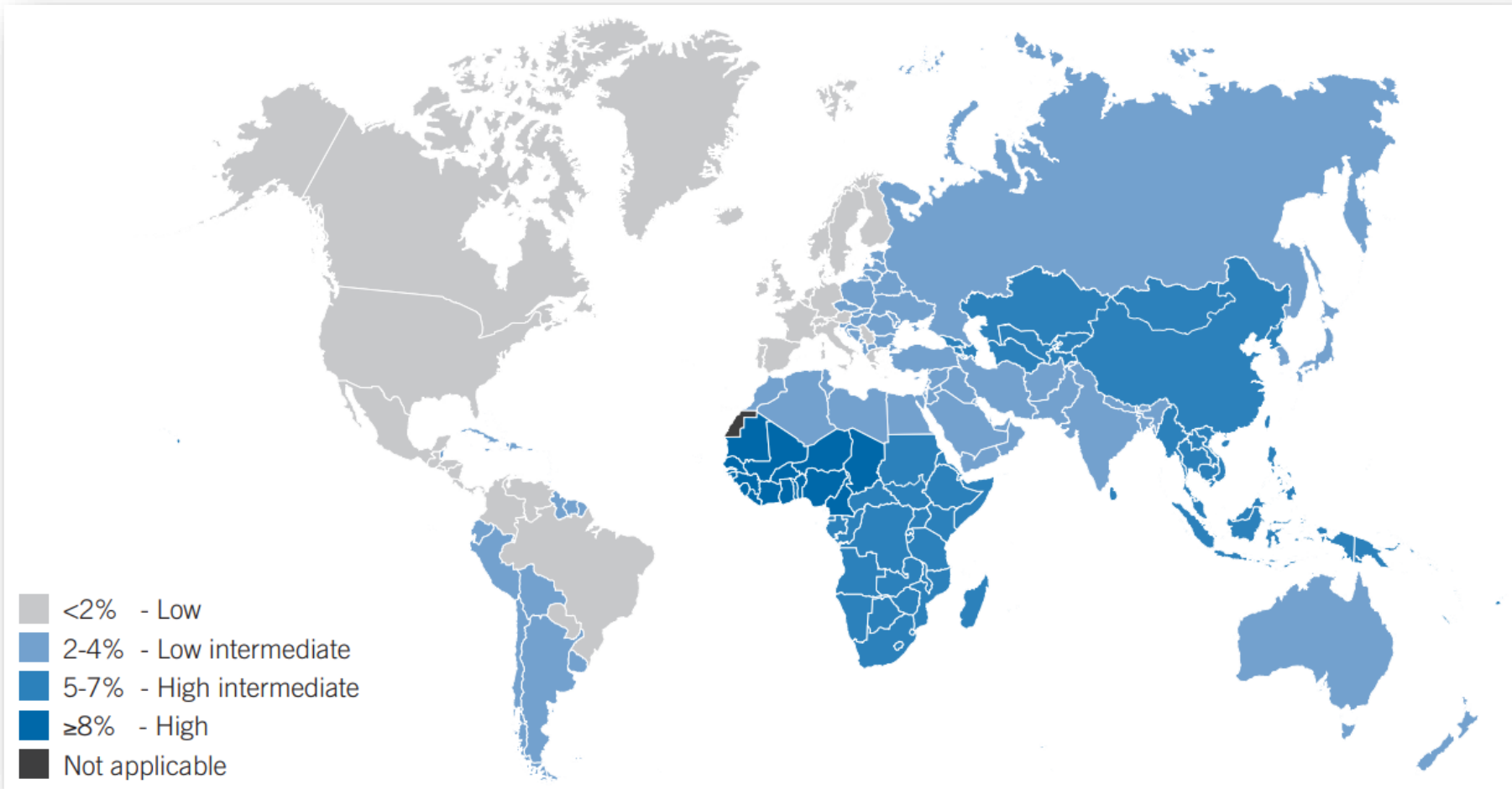
**None of the 12 LIC and LMIC countries have a strategy to tackle NAFLD**

