Estimating the impact of HBV vaccination policies

John Edmunds[1], Edward Jones[1], Andrea Apolloni[1], Fernando de la Hoz Restrepo[2], Pierre Gselle[3], Ximena Riveros Balta[3], Ana Maria Henao Restrepo[3]

[1] London School of Hygiene and Tropical Medicine
[2] Universidad Nacional de Colombia
[3] World Health Organisation

john.edmunds@lshtm.ac.uk

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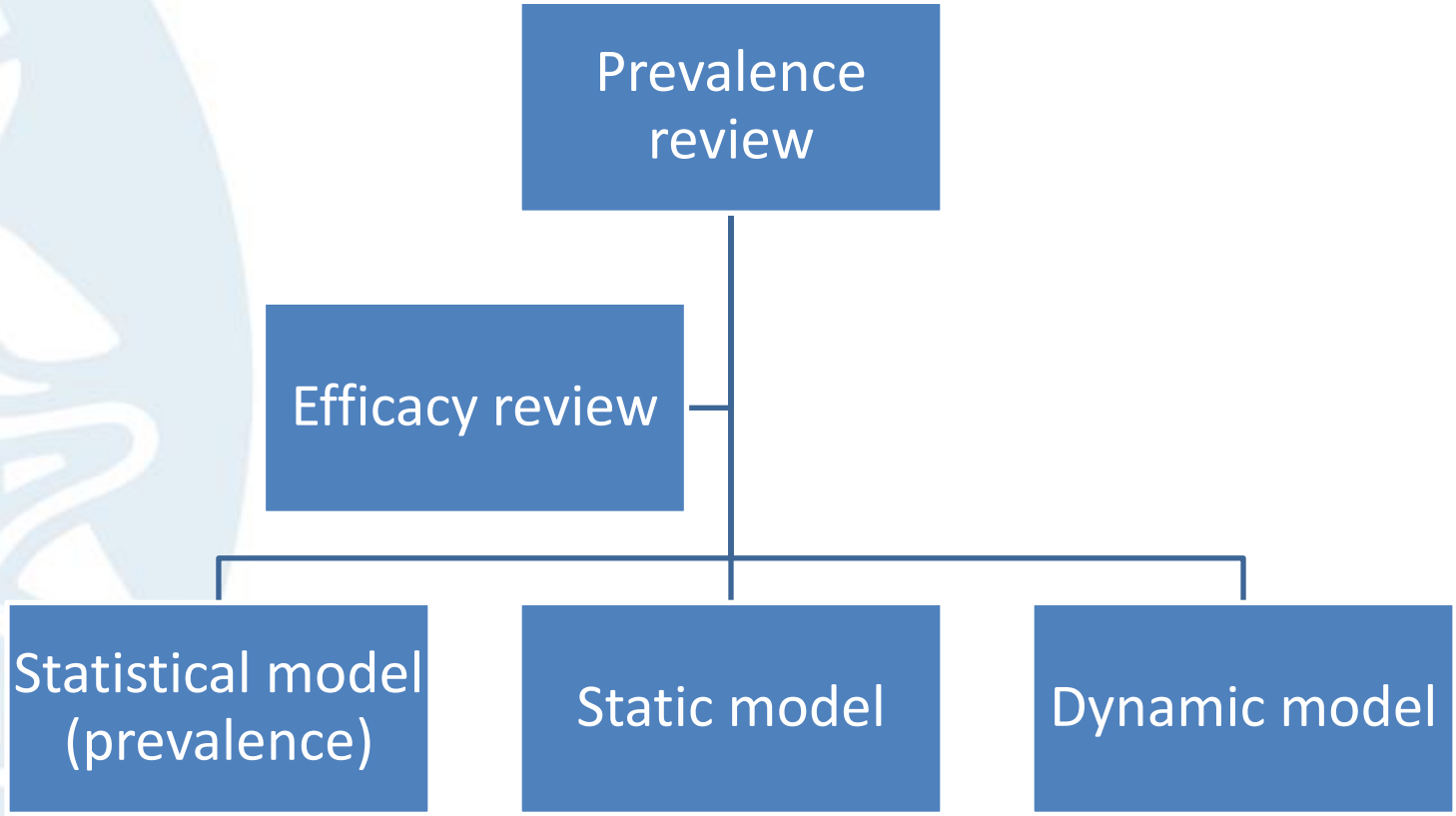
Project overview



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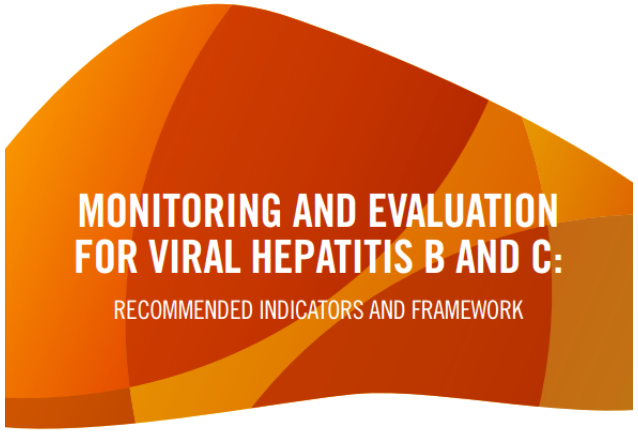
HBsAg prevalence

- Impact of HBV vaccination on liver cancer and cirrhosis takes many years to become apparent
- HBsAg carriage is necessary pre-condition for HBV-associated chronic disease
- Impact on carriage can be more rapidly assessed
  - Serological surveys in vaccinated age cohorts (and others)

www.who.int/hepatitis/publications/hep-b-c-monitoring-evaluation/en/

World Health Organization



Indicator C.9.a	Cumulated incidence of HBV infection in children 5 years of age
Indicator category	Core (GLOBAL INDICATORS)
Measurement method, sources of data	HBsAg biomarker prevalence survey in children 5 years of age (immunization coverage surveys and administrative vaccination coverage data) *(35)*

Systematic review of HBsAg prevalence studies

Schweitzer et al. Lancet 2015

- Systematic review of studies on HBsAg published 1965-2013
- 1800 reports on HBsAg from 161 countries.
- Seroprevalence was 3·61% (95% CI 3·61-3·61)

But

- Potentially relevant background data were not extracted, e.g.
  - Age group
  - Sex
  - Exact geographical location
  - Vaccine status of surveyed group
- Missing data
  - particularly recent studies in vaccinated cohorts


Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013

Aparna Schweitzer, Johannes Horn, Rafael T Mikolajczyk, Gérard Krause, Jördis J Ott

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Additional data extraction and search

- Papers in Schweitzer et al. study were retrieved and further data extracted on
  - Demographics of sample (age, sex, population group etc)
  - Geographical location (lat-long of centroid of study area)
- GDP per capita was assigned for each country using UN database.
- Vaccinated cohorts were identified for each database by linking with WHO/UNICEF data on HBV vaccine introduction (HBV3 & BD)

Additional search

- Targeted at countries with high/intermediate prevalence (>=2%) that had introduced vaccination
- Studies reporting local, regional or national data on HBsAg prevalence published in English, French Spanish, Portuguese between 2000 and 2016
- Similar inclusion and exclusion criteria to Schweitzer et al.

