BETTER WITH AGE: estimating age-specific susceptility

April 2017

Inference from Age of Cases

- We often focus on time series dynamics of infectious disease, but there is a long history of using age-specific information to infer past process

Inference from Age of Cases

- Observing a case tells you something about risk at that time and place
- Observing a case of known age, A, tells you about risk prior to A

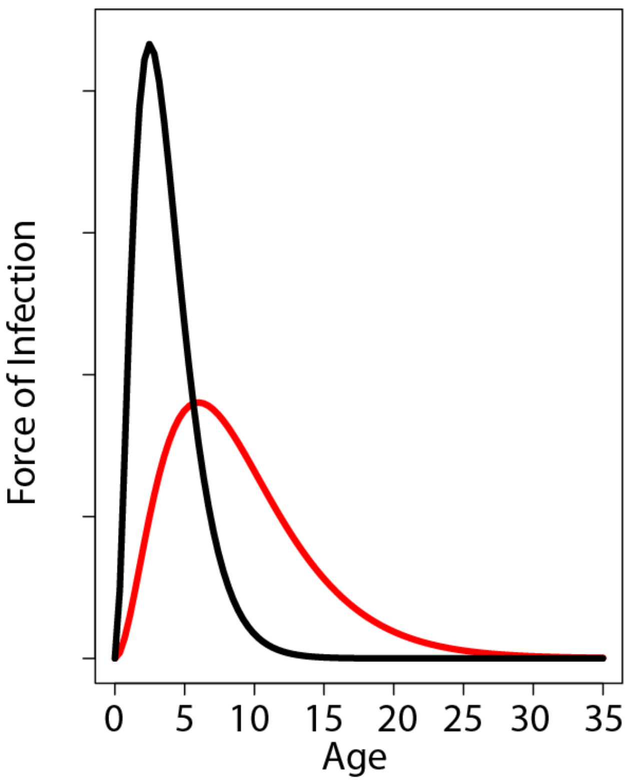
Inference from Age of Cases

- In a setting with homogeneous mixing:
  - $R_0 = L/A$
- Lower transmission rate, implies older mean age at infection

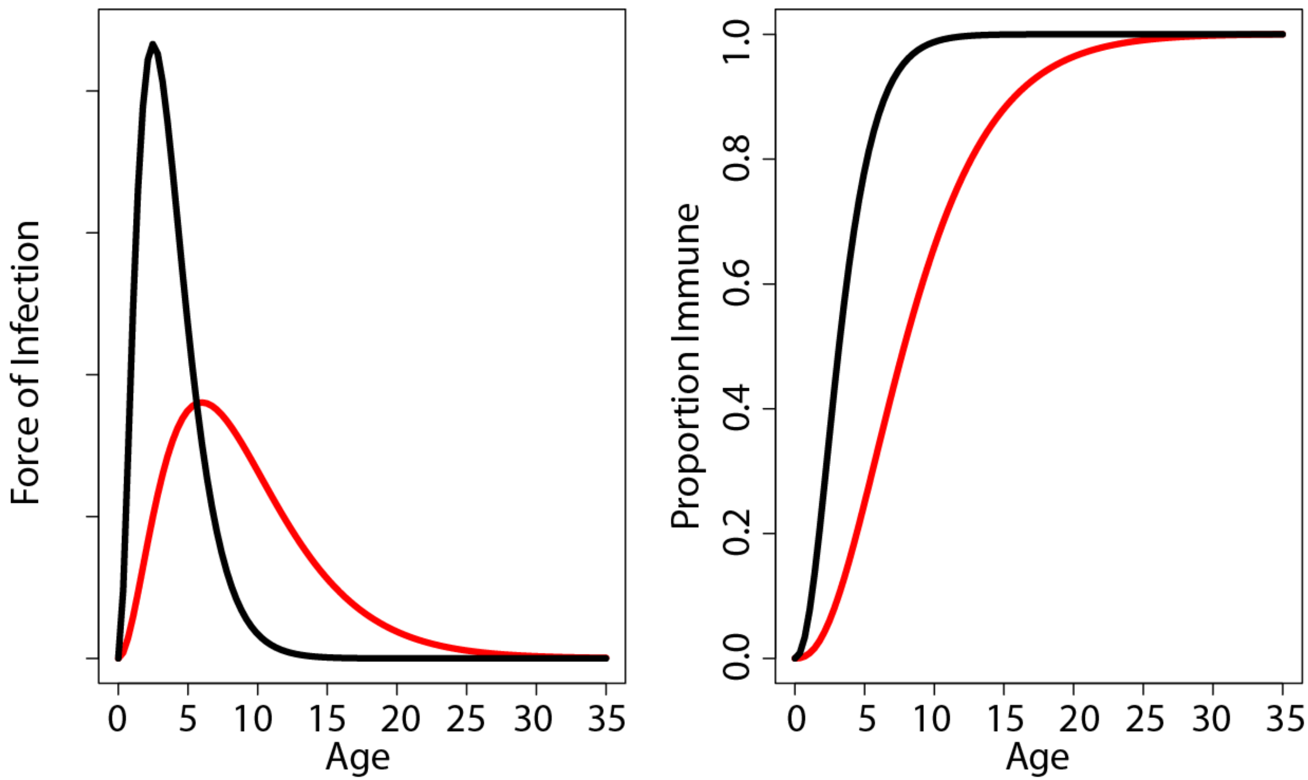
Inference from Age Distribution of Cases

- Differences in behavior and exposure result in age-specific risk, or **force of infection**
- The likelihood of observing a case at age A is related to the integral of all risk prior to A
- Basis of the **catalytic model**
  - Griffiths (1974)
  - Grenfell and Anderson (1985)