# Viral hepatitis in LMIC

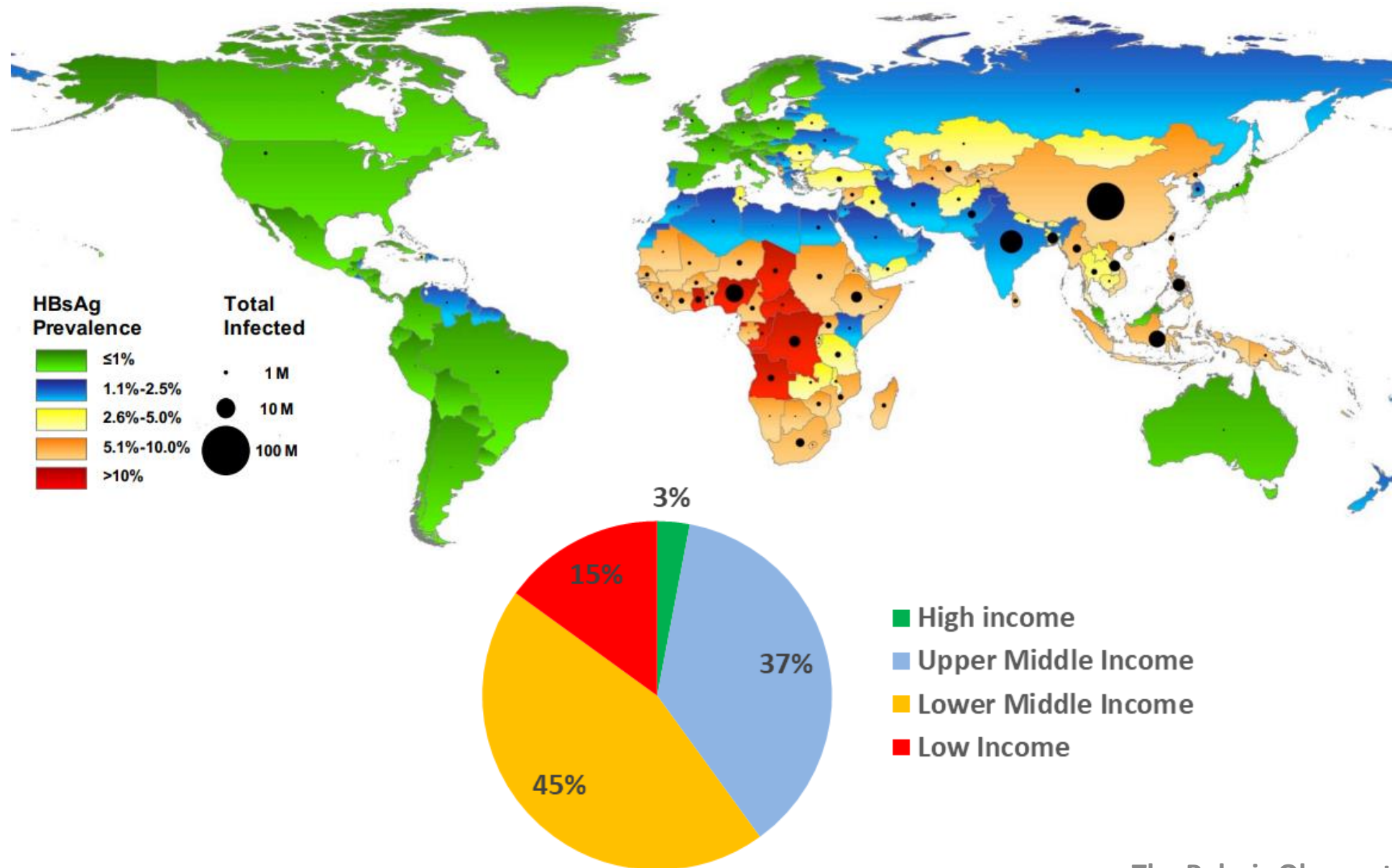


# 257 million persons living with HBV in 2015

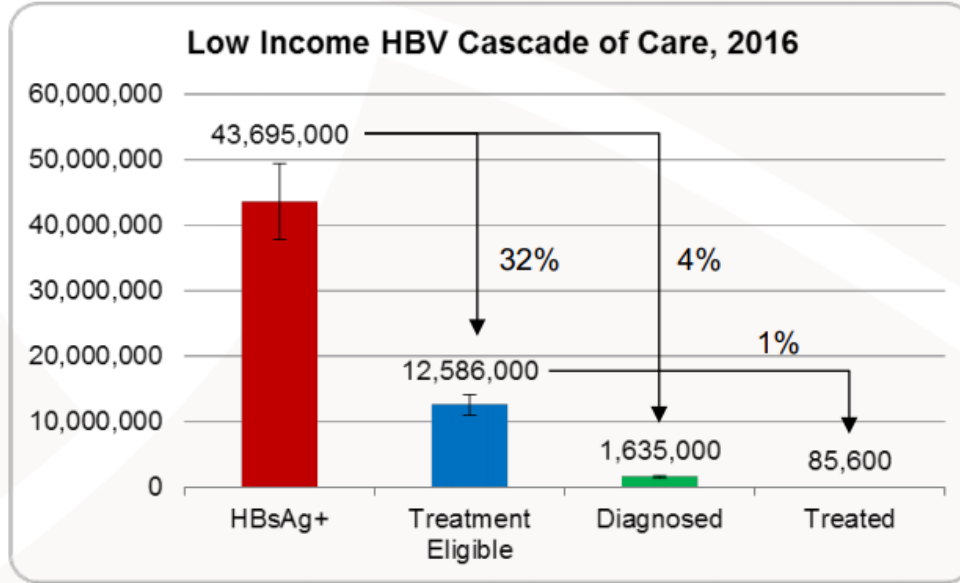
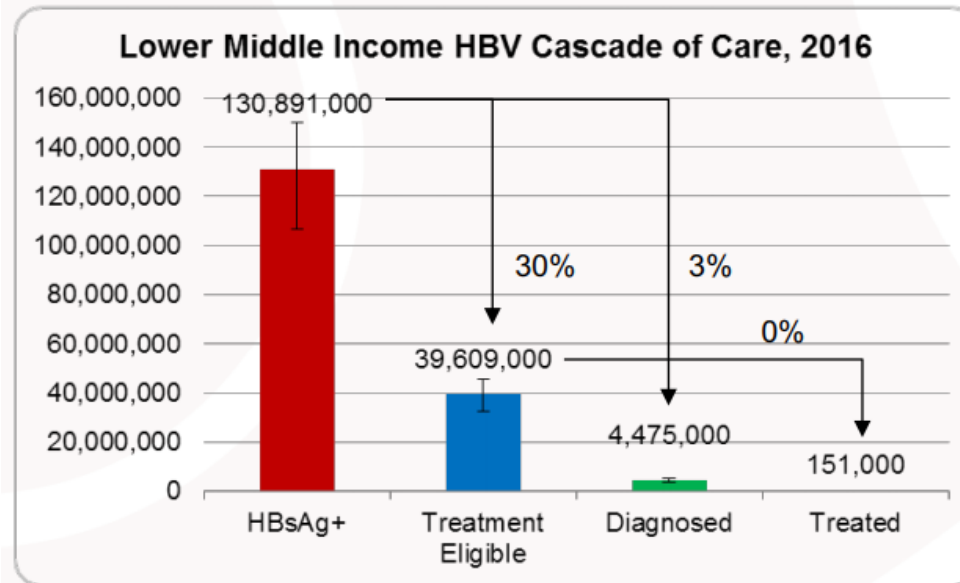
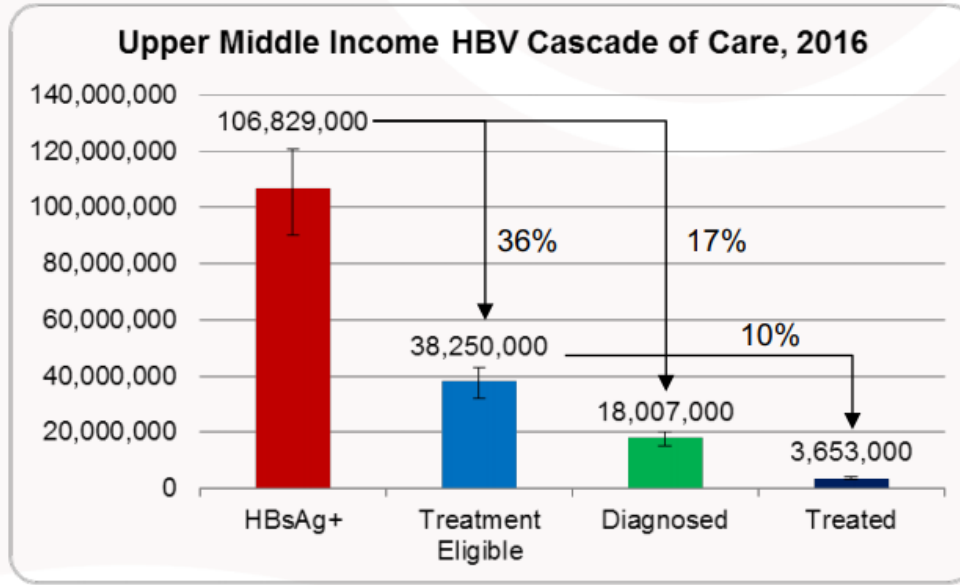
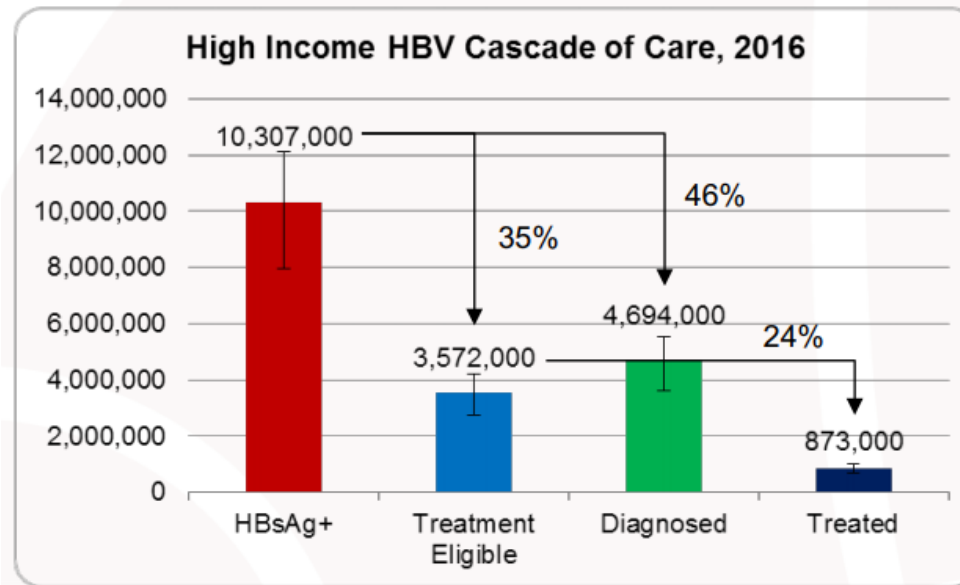
(3.5% of global population, among them 65 million fertile women)



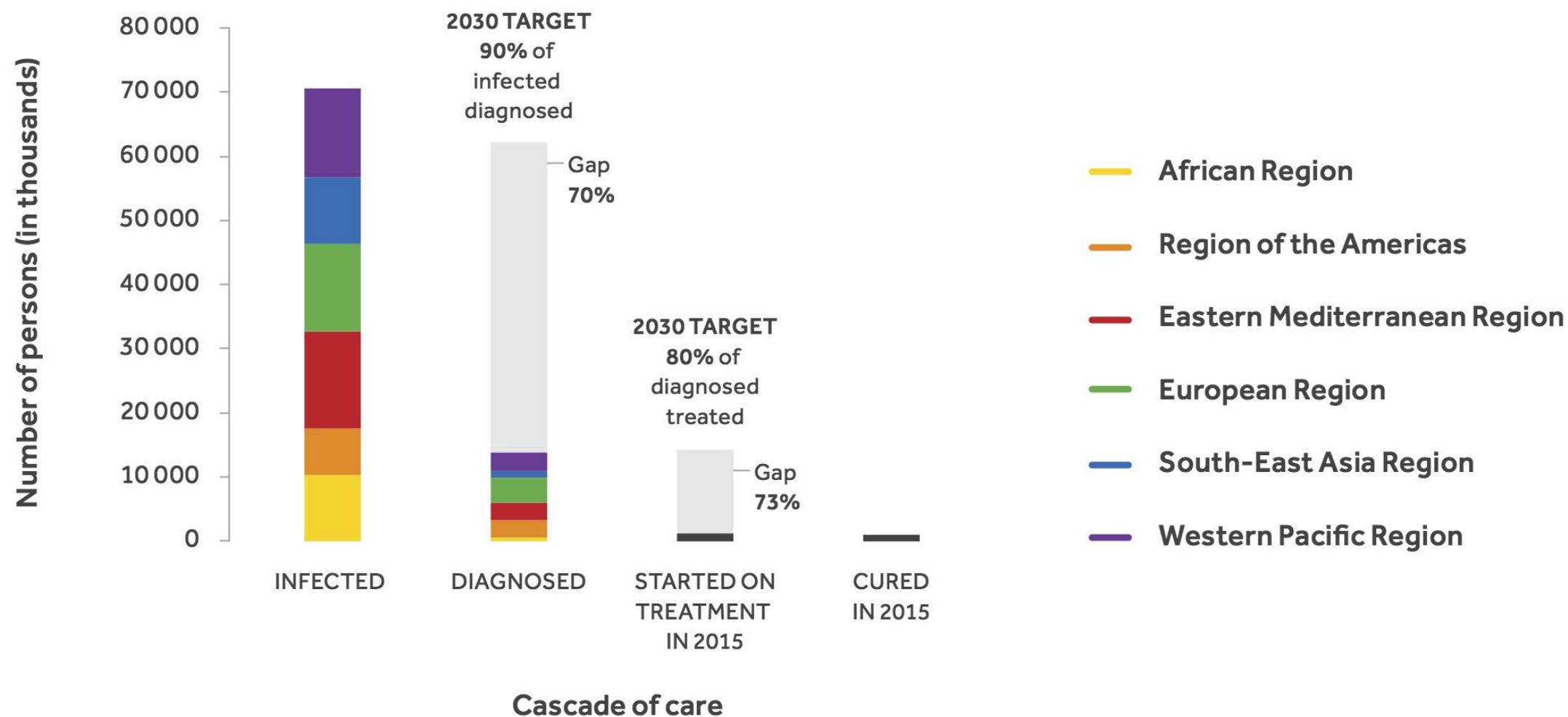
## In 2016, 60% of HBV infected persons were living in Low or Lower Middle Income countries