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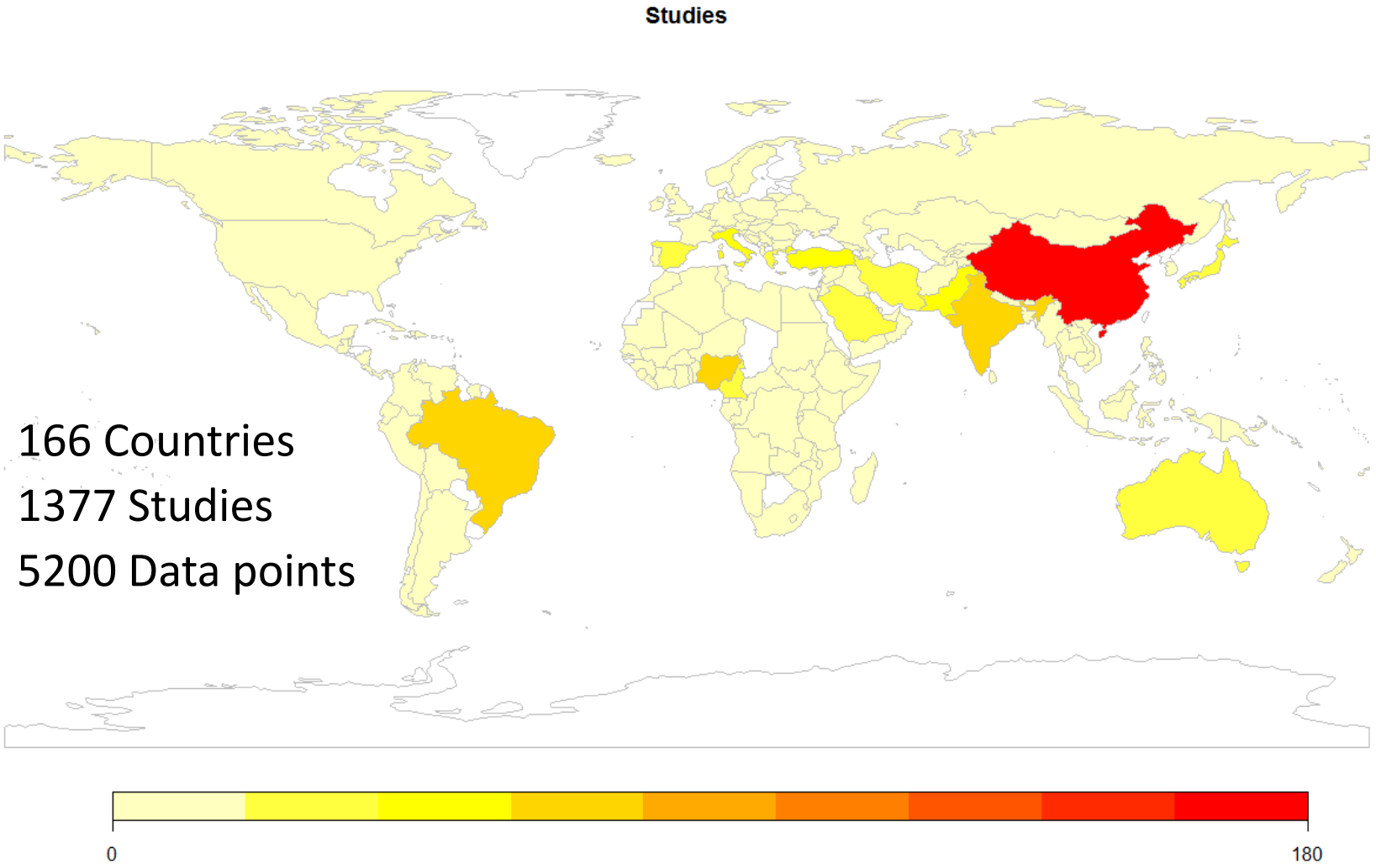
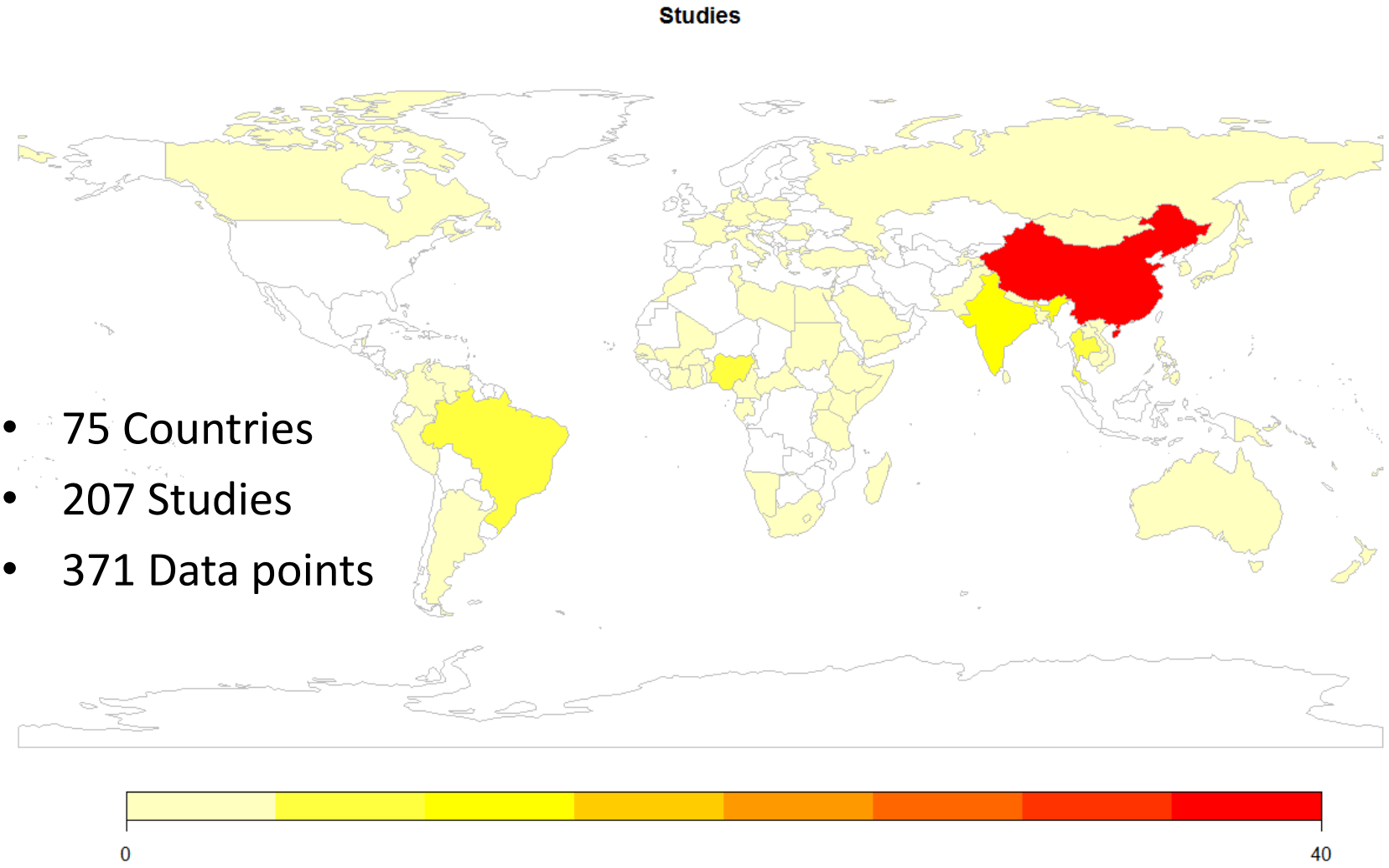
Total number of studies across countries