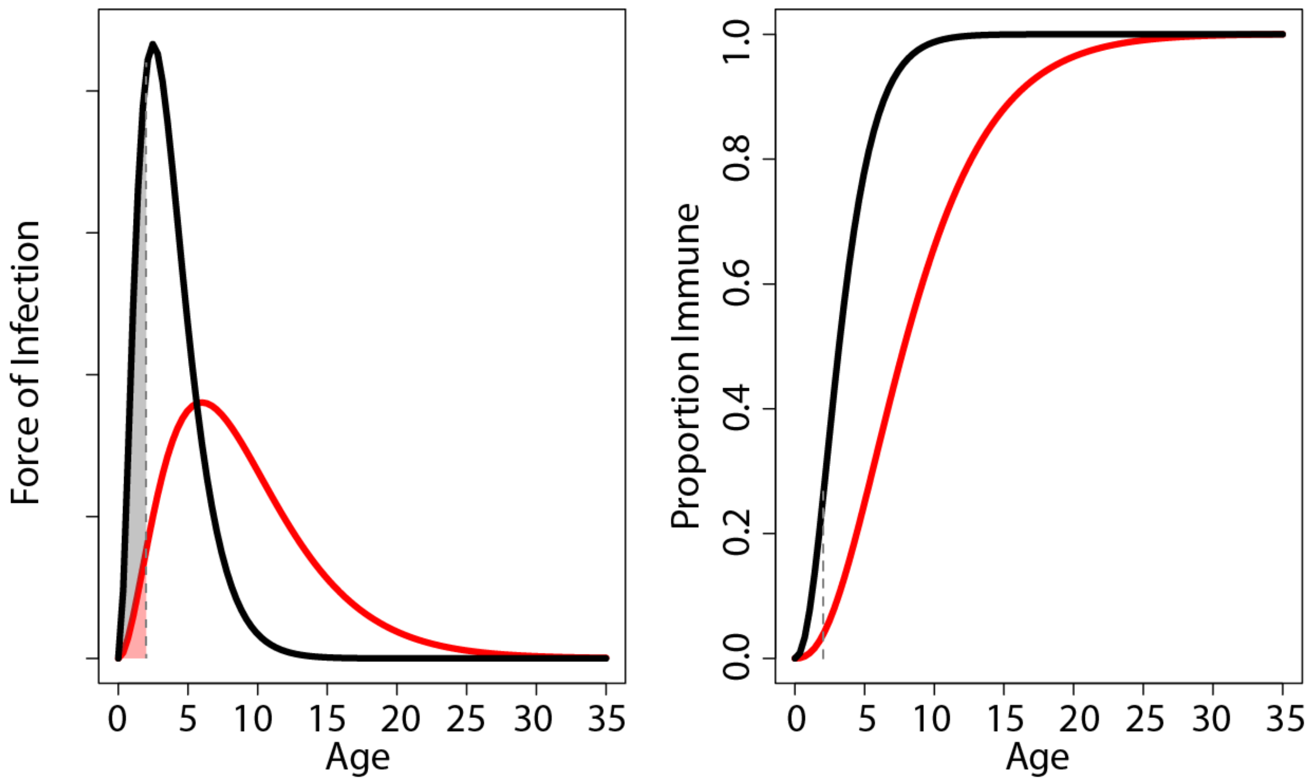
Catalytic Model



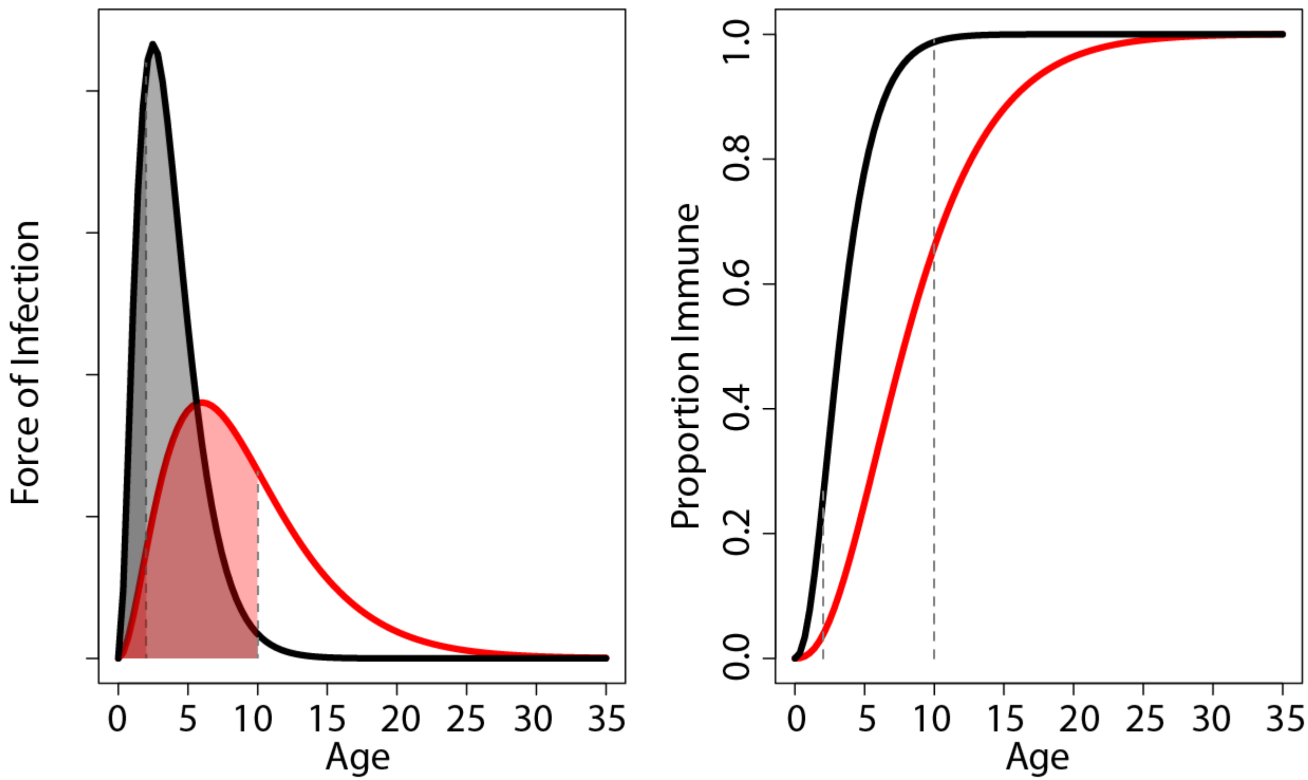
Catalytic Model



Catalytic Model



Catalytic Model



Fitting the Catalytic Model

- Serological Data

$$\phi(a) = \text{force of infection at age a}$$

$$P(sero(+) \mid age) = 1 - \exp\left(-\int_0^{age} \phi(x)\,dx\right)$$

$$\#\,sero(+)_{age} \sim \text{binomial}\left(N_{\text{tested, age}}, P(sero(+) \mid age)\right)$$

- Case Data
  - Expected age distribution of cases is a function of:
    - Remaining susceptible by age a
    - Force of infection at age a, conditional on remaining susceptible
  - Grenfell and Anderson (1985)
    - Multinomial likelihood

Extending the Catalytic Model

- Original formulation of catalytic model
  - doesn't include vaccination,
  - or assumes vaccination occurs instantaneously at "birth"
    - See Saki Takahashi's presentation tomorrow
- Straightforward to extend the model to include two sources of immunity

$$\phi(a) = \text{force of infection at age a}$$

$$\theta(\text{a}) = \text{vaccination rate at age a}$$

$$\alpha = \text{efficacy}$$

$$P(sero(+) \mid age) = 1 - \exp\left(-\int_0^{age} \phi(x)\,dx - \alpha \int_0^{age} \theta(x)\,dx \right)$$

Extending the Catalytic Model

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$$\alpha = \text{efficacy}$$

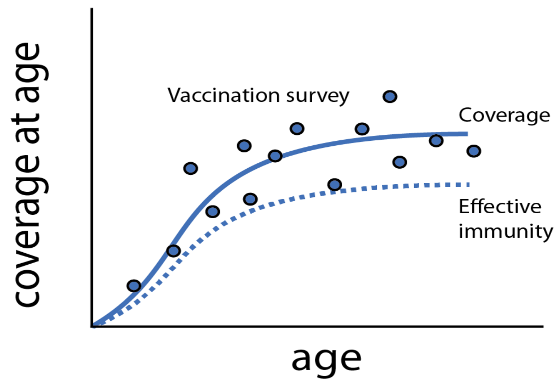
Not identifiable from serological data alone, requires independent data on vaccination

$$P(sero(+) \mid age) = 1 - \exp\left(-\int_0^{age} \phi(x)\,dx - \alpha \int_0^{age} \theta(x)\,dx \right)$$