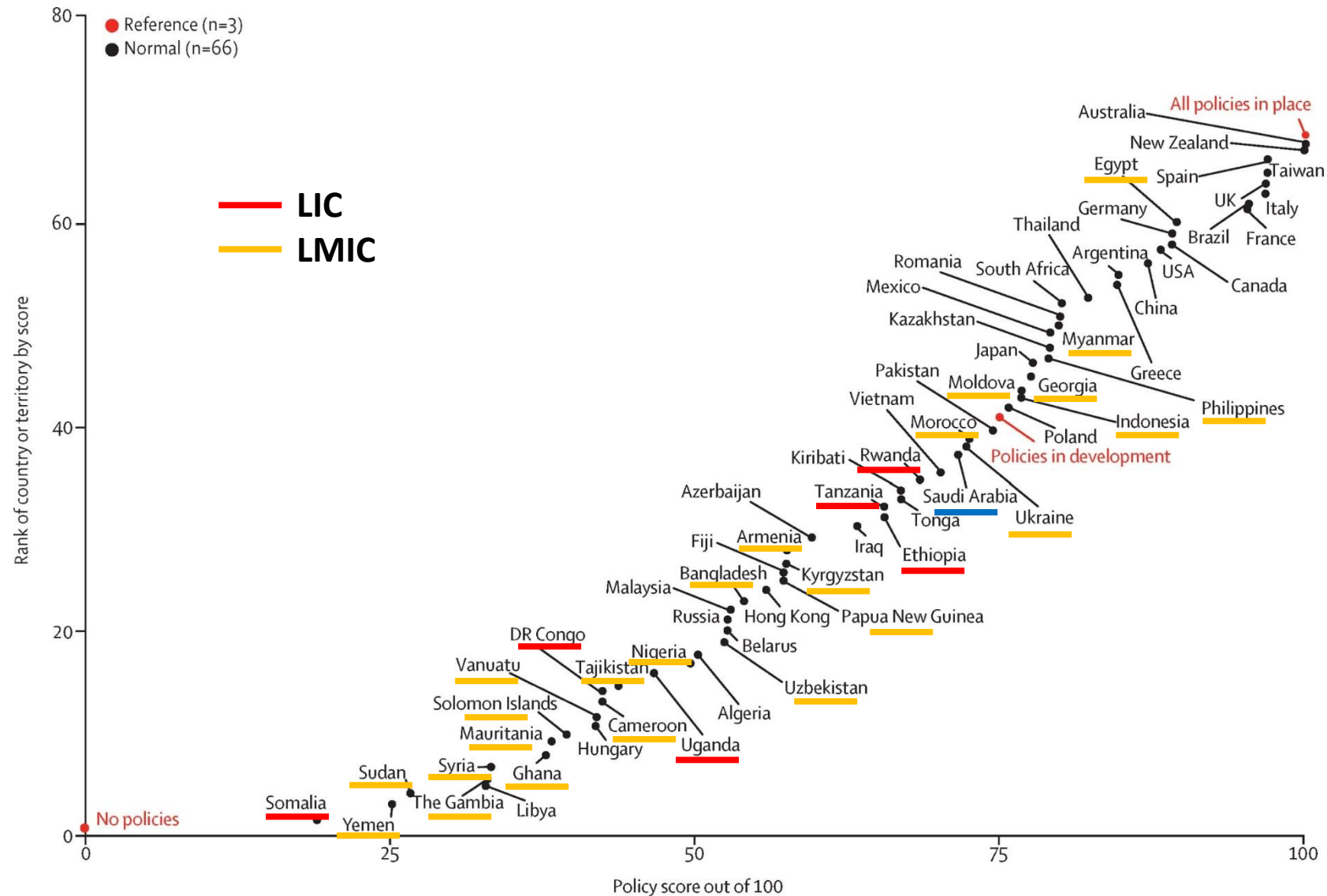
# HBV Cascade of Care According to World Bank Lending Classification



# Cascade of care for hepatitis C, by WHO region, 2015



# Status of 11 viral hepatitis policy indicators in 66 countries with the heaviest burden by global region



# The hurdles to diagnose viral hepatitis in LMIC

- Lack of awareness, advocacy, national strategies, infrastructure
- Poor quality assays (no WHO prequalification)
- Although first-level screening assays are inexpensive, confirmatory assays for ongoing infection may cost more than generic medicines
- OK to diagnose, but then ...????



## DISEASE AREAS



ANTIMICROBIAL  
RESISTANCE



HEPATITIS C & HIV



MALARIA & FEVER



NEGLECTED  
TROPICAL DISEASES



PANDEMIC  
PREPAREDNESS



TUBERCULOSIS

### Projects

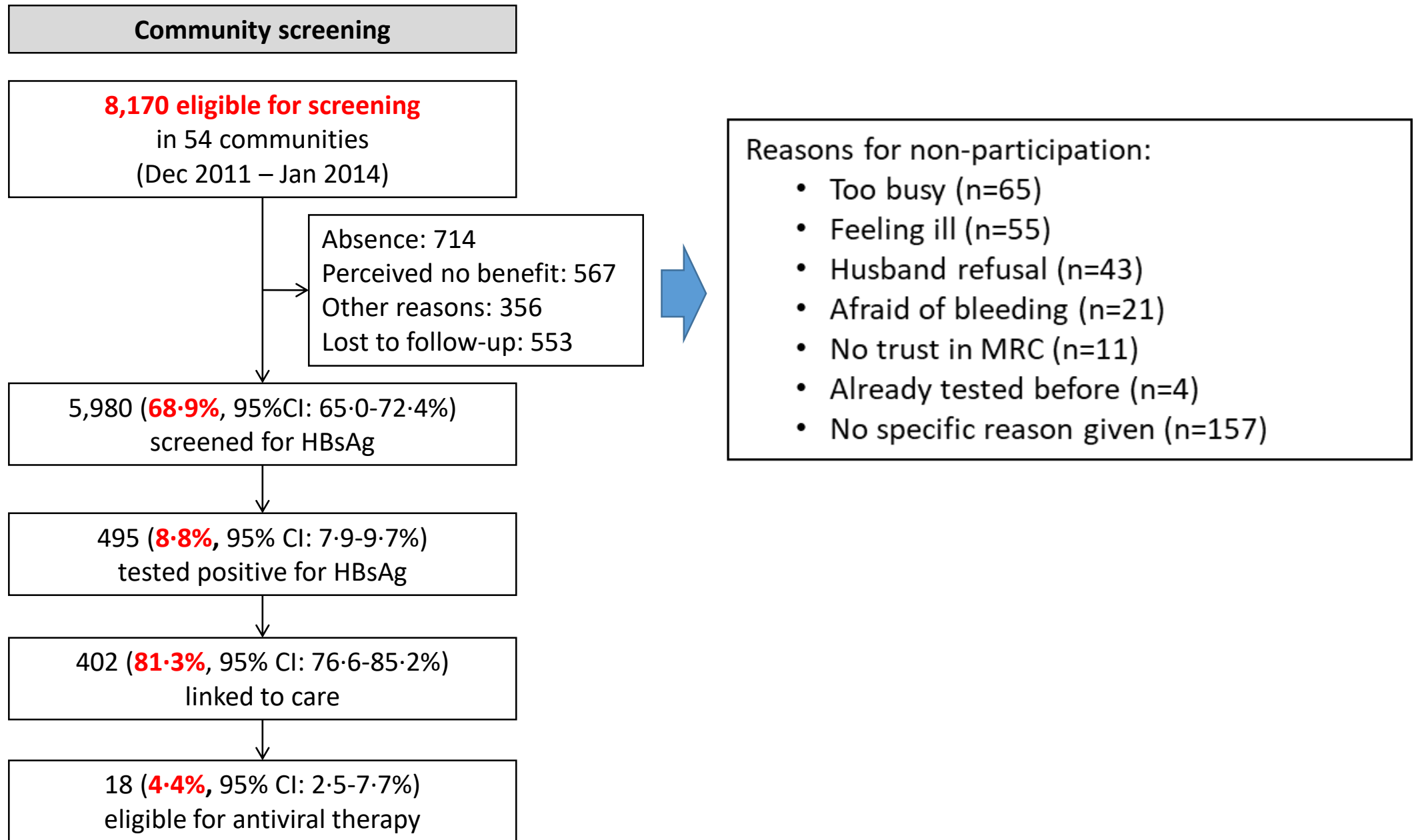
- R&D
- Clinical trials
- Access

### Offices

Geneva, Switzerland (HQ)  
Hanoi, Viet Nam  
New Delhi, India  
Cape Town, South Africa  
Nairobi, Kenya