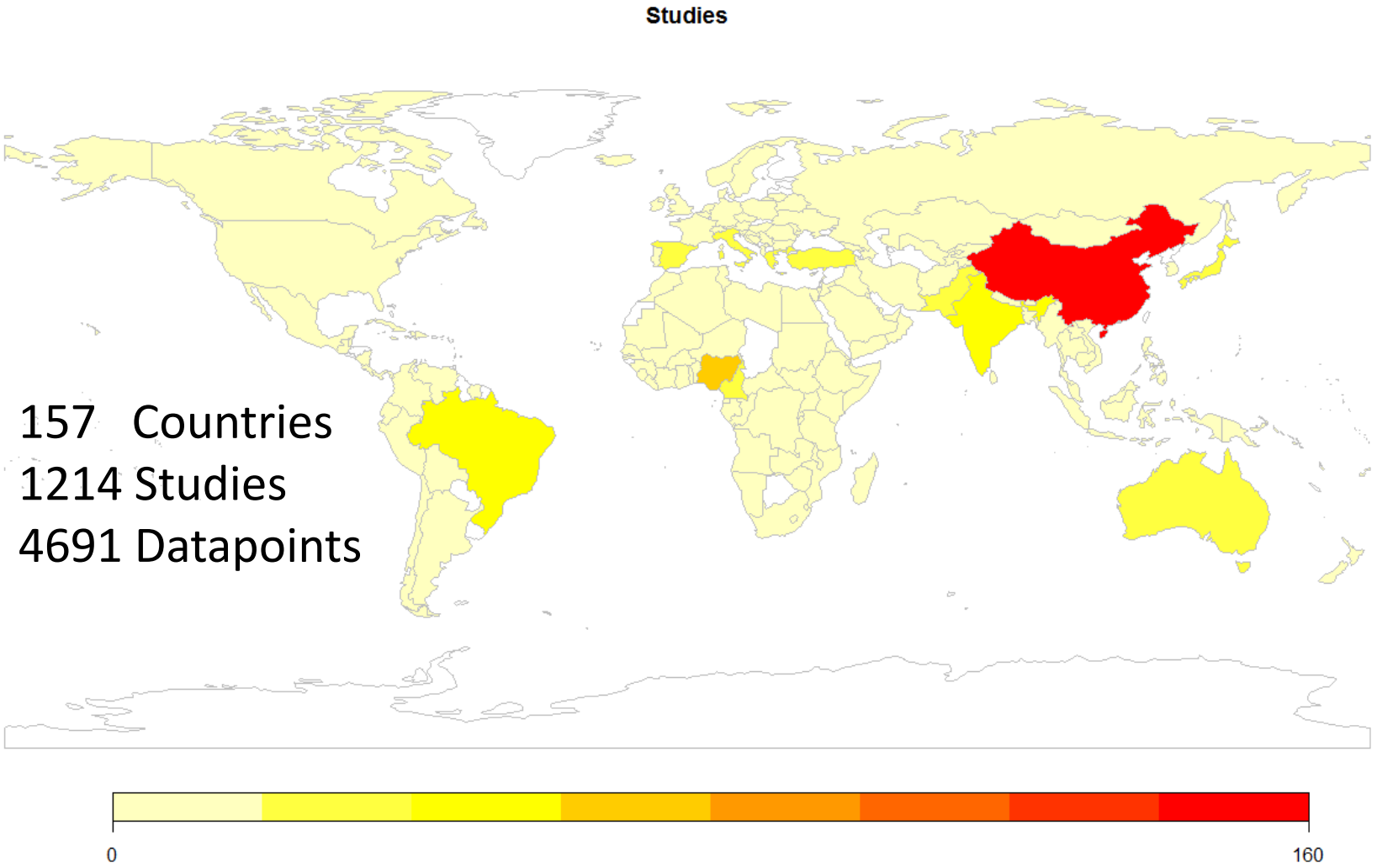
- 166 Countries
- 1377 Studies
- 5200 Data points

Studies with U5 data



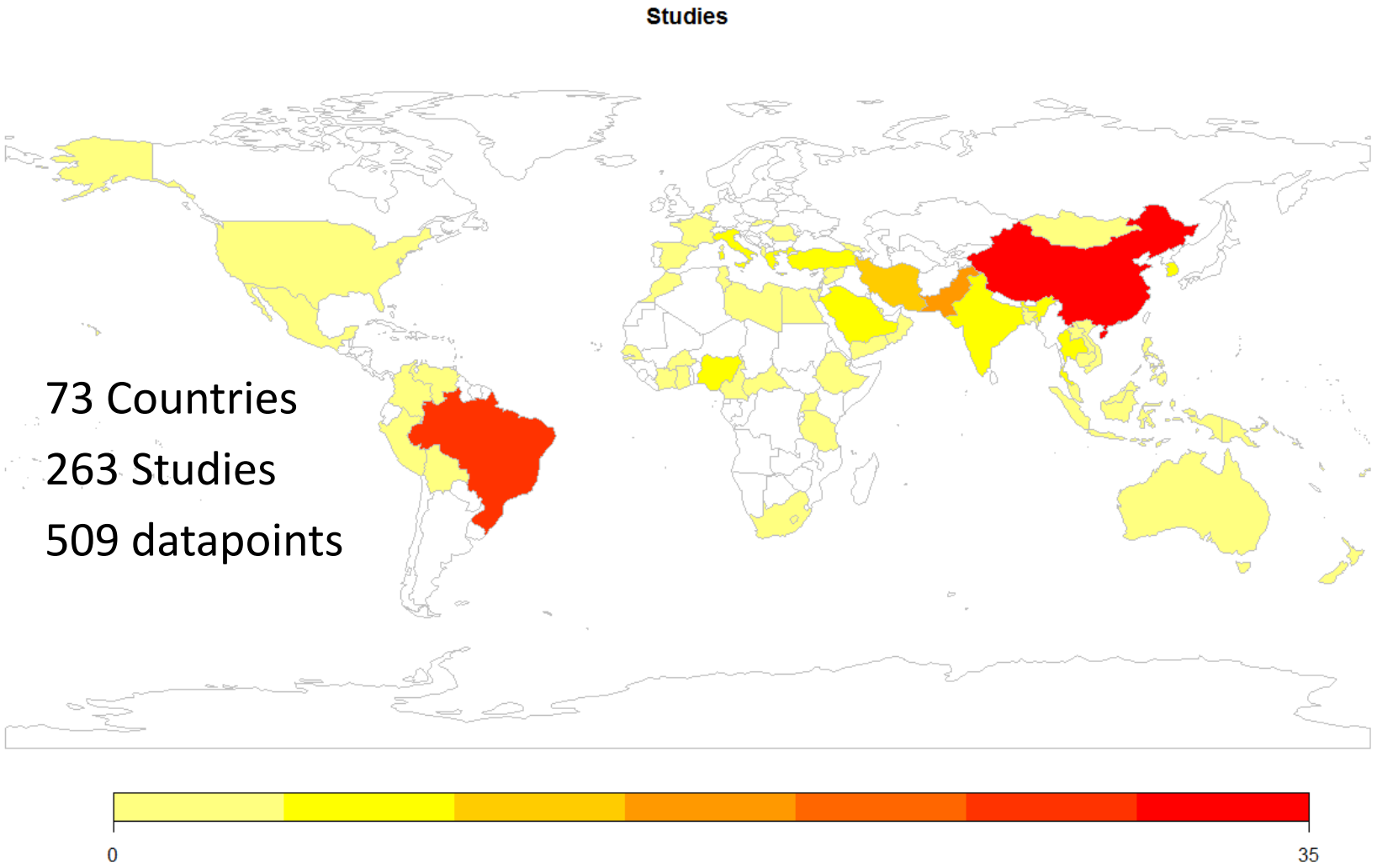
- 75 Countries
- 207 Studies
- 371 Data points