Extending the Catalytic Model

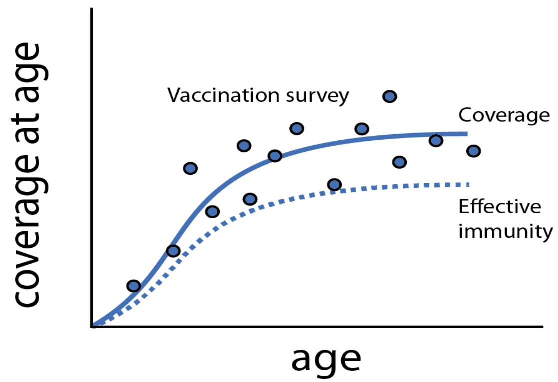
- Catalytic model assumes that historical dynamics have been constant, or at least stationary (see Whitaker and Farrington)
- Increasing routine coverage, declining prevalence, erratic outbreaks, and pulsed campaigns all violate these assumptions
  - Ferrari et al 2010 presented an extension of this model to account for impact of non-stationary processes
  - Li et al 2017 extended this further to allow use of longitudinal observation of age-distribution

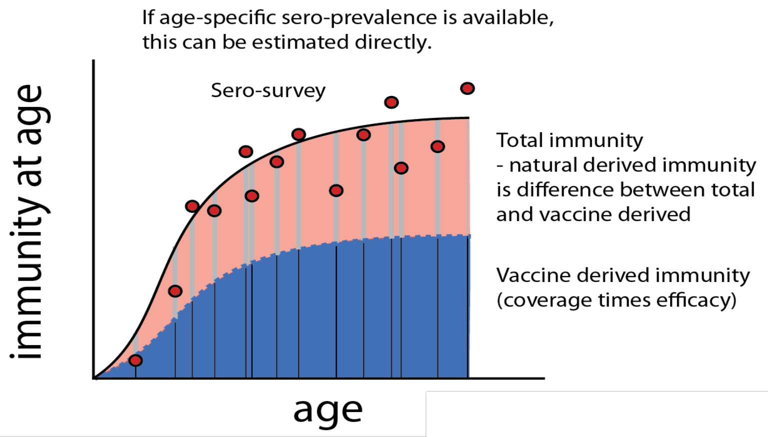
Estimating Proportion Immune



Age-specific vaccination coverage from DHS surveys. Note that immunity due to vaccination should be lower than vaccination coverage due to imperfect efficacy.

Estimating Proportion Immune

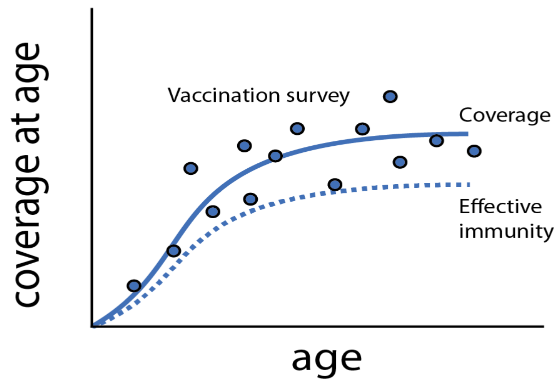




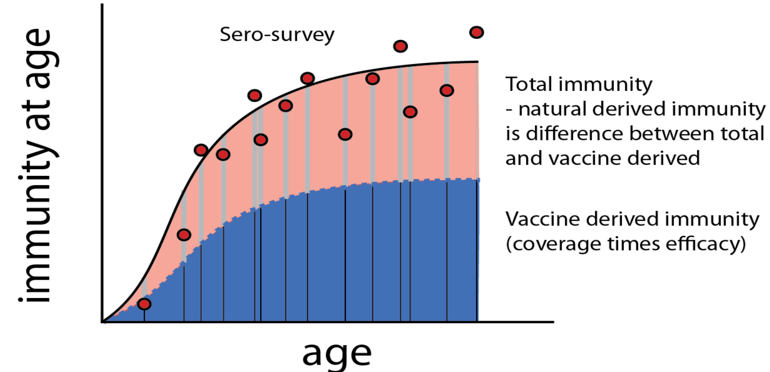
Age-specific vaccination coverage from DHS surveys. Note that immunity due to vaccination should be lower than vaccination coverage due to imperfect efficacy.

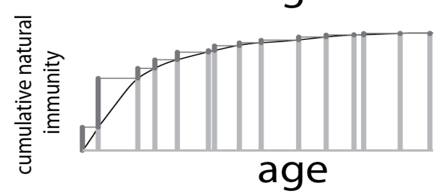
With age-specific serology, immunity can be estimated directly and the contribution of natural infection (here the light grey bars) are the difference between vaccine derived immunity and total immunity

Estimating Proportion Immune



If age-specific sero-prevalence is available, this can be estimated directly.

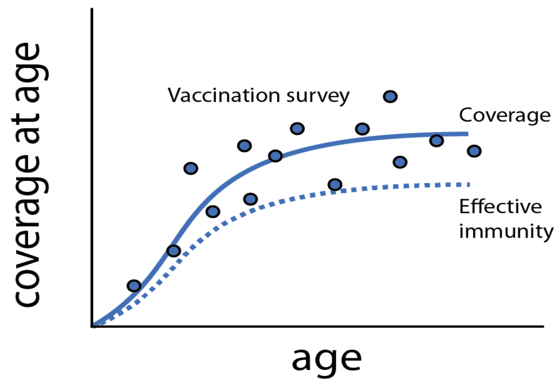


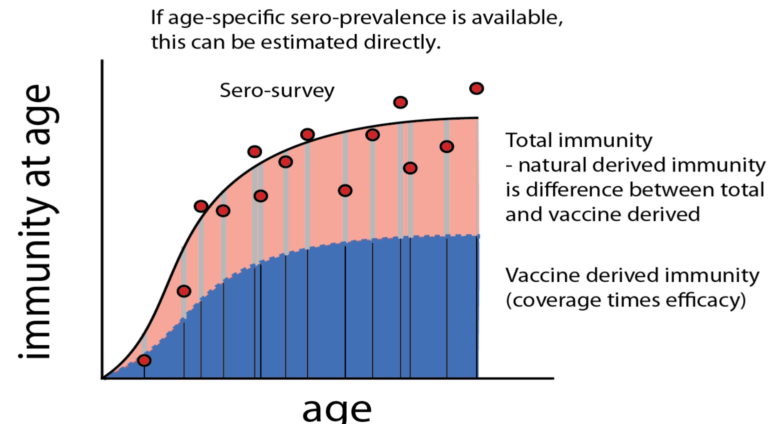


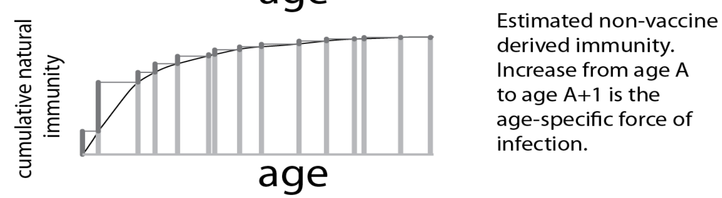
Estimated non-vaccine derived immunity. Increase from age A to age A+1 is the age-specific force of infection.