# 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*

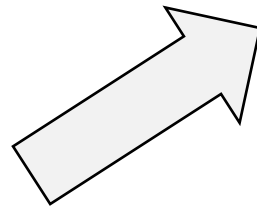


## Cost of DAA as % of median annual income per capita

---

Egypt	110%
Ethiopia	214%
Nigeria	152%
DRC	244%
Cameroon	186%
Rwanda	319%
South Africa	62%

---



**Switzerland**  
**CHF 30,829 / 49,905 = 62%**

## Required increase in total health expenditure (THE) by different sources to provide HCV treatment to seven African countries (tiered pricing model, 2014)

Country	Total price of Generic	Increase in THE as % of GDP	Increase in THE	Increase in GovtE	Increase in PrvtE	Increase in OOPE	Increase in ODA	Increase in THE plus ODA
Egypt	\$5681.3	5.6%–7.3%	31%	80%	50%	55%	2390%	30%
Ethiopia	\$507.0	4.9%–5.7%	17%	29%	41%	52%	40%	12%
Nigeria	\$6086.3	3.7%–5.0%	34%	136%	46%	48%	510%	32%
DRC	\$82.5	4.3%–4.5%	5%	15%	9%	14%	14%	4%
Cameroon	\$1104.8	4.1%–7.9%	92%	403%	120%	139%	831%	83%
Rwanda	\$356.3	7.5%–11.9%	59%	154%	95%	210%	127%	40%
South Africa	\$474.8	8.8%–9.0%	2%	4%	3%	27%	98%	2%

## Sources of health financing and their percentage distribution in seven African countries (2014)

Country	Total Health Expenditure (THE) = GovtE+PrvtE <sup>a</sup>								Overseas development assistance (ODA) <sup>a</sup>		THE plus ODA
	Government expenditure (GovtE)		Private expenditure (PrvtE)		Out of pocket expenditure (OOPE)		THE				
	N	% of THE	N	% of THE	N	% of PrvtE	N	% of THE+ ODA			
Egypt	7076	38.2%	11,448	61.8%	10,318	90.1%	18,524	98.7%	238	1.3%	18,762
Ethiopia	1770	58.7%	1245	41.3%	974	78.2%	3015	70.6%	1257	29.4%	4272
Nigeria	4468	25.1%	13,332	74.9%	12,763	95.7%	17,800	93.7%	1193	6.3%	18,993
DRC	559	36.9%	956	63.1%	588	61.5%	1515	72.6%	573	27.4%	2088
Cameroon	274	22.9%	923	77.1%	794	86.0%	1197	90.0%	133	10.0%	1330
Rwanda	231	38.1%	376	61.9%	170	45.2%	607	68.4%	280	31.6%	887
South Africa	13,264	48.2%	14,255	51.8%	1789	12.5%	27,519	98.3%	487	1.7%	28,006



## How to make an expensive treatment affordable

- Prioritization: is it compatible with distributive justice?
- Price-volume agreements
- Government/NGO/industry partnerships
- Parallel importation of generic medicines (e.g. Buyers' Clubs)
- Voluntary licensing (MPP)
- Compulsory licensing

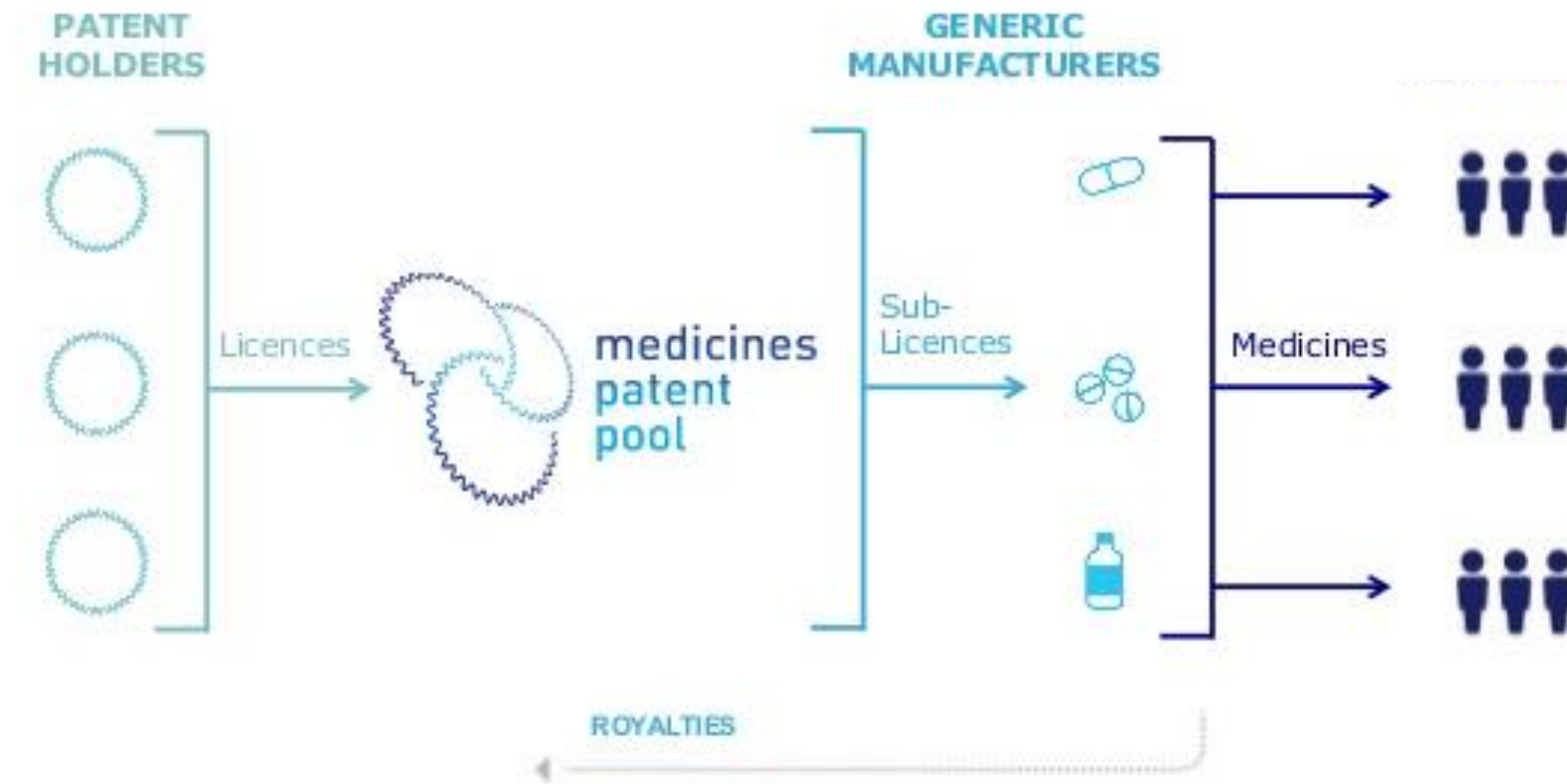
## Buyer's Club are providing a solution to individual patients



~~Fix~~ HepC

- Generic DAAs can be bought online, at competitive, steadily declining prices
- Medicines sent worldwide from India, Bangladesh, China, Egypt
- As per Article 60 of the TRIPS agreements, most countries allow generics importation for personal use  
([http://www.who.int/medicines/areas/policy/wto\\_trips/en/](http://www.who.int/medicines/areas/policy/wto_trips/en/))