Pre-vaccination



- 157 Countries
- 1214 Studies
- 4691 Datapoints

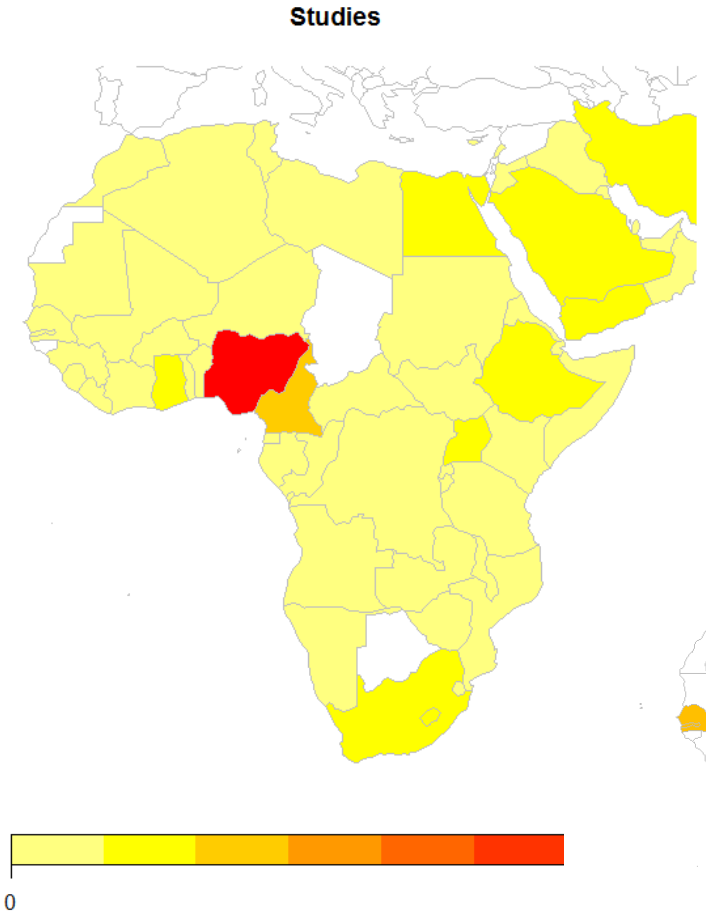
Post vaccination studies

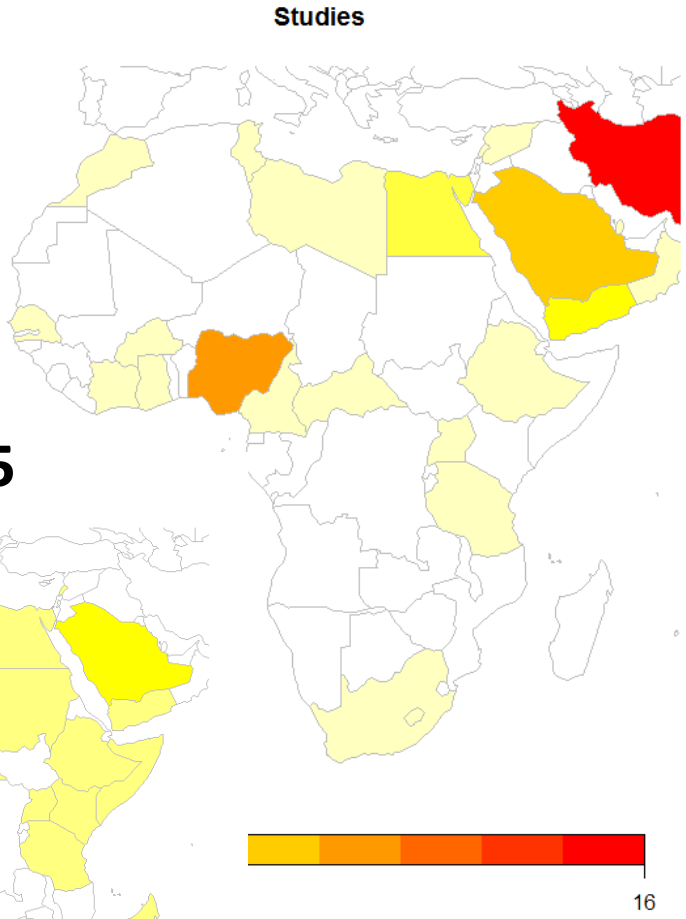


- 73 Countries
- 263 Studies
- 509 datapoints

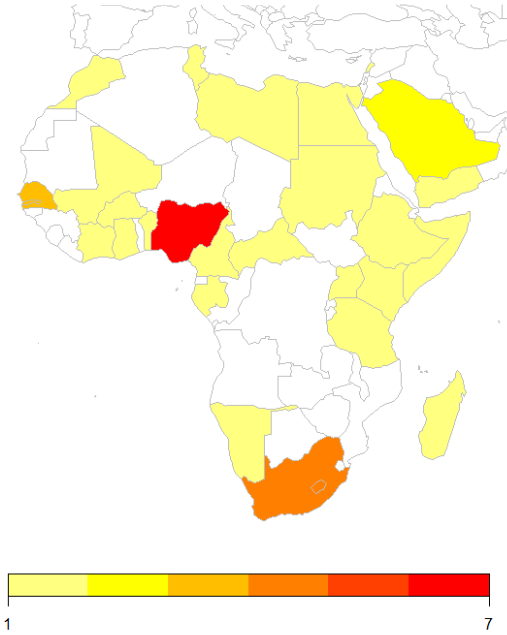
Pre-vac

Post-vac





Under 5



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Estimating the HBsAg prevalence

- Logistical regression with geospatial random effects
  - Included geographic and GDP difference in a distance matrix as part of the correlated autoregressive function.
- Variables
  - sex, age, bias (e.g. indigenous peoples), vaccinated cohorts, birth dose
- $Y_i \sim \text{Binomial}(\pi_i, N_i)$, $\log \frac{\pi_i}{1-\pi_i} = \beta_0 + \sum_{j=1}^{p} \beta_j x_{ij} + u_i$
- Bayesian statistical package WinBUGS
- Validation on random sample of studies (10%)

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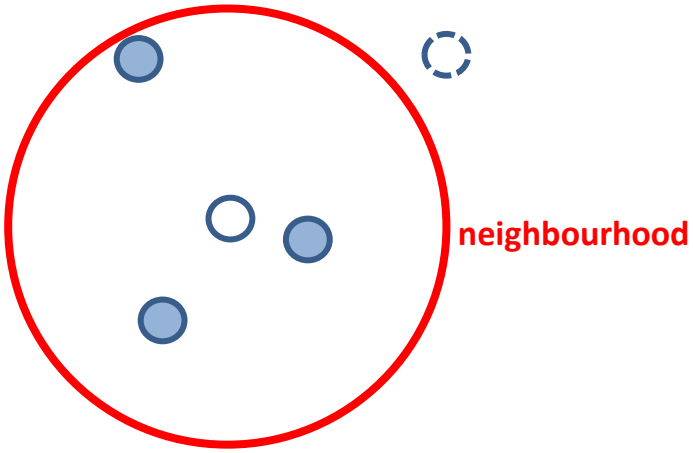
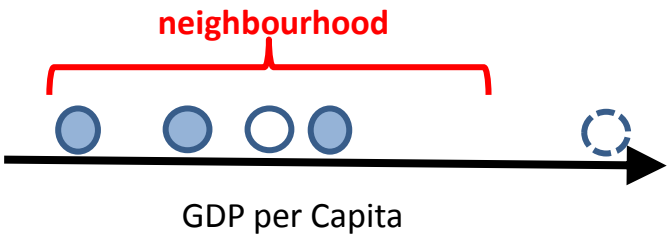
Country-level random effects: measures of distance

- Geographical distance (space)
  - Define neighbourhood around point of interest
  - Data points within neighbourhood contribute to estimate
  - Can either weight the points according to their distance or not



- Socio-economic distance (GDP per capita)



- Both “distance” measures used in the model
  - Weighted 2:1 in favour of GDP distance

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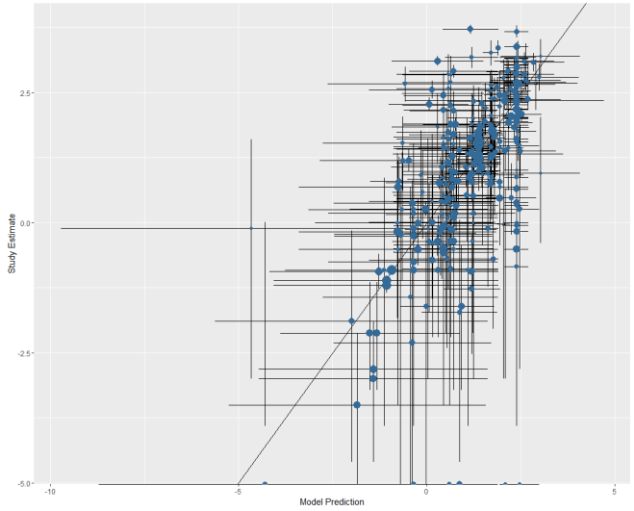
Model validation