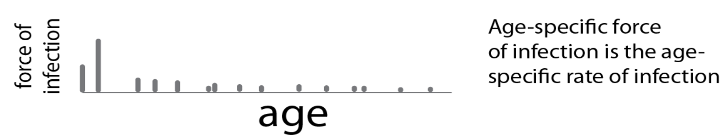
Projecting the light grey bars to the X-axis we see the cumulative immunity due to natural infection. Rate of increase between age classes is the **age-specific force of infection**

Estimating Proportion Immune



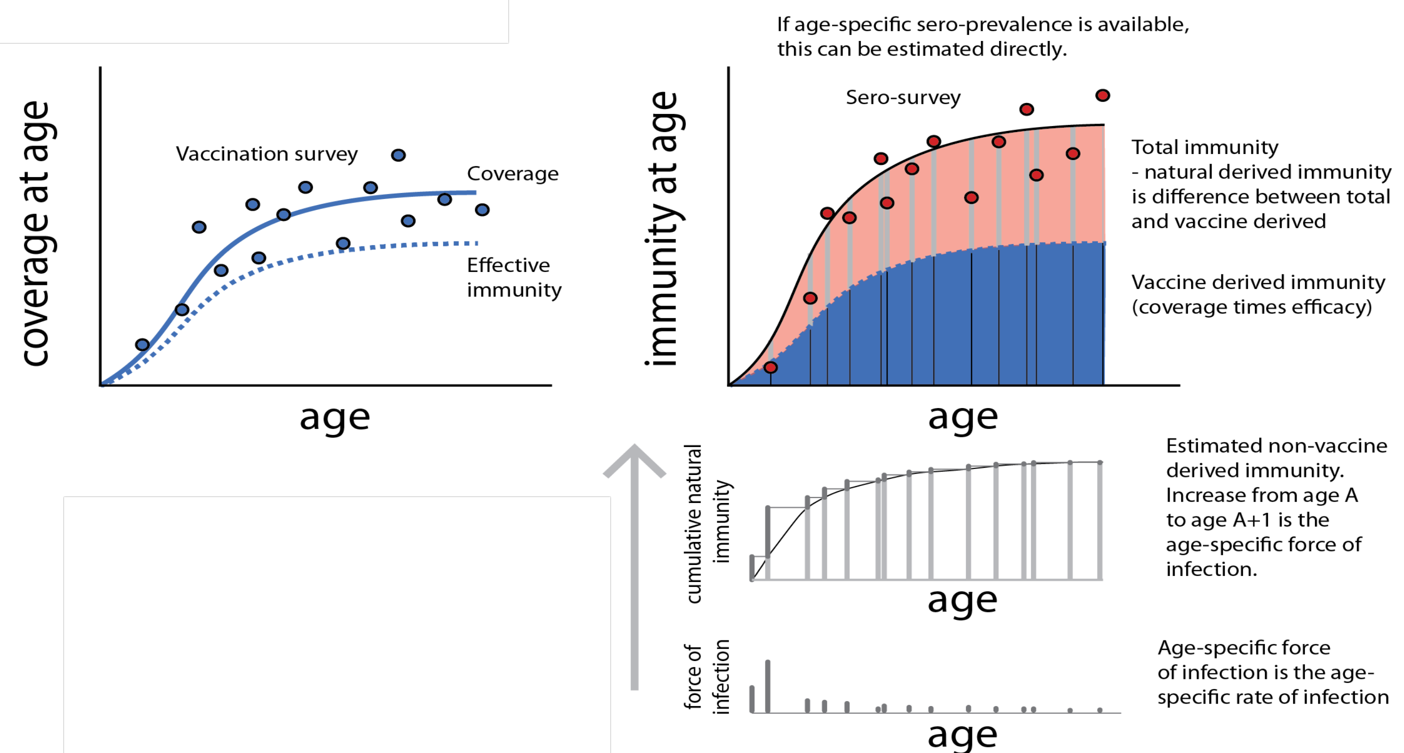




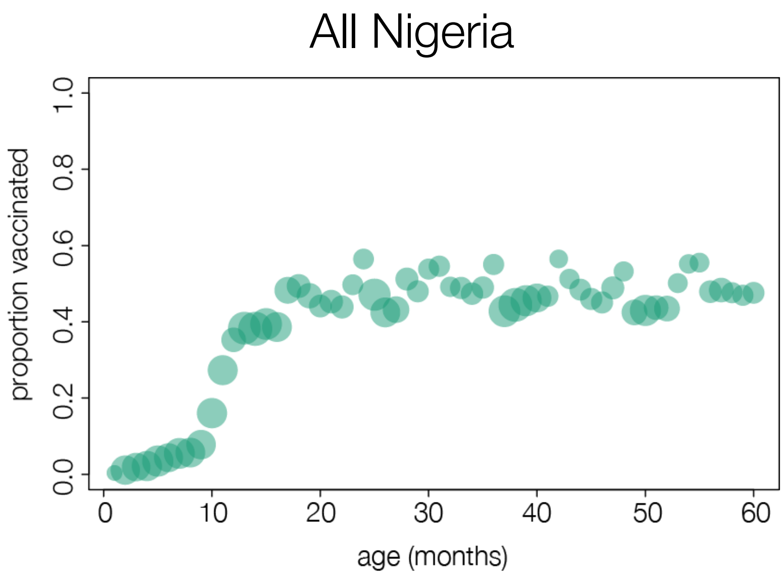


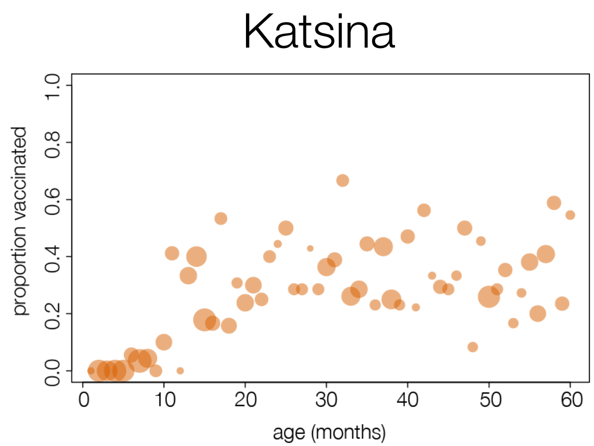
Force of Infection is commonly age dependent due to variable mixing