# THE MEDICINES PATENT POOL MODEL

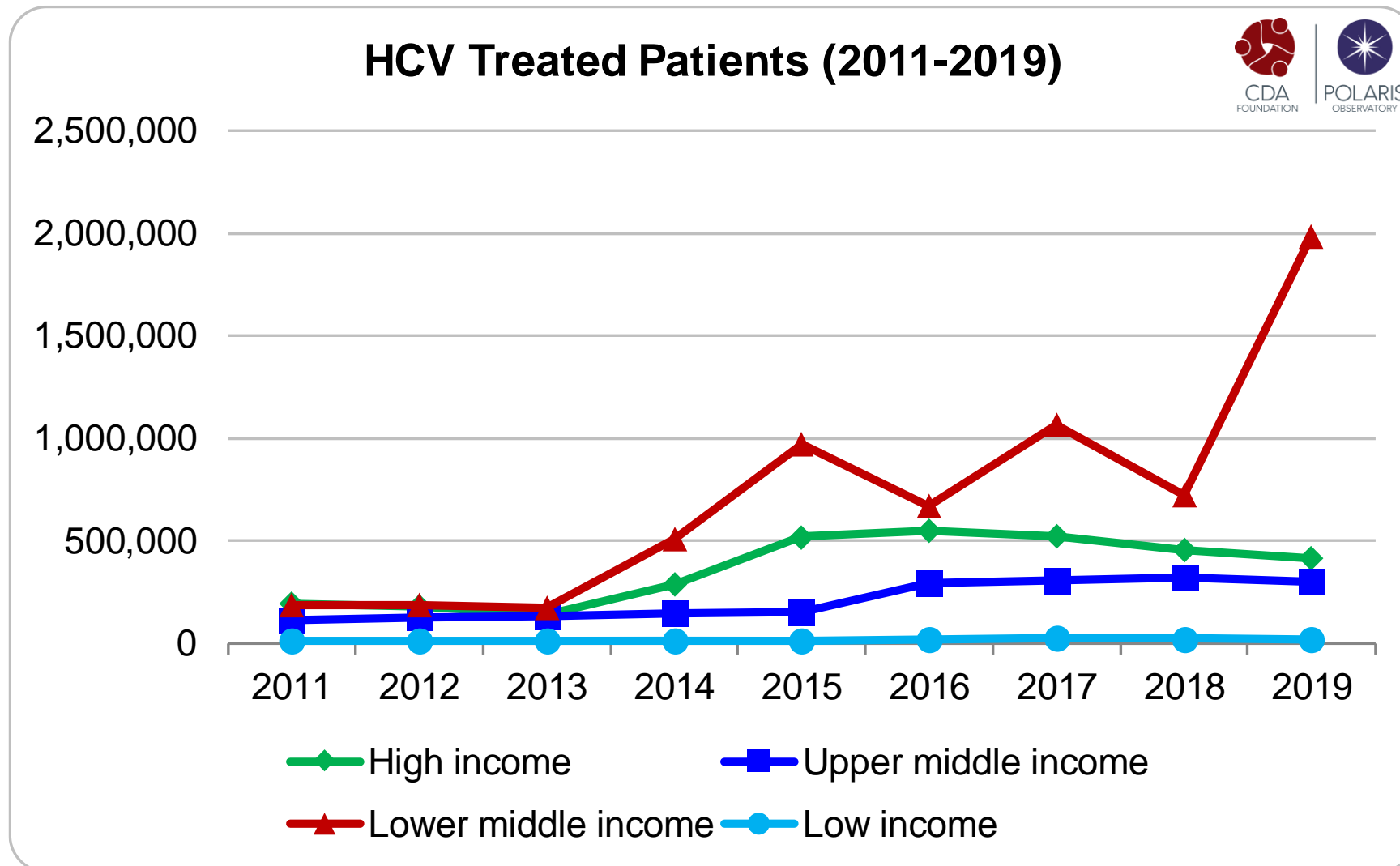


**Founded in 2010 by UNITAID, and endorsed by WHO and the UN General Assembly**  
**Initially focused on HIV, in 2015 expanded to HCV and TB**  
**Works through access oriented licences**

## Patent transfer is possible to allow distribution and sale of generic medicines in 91 countries

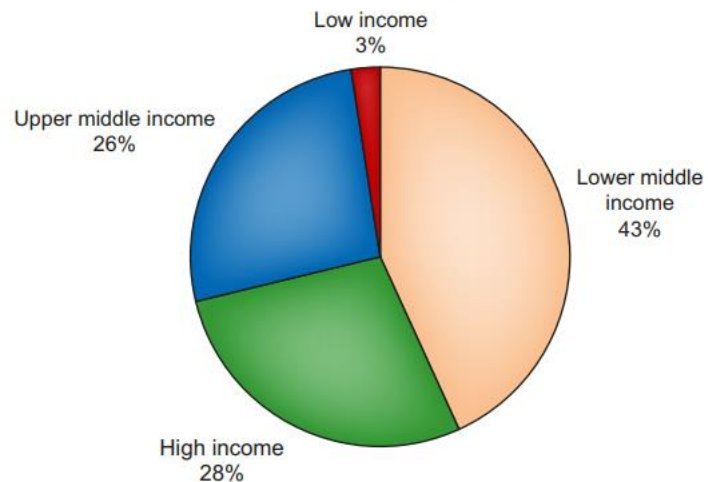
Afghanistan	Chad	Guatemala	Maldives	Papua New Guinea	Swaziland
Angola	Comoros	Guinea	Mali	Rwanda	Tajikistan
Antigua and Barbuda	Congo, DR	Guinea-Bissau	Mauritania	Samoa	Tanzania
Bangladesh	Congo, Rep.	Guyana	Mauritius	Sao Tome & Pr.	Timor Leste
Benin	Cote d'Ivoire	Haiti	Mongolia	Senegal	Togo
Bhutan	Cuba	Honduras	Mozambique	Seychelles	Tonga
Bolivia	Djibouti	India	Myanmar	Sierra Leone	Turkmenistan
Botswana	Dominica	Indonesia	Namibia	Solomon Islands	Tuvalu
Burkina Faso	Egypt	Kenya	Nauru	Somalia	Uganda
Burundi	Equatorial Guinea	Kiribati	Nepal	South Africa	Uzbekistan
Cambodia	Eritrea	Kyrgyz Republic	Nicaragua	South Sudan	Vanuatu
Cameroon	Ethiopia	Lao PDR	Niger	Sri Lanka	Vietnam
Cape Verde	Fiji	Lesotho	Nigeria	St. Vincent and the Grenadines	Zambia
Central African Republic	Gabon	Liberia	North Korea	Sudan	Zimbabwe
	Gambia	Madagascar	Pakistan	Suriname	
	Ghana	Malawi	Palau		

## Most HCV treatment uptake increase between 2011 and 2019 has occurred in LMIC

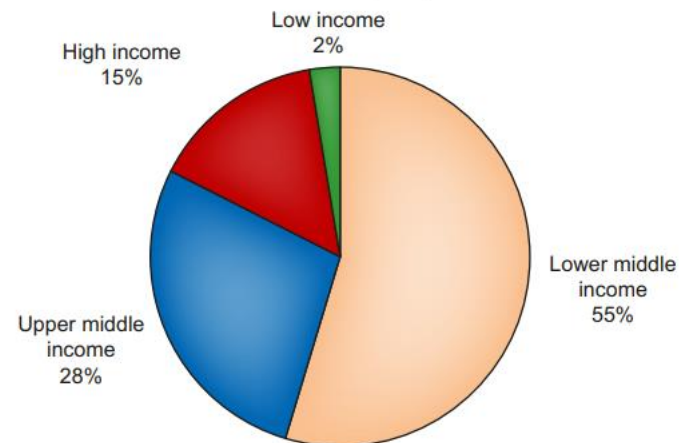


# Impact of COVID-19-related delays in hepatitis C management on treatment uptake and liver-related outcomes, 2020-2030

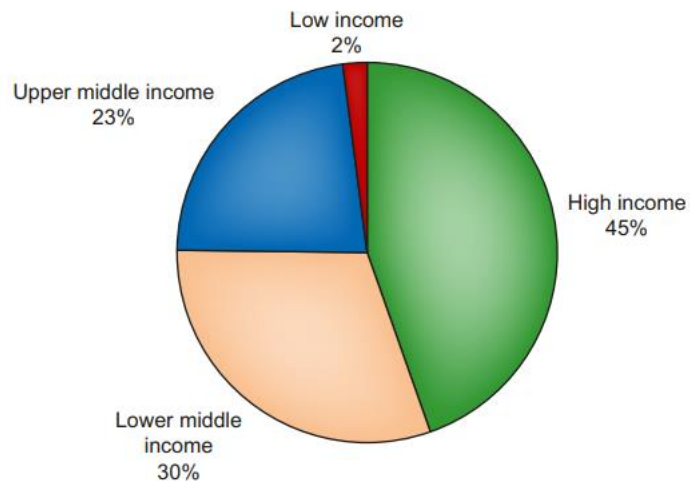
**Missed treatments, WB, 2020-2030**



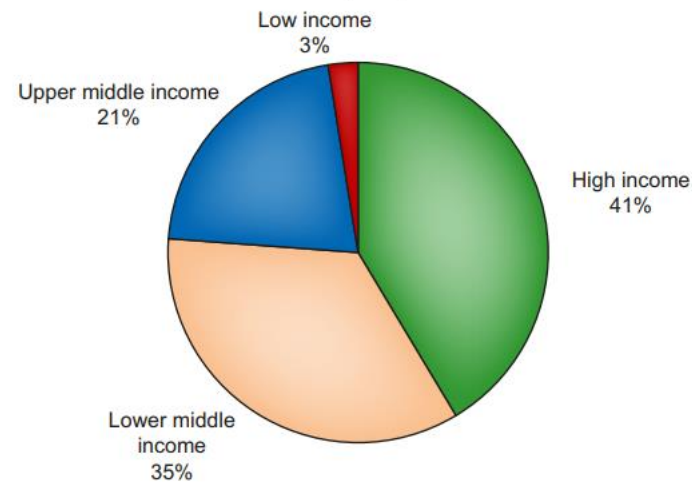
**Excess incident HCV, WB, 2020-2030**



**Excess HCC, WB, 2020-2030**



**Excess LRDs, WB, 2020-2030**



# Treatment capacity matters: the example of Indonesia

Population 250 million

>12 million HBsAg+

>1.4 million anti-HCV+

>6,000 inhabited islands

110 hepatologists

(~13,000 patients/hepatologist)