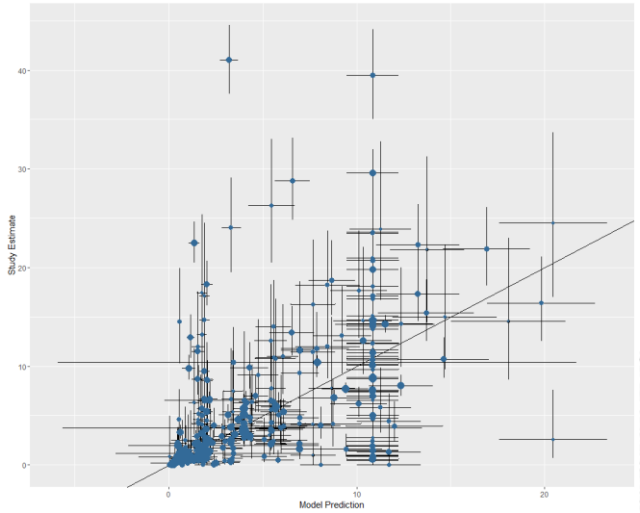
Validation

- Final model run using 90% of data
- Verified against remaining 10%

- Final model predictions incorporate all data



Log scale



Linear scale

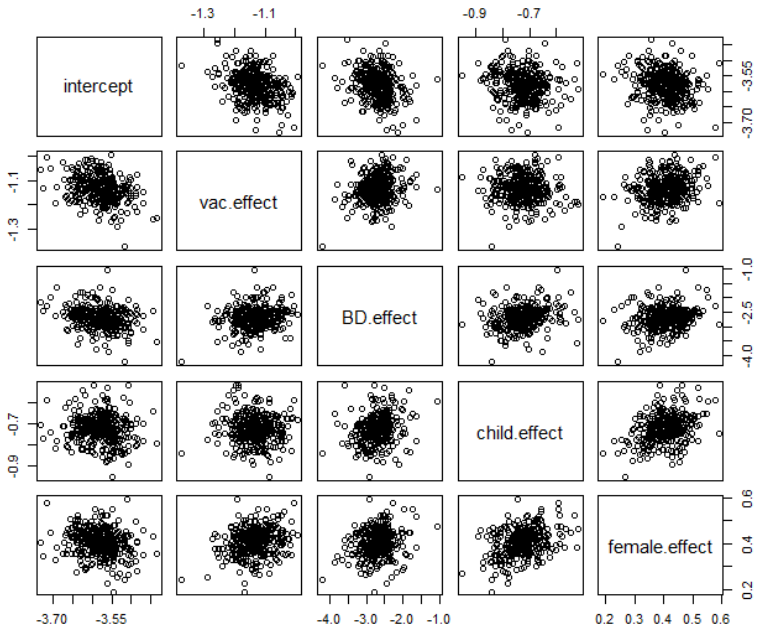
Model selection and results

Selection

- Sensitivity analysis performed on assumptions
  - Incorporation of birth dose
  - Different methods for incorporating gender
  - “Bias”
  - GDP vs geographical distance
- Best fitting model selected based on deviance

Key result

- Vaccination significantly reduces prevalence
- Incorporation of birth dose significantly improves model fit & further reduces prevalence



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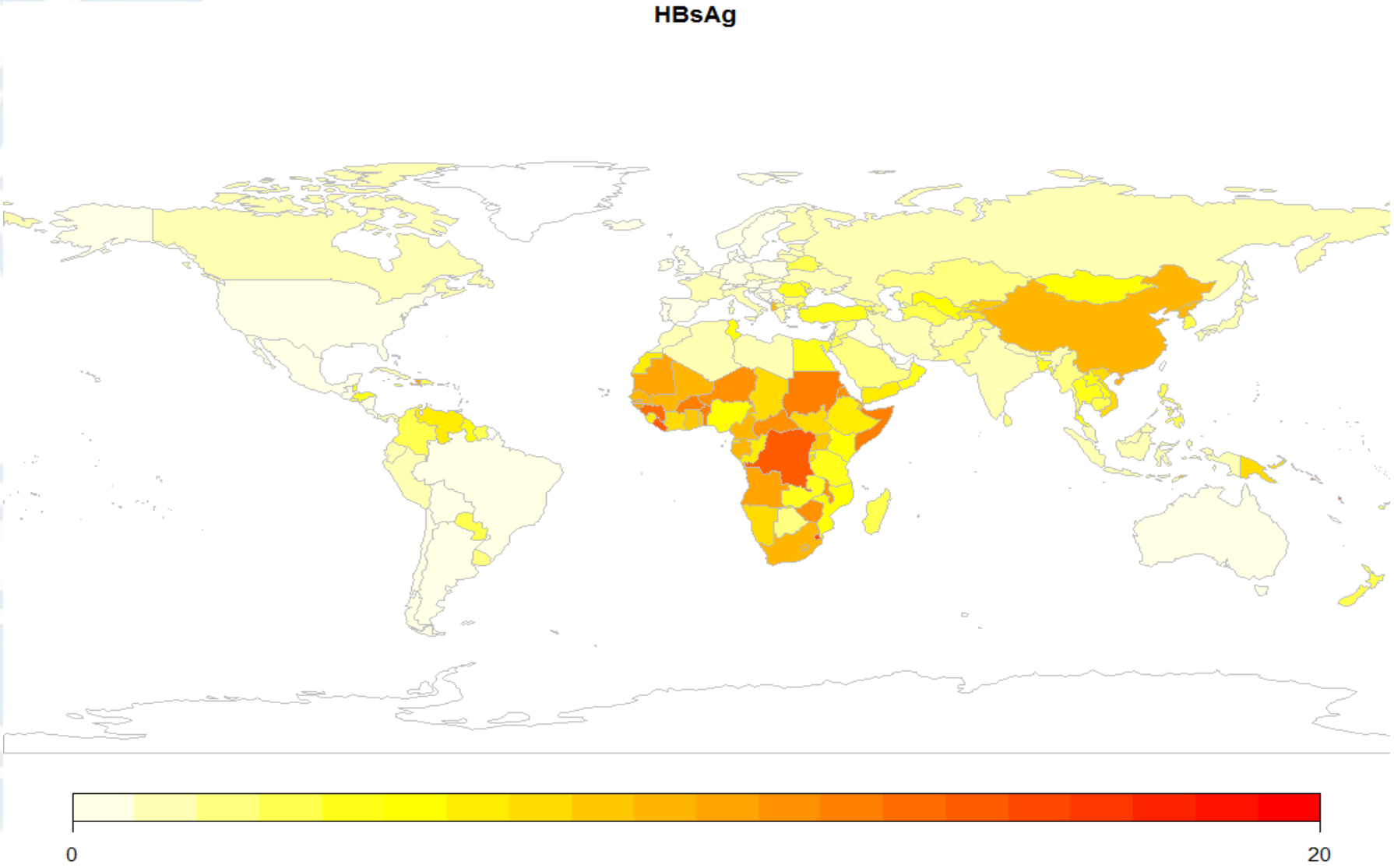
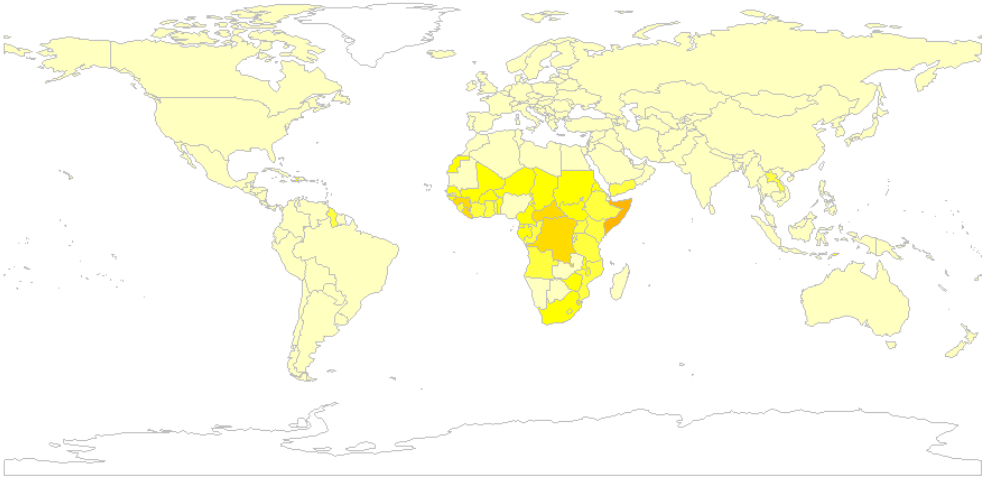
Adult prevalence estimate pre-vaccination