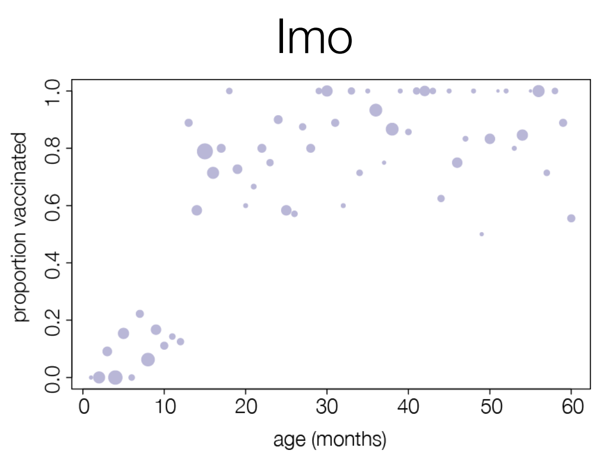
Estimating Proportion Immune



DHS vaccination coverage

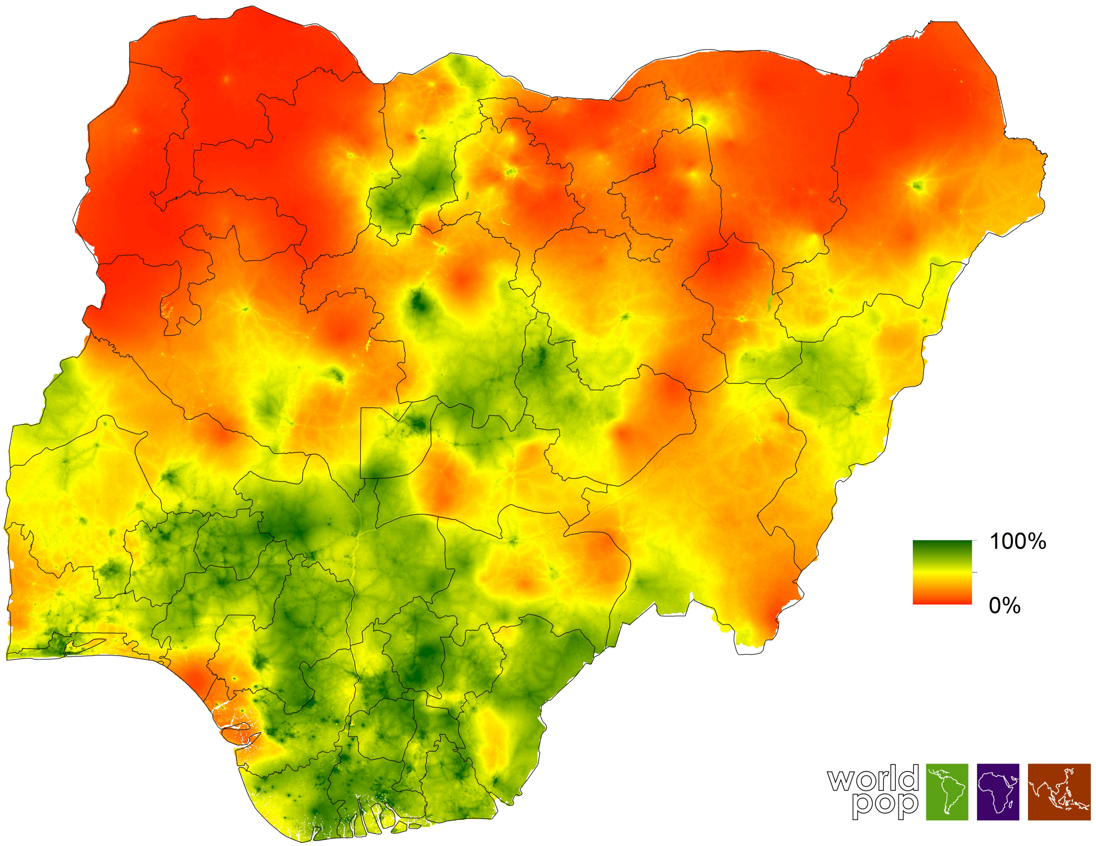




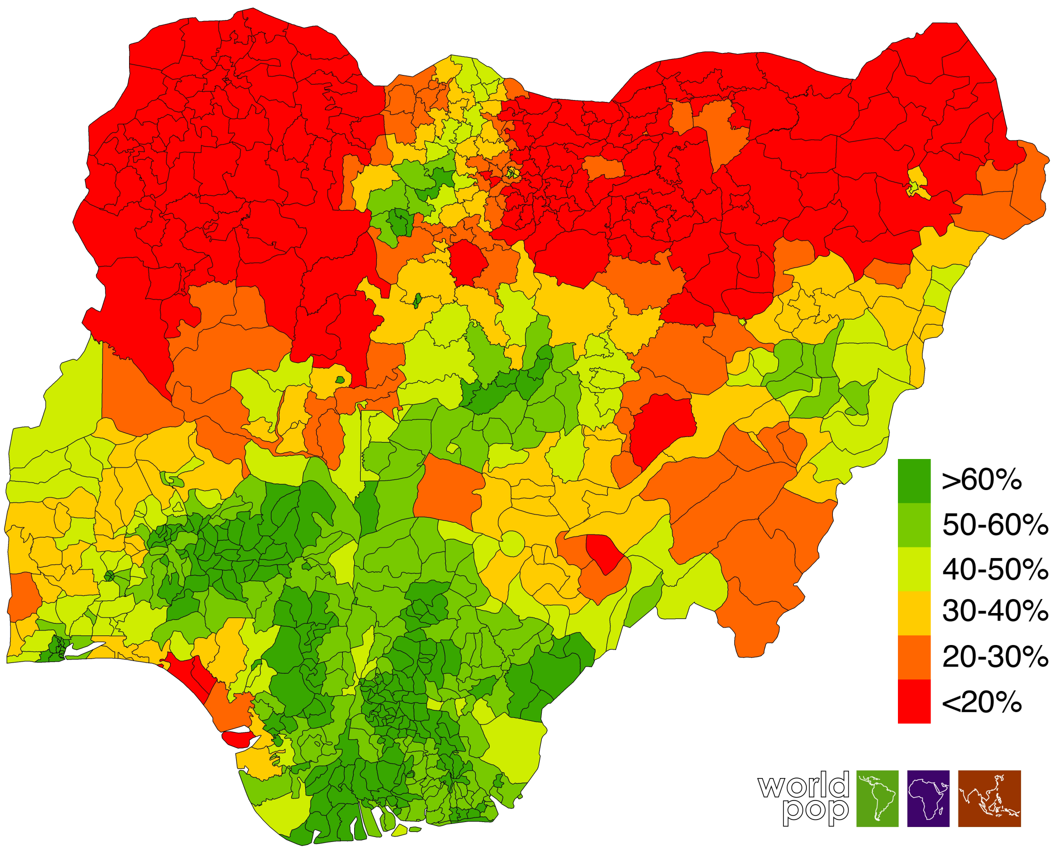


- All cause vaccination, doesn't discriminate routine from SIAs
- Relies on maternal recall
- Last survey done in 2013
  - See Saki's talk