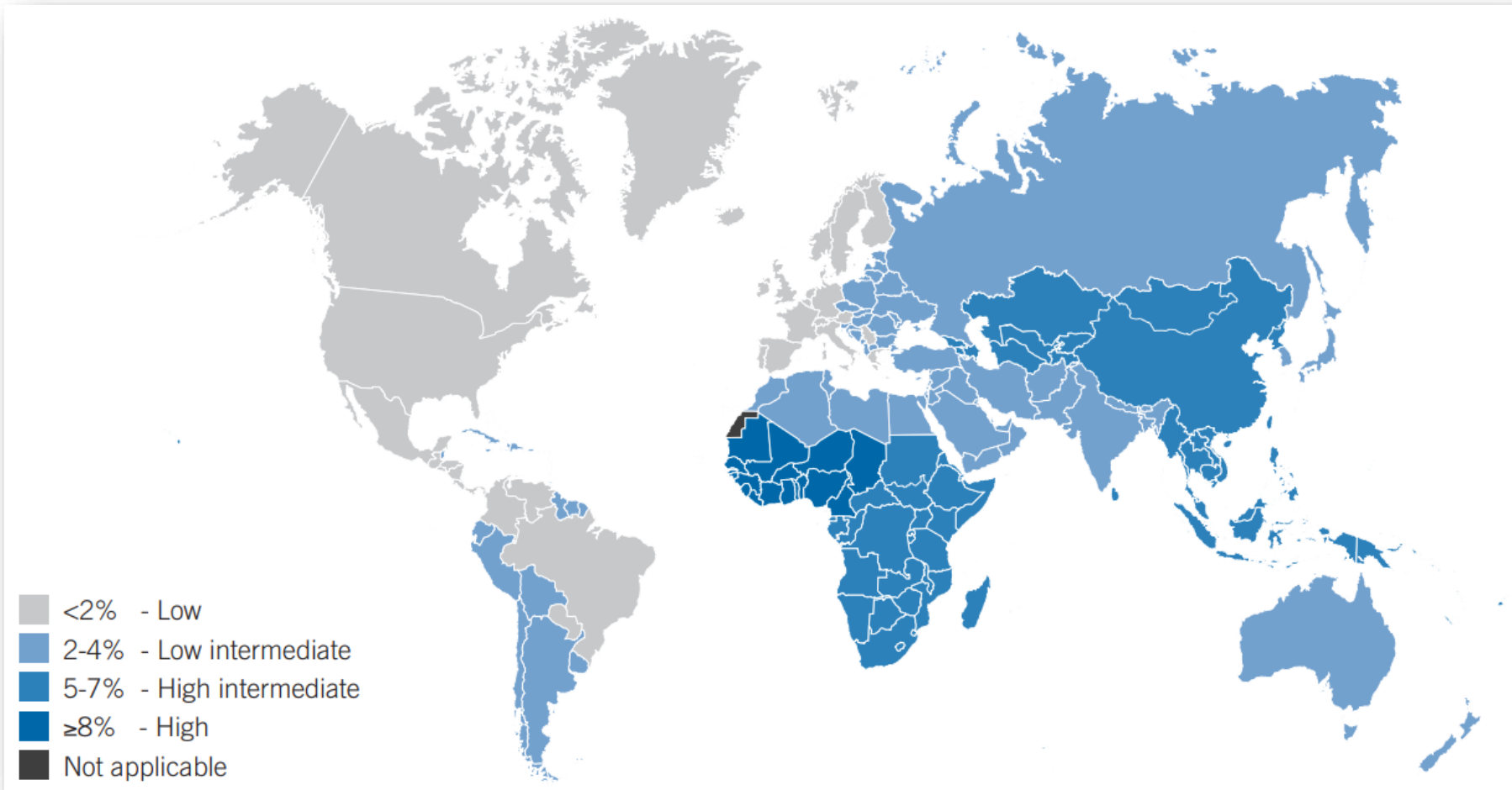




# 257 million persons living with HBV in 2015

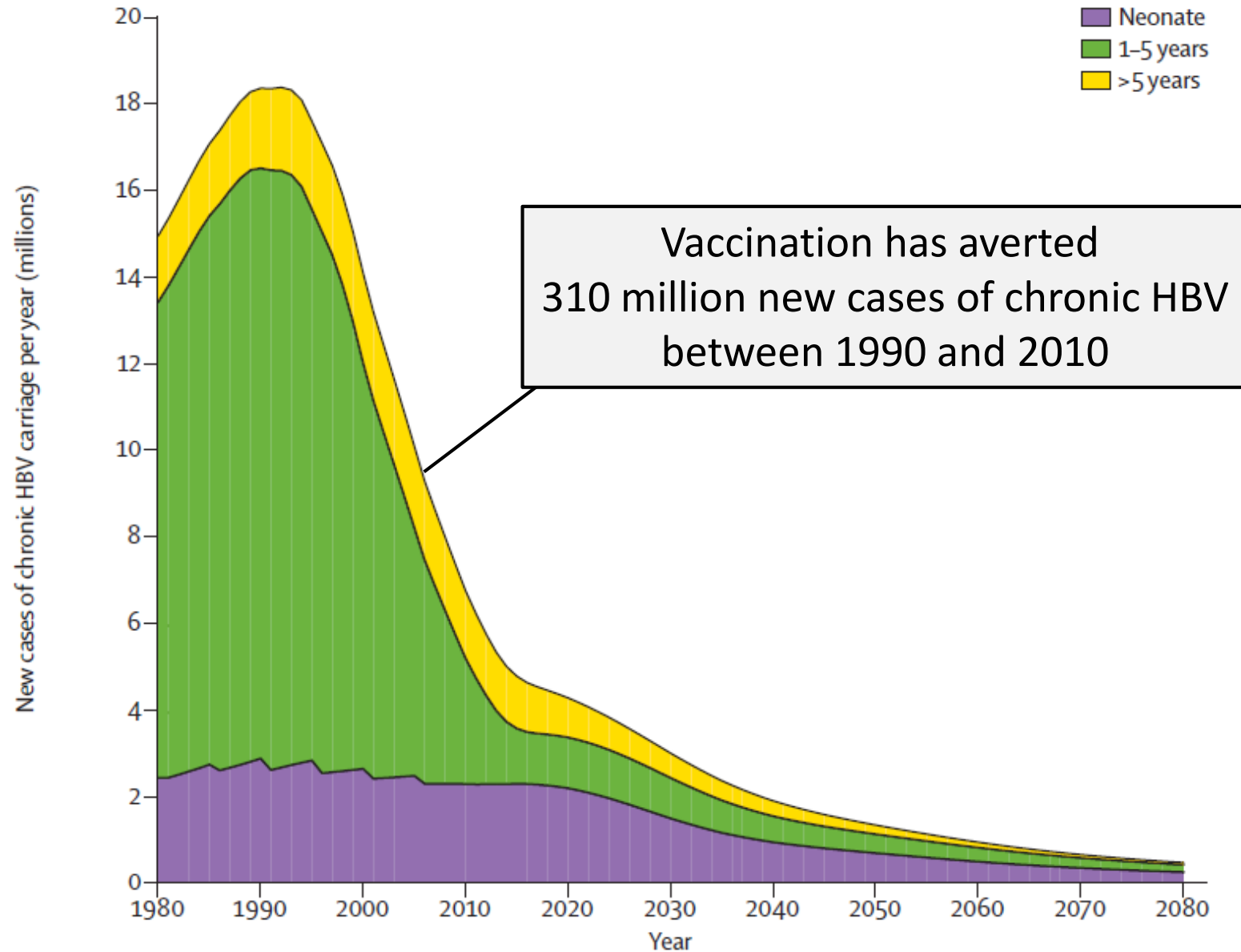
(3.5% of global population, among them 65 million fertile women)