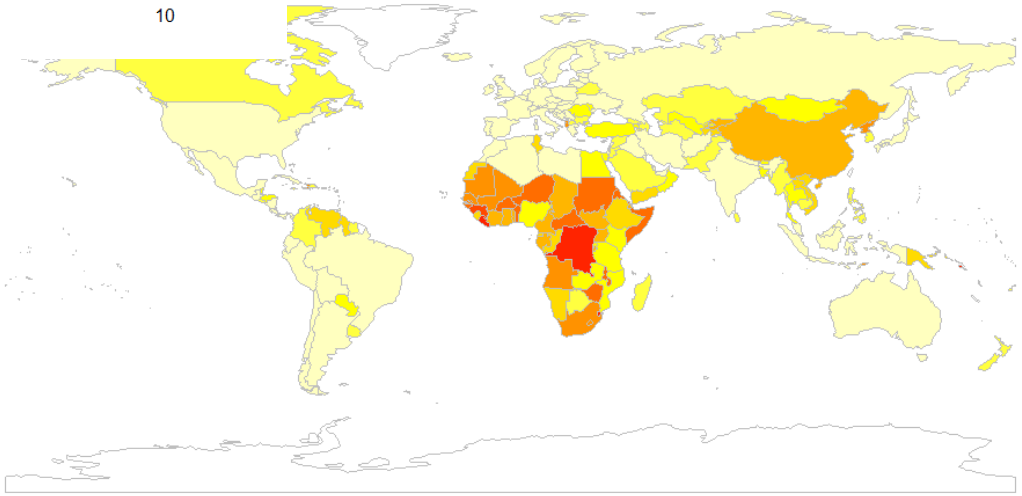


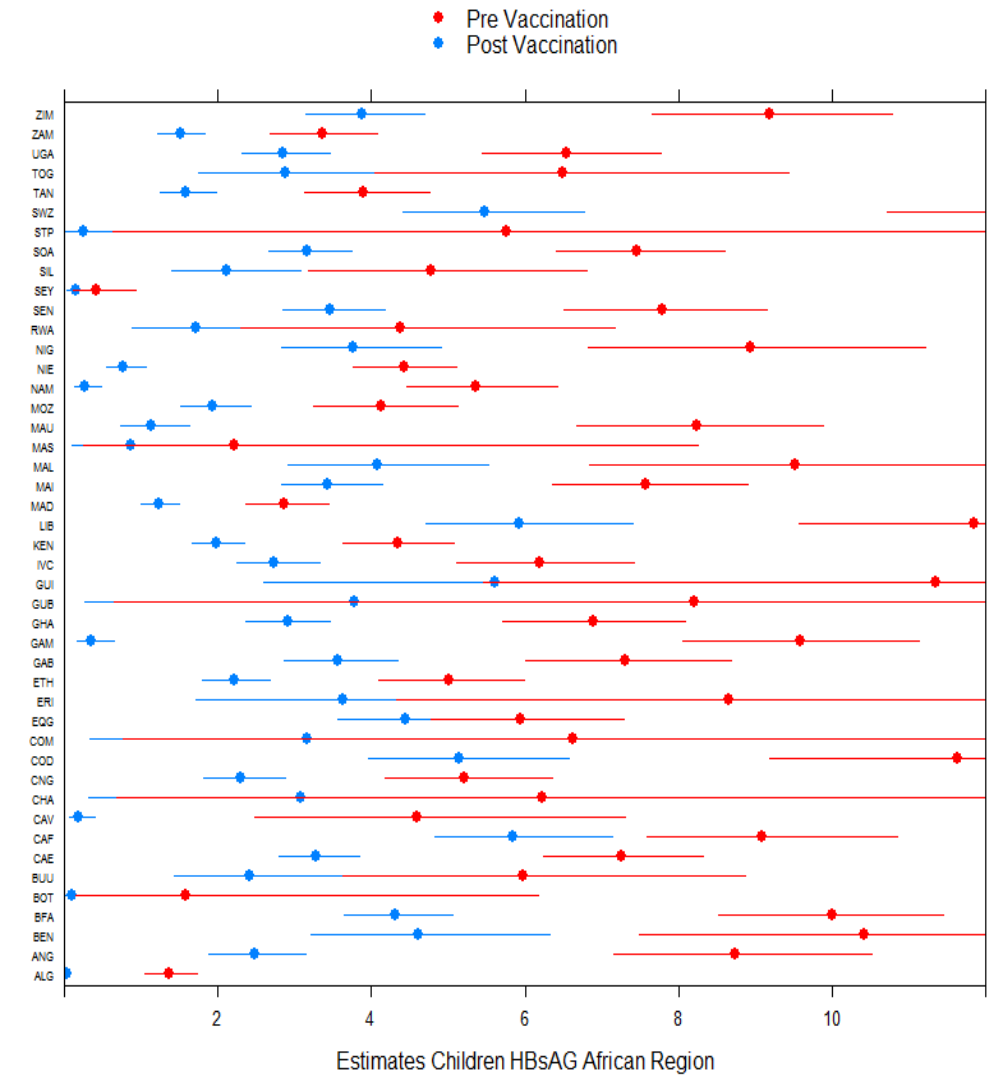
HBsAg



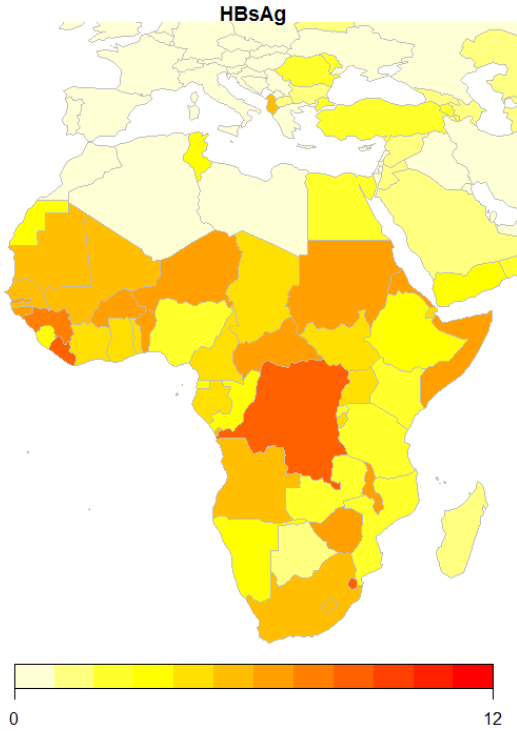
U5 prevalence estimate post & pre vaccination