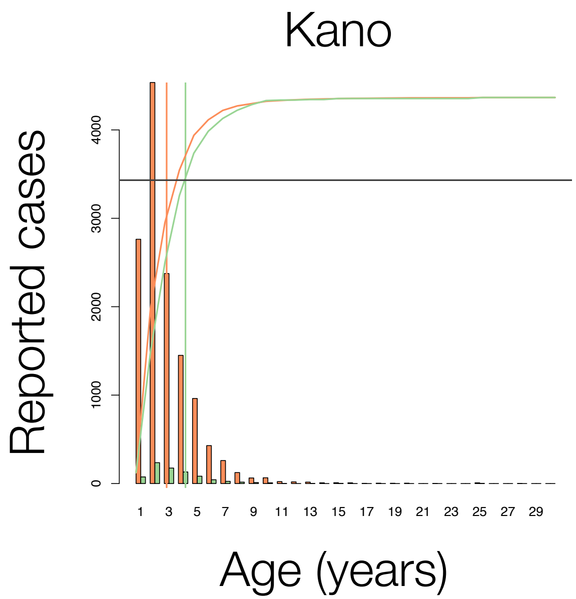
Estimated Measles Vaccination Coverage



Estimated Measles Vaccination Coverage



Reported Case Surveillance

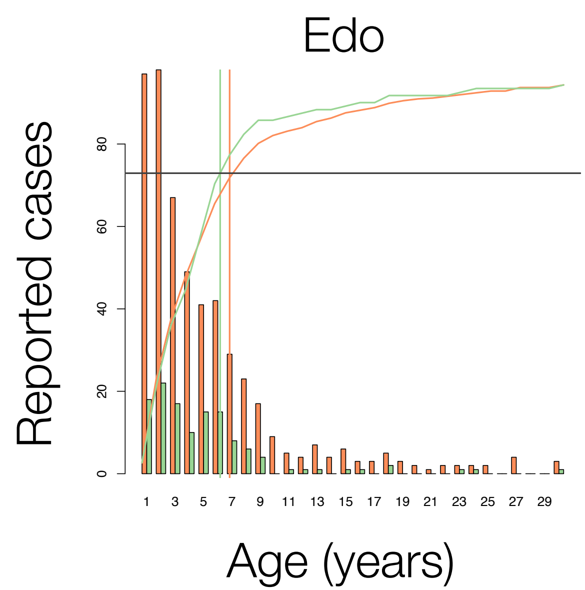


Suspected Measles Cases

Lab Confirmed Measles Cases

80th percentile of suspected age distribution

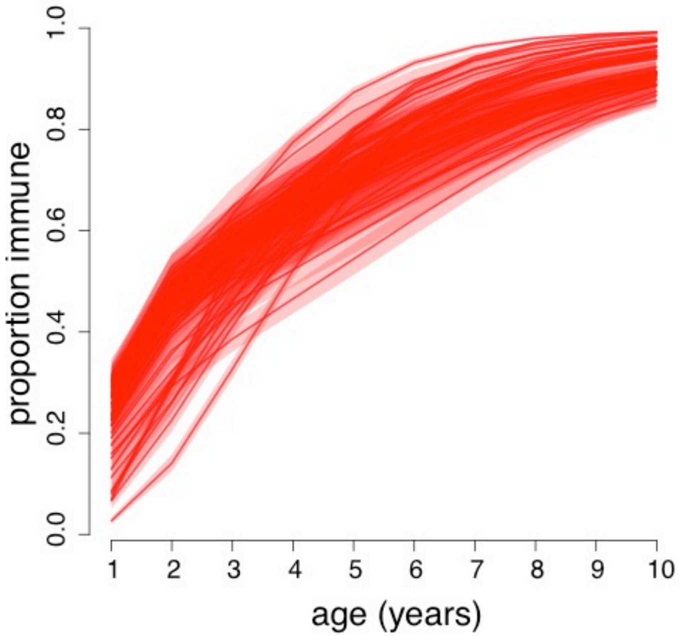
80th percentile of age distribution



Kano State: mean age 3-4y
few cases observed >15y

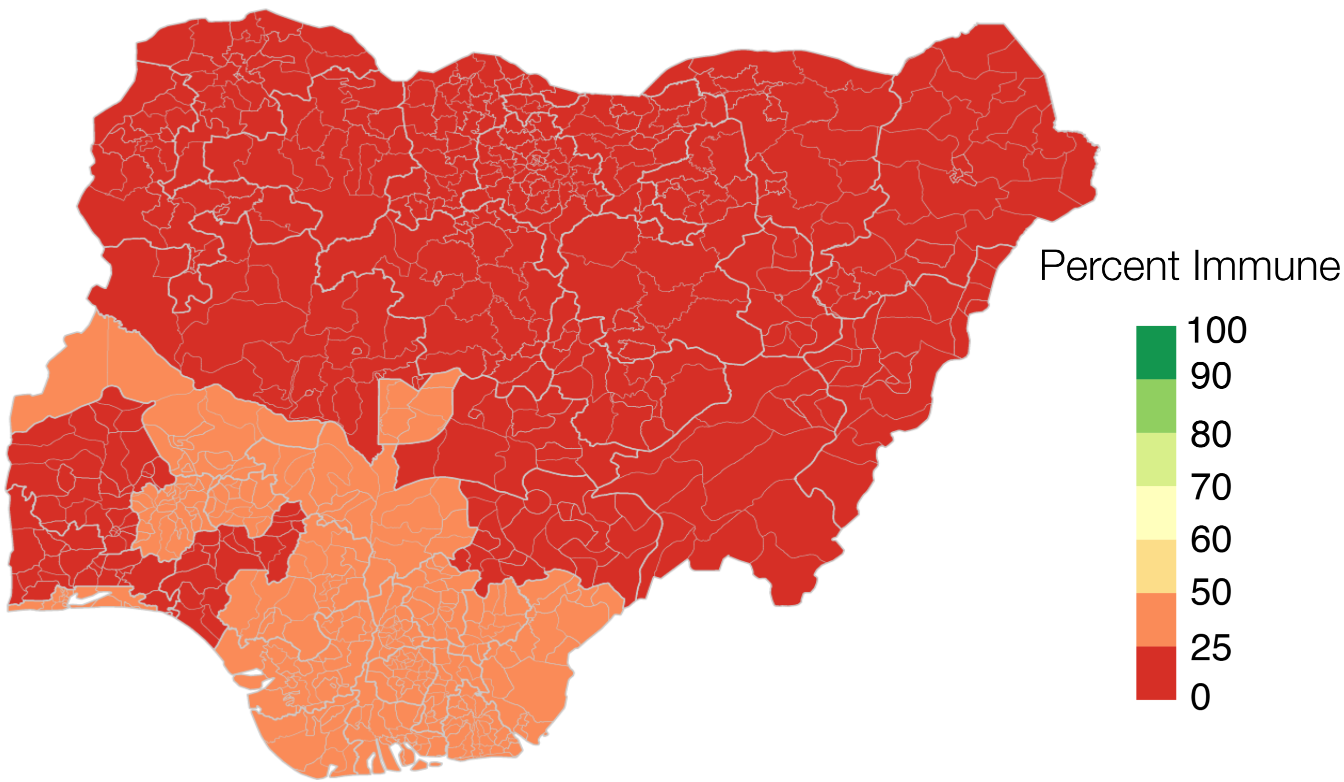
Edo State: mean age 6-7y
many cases observed >15