**~600,000 children develop chronic HBV infection each year**

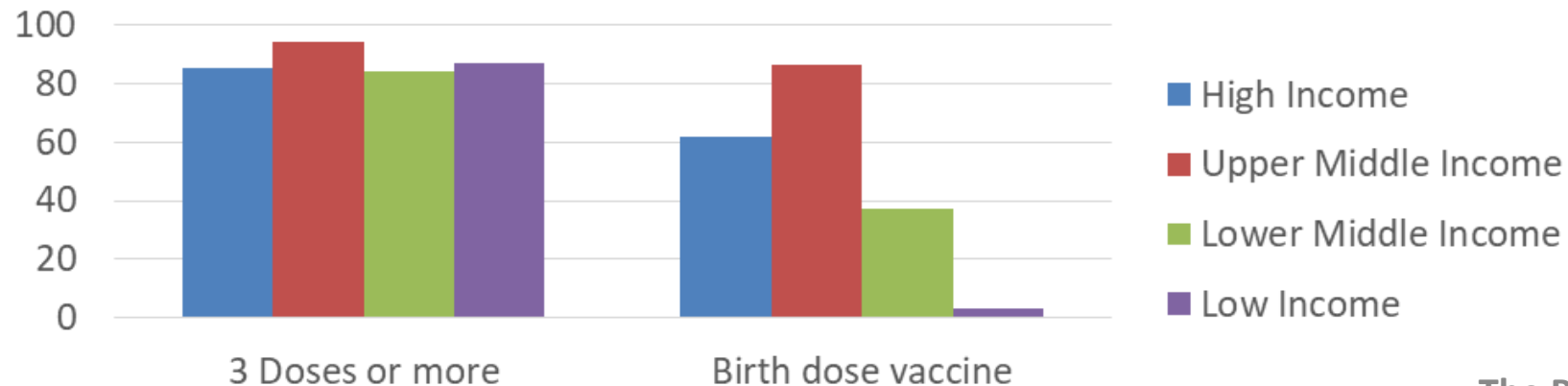
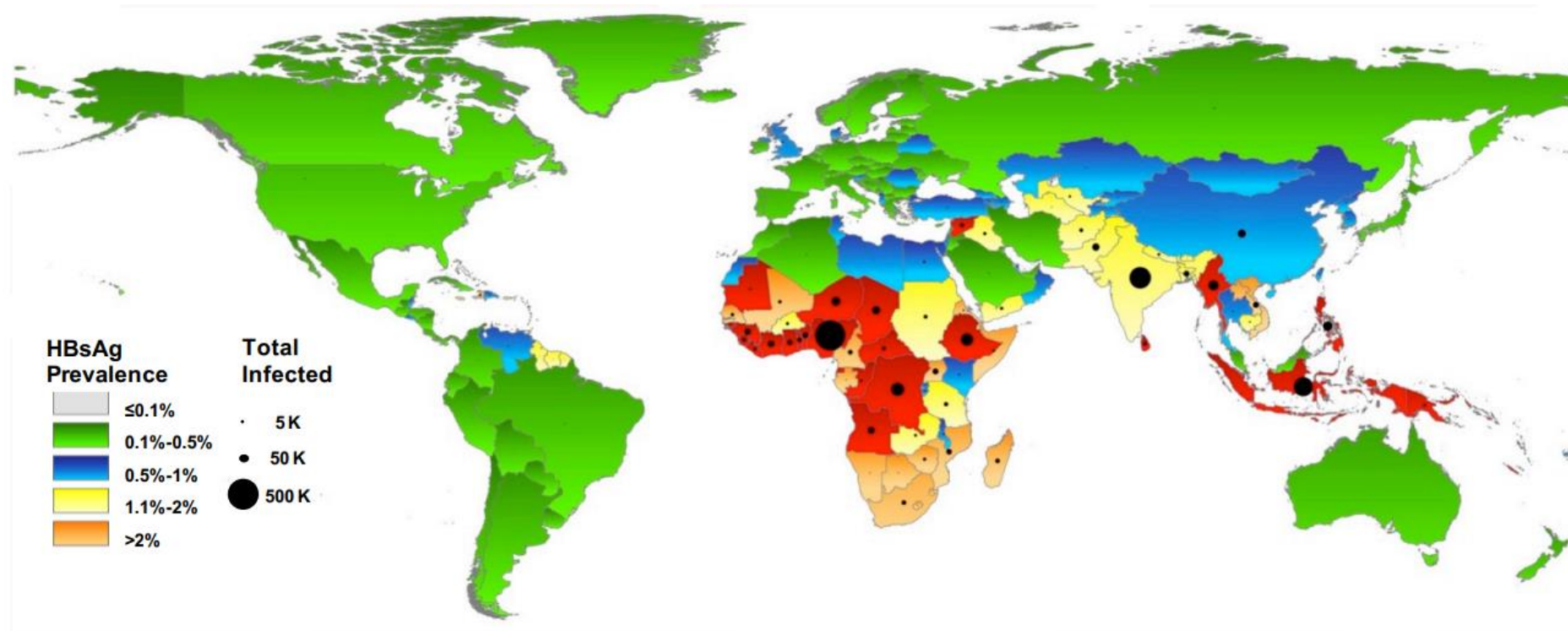




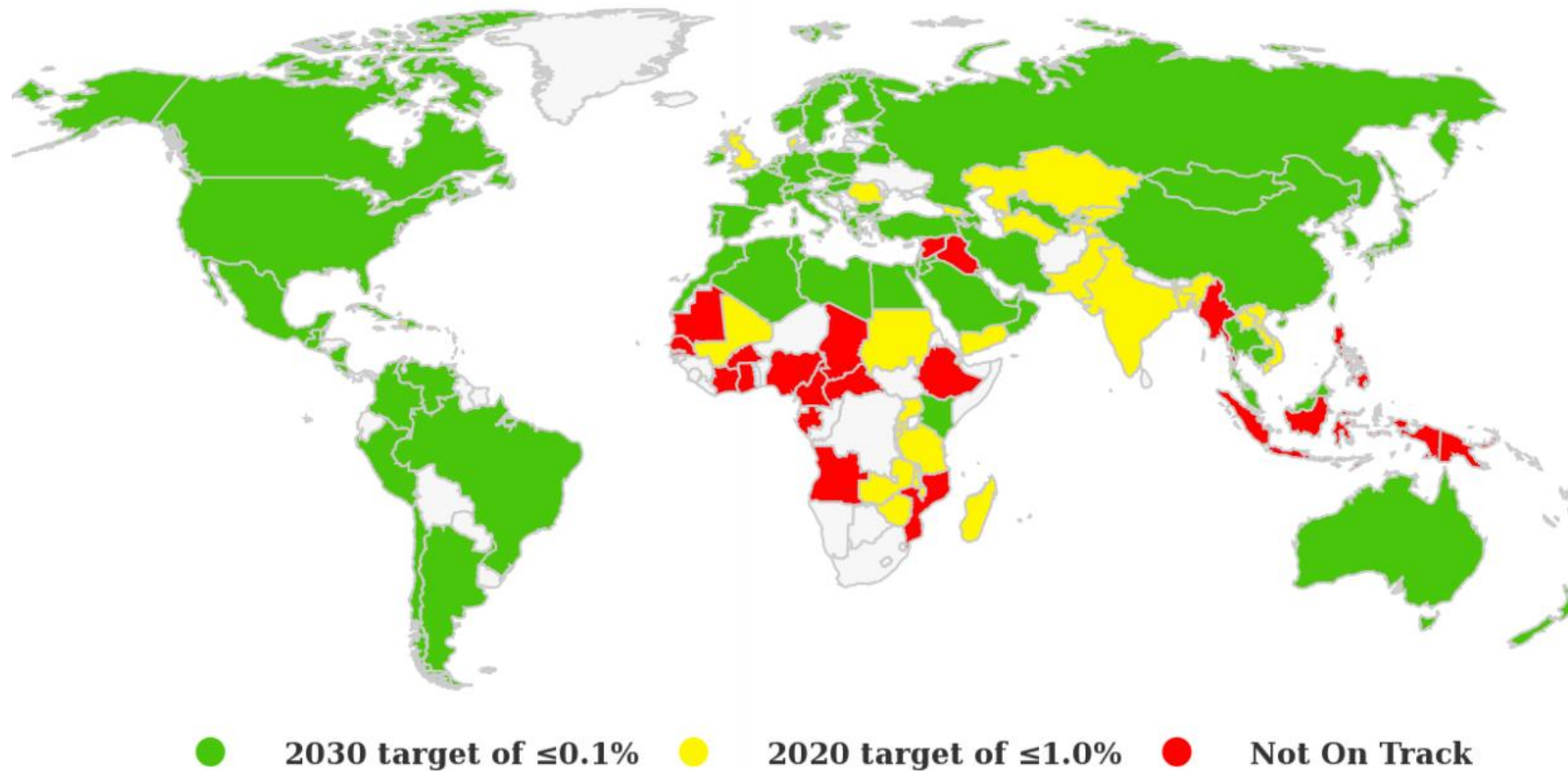
# The global HBV vaccination campaign is a success story