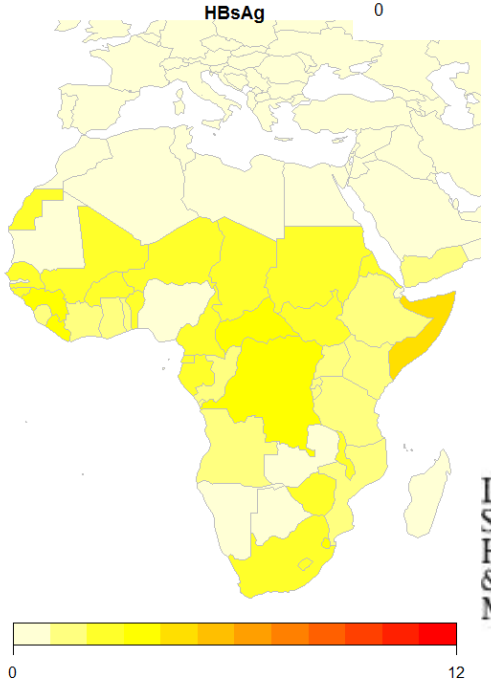
HBsAg





Pre-vaccine





Post-vaccine

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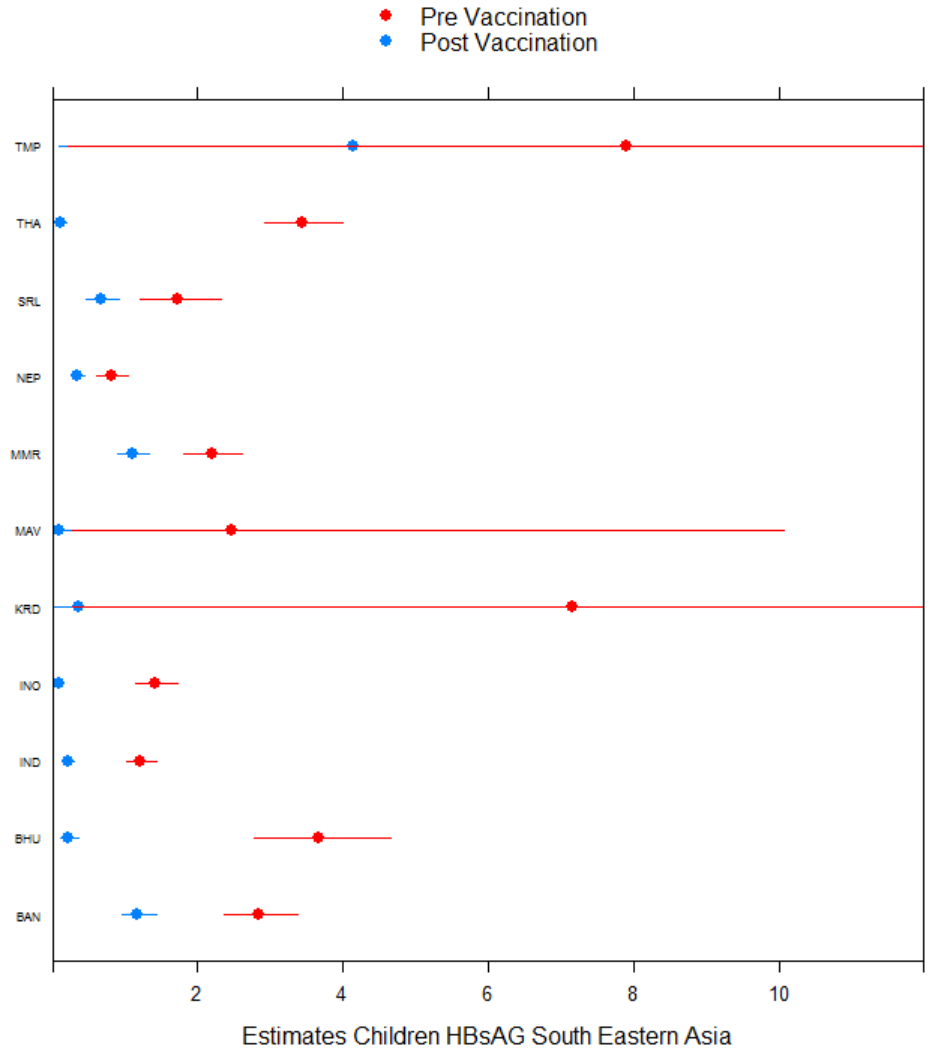
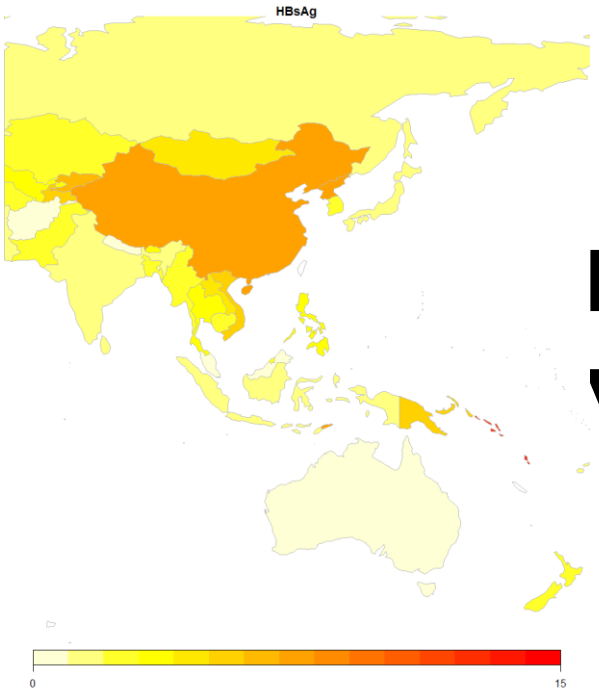
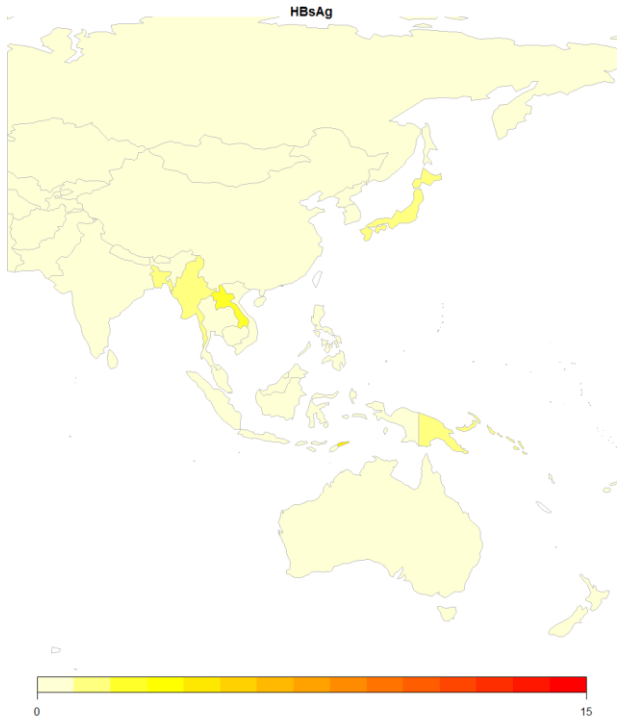




Pre-vac



Post-vac

Global estimate carriage without vaccination

	Total number	Overall HBsAg	Under 5 HBsAg
Europe	15,453,613	1.8%	1.1%
Americas	10,714,549	1.1%	0.7%
W. Pacific	137,947,933	7.9%	4.0%
Africa	71,671,384	8.6%	4.3%
SE Asia	38,135,460	2.1%	1.0%
East Med	21,219,990	3.7%	2.0%

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Predicted current under 5 carriage

	Prevalence (%) HBsAg	
	pre-vac	post-vac
Europe	1.1	0.1
Americas	0.7	0.1
W. Pacific	4.0	0.2
Africa	4.3	1.6
SE Asia	1.0	0.2
East Med	2.0	0.6

	pre-vac	post-vac
Europe	633,217	72,286
Americas	500,323	81,530
W. Pacific	4,765,849	258,441
Africa	6,786,242	605,557
SE Asia	1,852,959	370,431
East Med	1,569,459	473,973