Estimated Proportion Susceptible

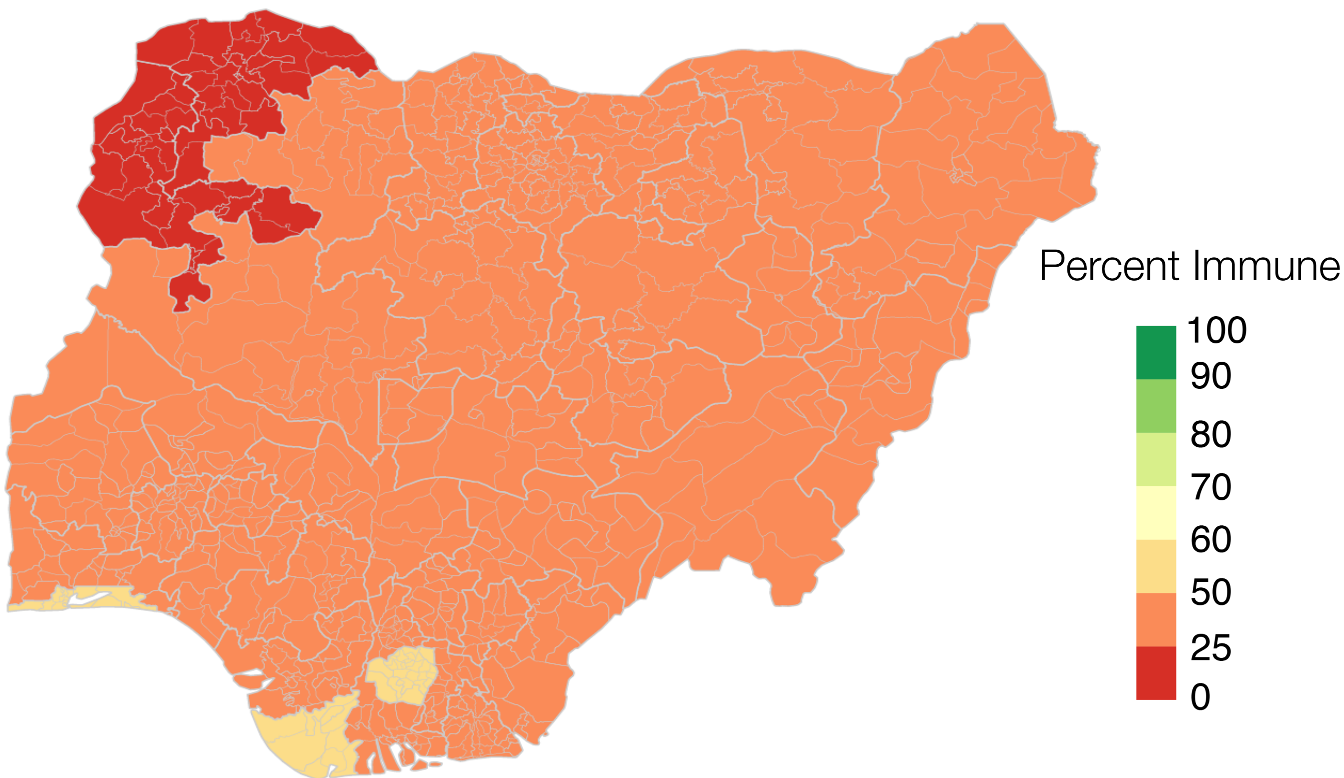


- We estimate the total fraction immune in each age class at the **state-level**
  - Data below state level often too sparse
- At left, the estimated proportion of children immune in each state, due to vaccination or natural infection, as a function of age. Each line indicates one state; shading around each line indicates 95% confidence bounds