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**





# Vaccine programs supported by GAVI

- Human papilloma virus
- Polio vaccine
- Japanese encephalitis virus vaccine
- Meningococcal vaccine (*Neisseria meningitidis* type A)
- Measles and rubella virus vaccine
- Typhoid vaccine (*Salmonella enterica*)
- Cholera vaccine
- Rotavirus vaccine
- Yellow fever vaccine
- ***Pentavalent vaccine (diphtheria, tetanus, pertussis, Haemophilus influenzae type B, hepatitis B)***
- Ebola vaccine

# Why is hepatitis B vaccine coverage at birth so low in many African countries?

By *Jenny Lei Ravelo* // 28 July 2020

Global Health

Funding

Trade & Policy

Gavi

WHO

Central Africa

Southern Africa

West Africa



*Hepatitis B vaccine. Photo by: Larry McCormack / The Tennessean via Imagn Content Services, LLC*

MANILA — More children are receiving the hepatitis B vaccine today, but coverage, especially at birth, remains uneven across regions. Coverage of the first critical dose, which the World Health Organization says should be given within 24 hours from birth, is only at 43% globally. The proportion is even lower when broken down regionally, with only 6% in the countries that are part of the WHO regional office for Africa.

High number of out-of-facility births (~50%)

Limited number of skilled birth attendants

Male domination in maternal health care workforce

Unwillingness to be examined by male care providers

Poor gender and cultural sensitivities for women

Unmarried adolescent girls are denied access to family planning services because of unfriendly provider attitudes to premarital sex



**Barriers to maternal health**

Administration of the vaccine beyond 24-hour time frame

Cold chain storage requirements

Low cost per dose equal to the minimum amount  
countries co-finance as per GAVI cofinancing policy



**Barriers to birth dose provision**



**Low HBV birth dose coverage in Africa**

**Europe: 20 maternal deaths per 100,000 live births**  
**WHO AFRO Region : 480 maternal deaths per 100,000 live births**

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

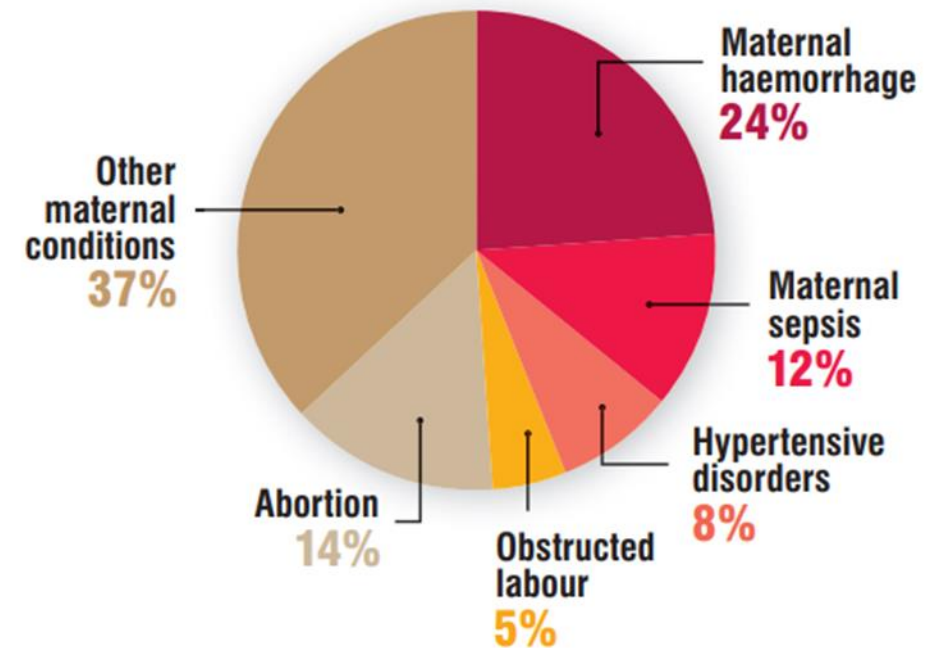
**Antenatal and delivery care coverage**

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)**







## Ten threats to global health in 2019

**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**

## 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 can infect more than a dozen people, typically infants who have received their first dose. Such high levels of infection that when the percentage of the community who have

[measles vaccine](#) falls below 90 percent to 95 percent, we see major outbreaks, as in the 1950s when four million Americans were infected and 450 died. Worldwide, measles still kills about 1 million children each year.

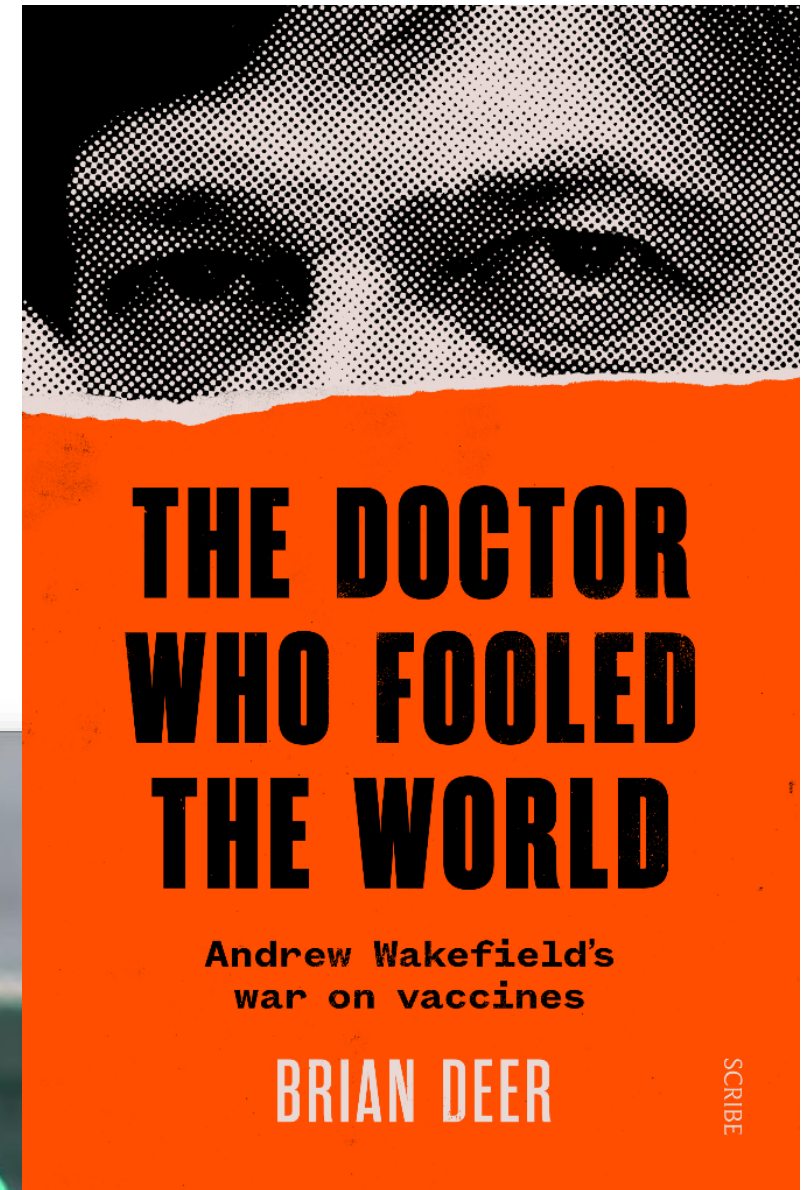


MEASLES OUTBREAK

WHY PARENTS REFUSE TO VACCINATE


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# 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

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**"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

**To conclude....**





Lunch in a toulou at Tianluokeng (Fujian, South China, 2016)





**A wet market somewhere in South East Asia (not my picture)**





Near Hora Lake, Dere Zeit, Ethiopia, 2017





With Homie Razavi, we preferred PLOV (with tea and vodka) to foreign delicacies.... (Samarqand 2018)





**Professor Olzvoi (here in Ulaanbaatar, 2017) published the first paper on viral hepatitis in Mongolia in 1982**





With Dr Tiruwork Fekadu, the first female hepatologist in Ethiopia, Addis Abeba, 2016

## Hepatology in resource-poor countries

- Poor data, poor awareness, inadequate policies
- Lack of skilled health workers (poor working conditions, poor pays)
- Most liver disorders managed by GP's, with specialists (GI, ID) are concentrated in major cities
- Priority should be given to infrastructure (communication, utilities....)
- Geographic barriers (distances, remote locations, islands)
- Corruption
- Beware that improved socioeconomic status may lead also to:
  - Metabolic syndrome
  - Alcohol drinking among females
  - Vaccine hesitancy
- Gender equality is lagging behind