14.2m under 5 carriers prevented

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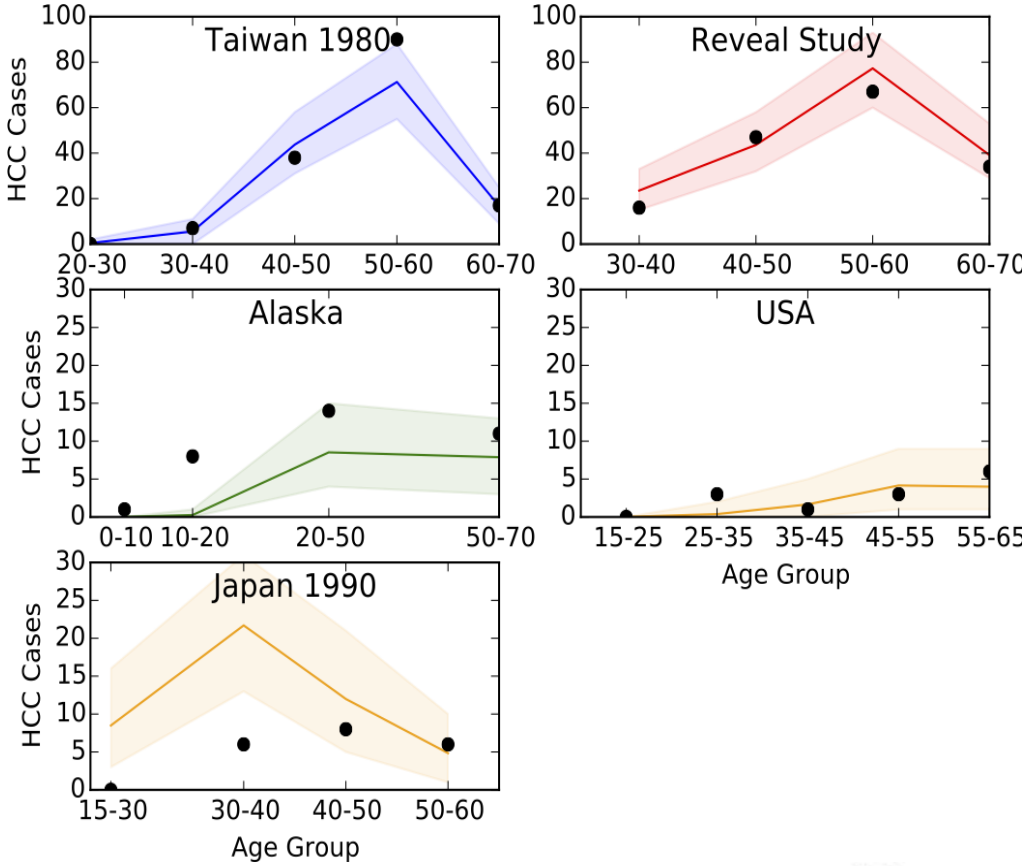
Predicting the impact on HBsAg carriage-related deaths

- Static model for 169 countries
- Markov-Model including perinatal infections
- Inputs
  - Country-level estimates of HBsAg prevalence
  - Demographic trends (UN)
  - Vaccine coverage (WHO/UNICEF)
    - Timing (Sanderson)
  - Vaccine efficacy (lit review)
- Outputs (country level)
  - Estimate of burden of HBV
  - Estimates of HCC cases and HBV-related deaths
  - Conservative estimates of vaccination effect



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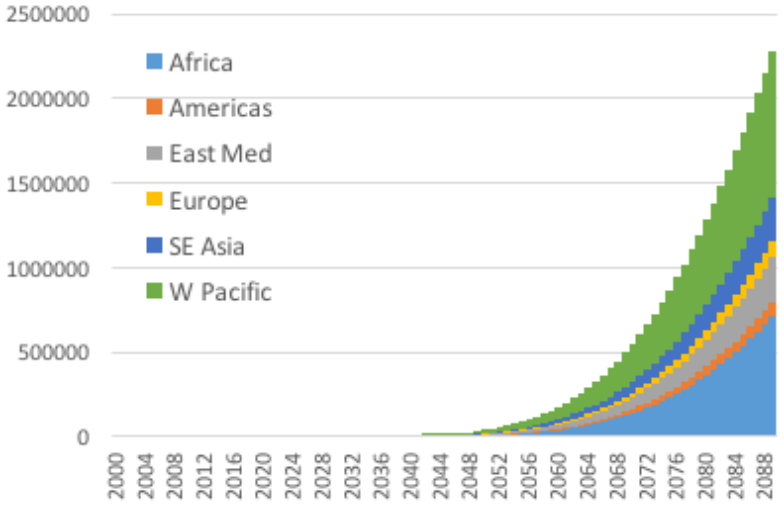
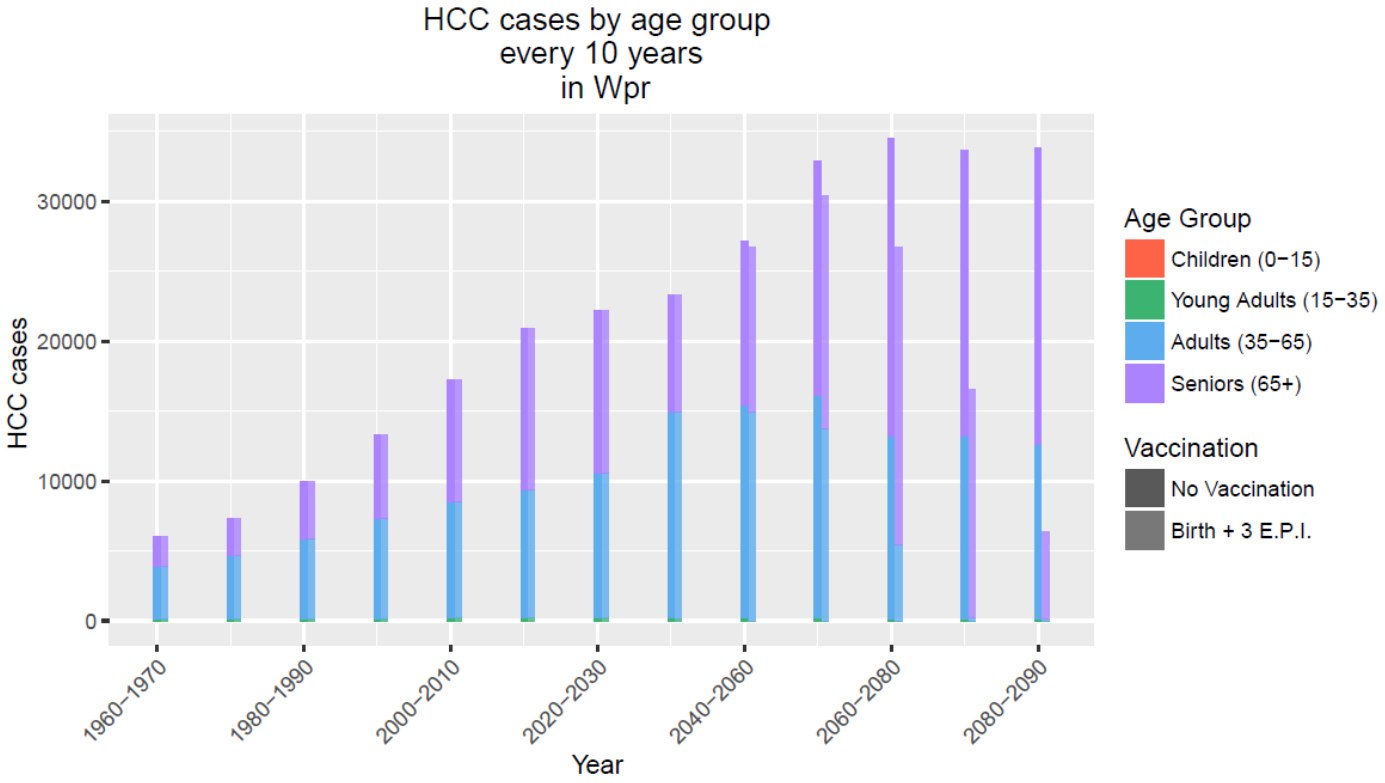
Predicted impact on carriage-related deaths





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Summary

- Constructed an updated global database on HBsAg prevalence
  - Enhanced data for each point
    - Age group, vaccine status, GDP per capita
- Database very large, but has gaps (e.g. U5 post-vaccination)
- Used this database to construct and validate a statistical model to
  - Examine factors influencing prevalence (e.g. HBV3 and HBVBD coverage)
  - Predict the prevalence in areas where data are lacking
- Data and model demonstrate dramatic reduction in prevalence in children under 5 years of age post vaccination
- Prevalence estimates inform static model to predict the impact of vaccination on deaths associated with chronic HBsAg carriage
  - Large reductions in deaths expected in the long run
  - Meanwhile HBV-associated deaths expected to increase
    - Due to past population growth and increasing life-expectancy

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