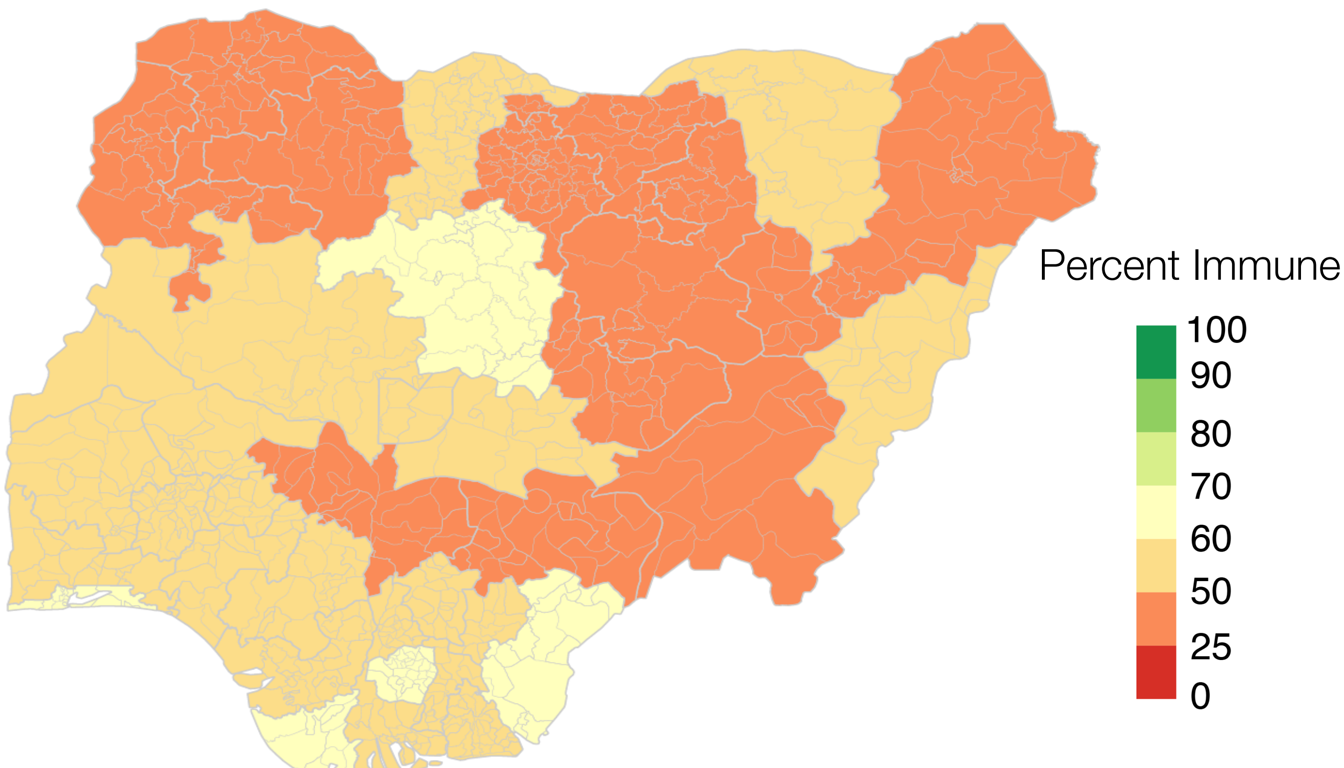
Proportion Immune: 1y old



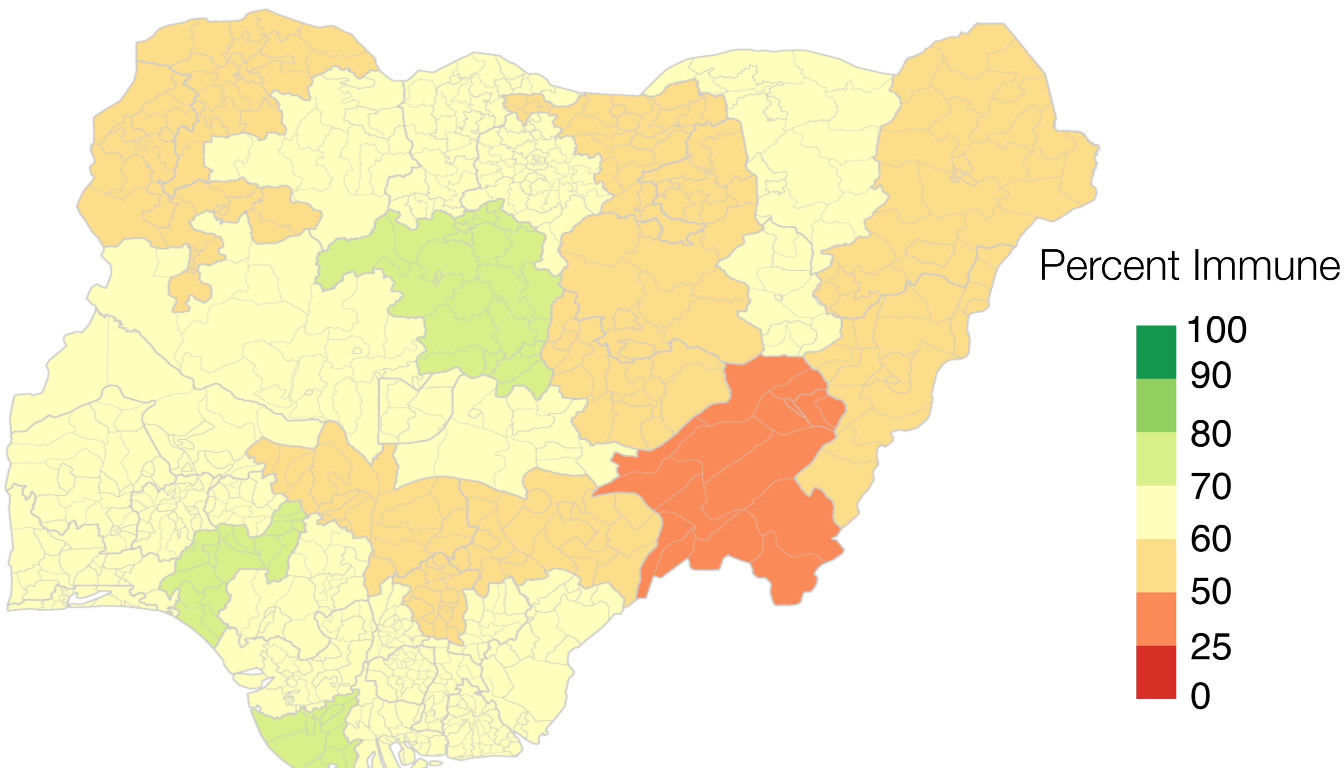
Proportion Immune: 2y old



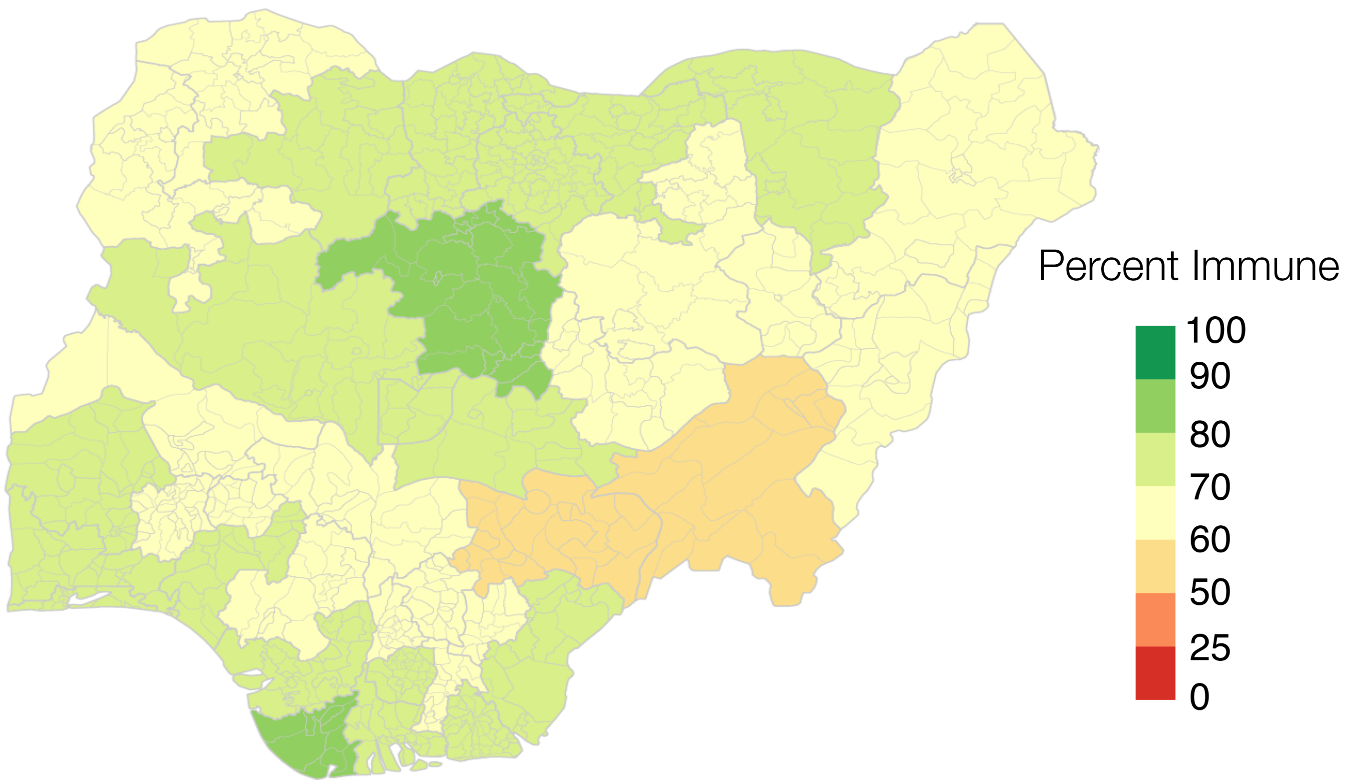
Proportion Immune: 3y old



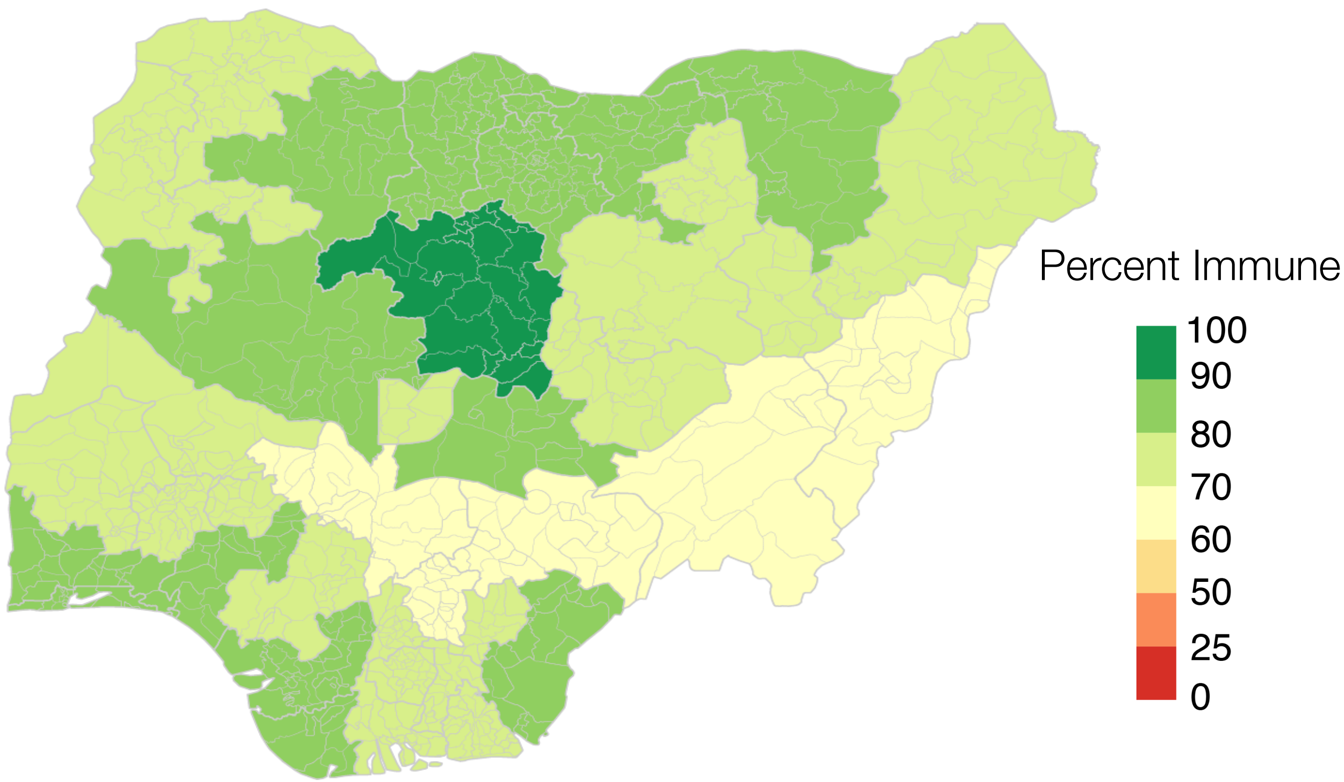
Proportion Immune: 4y old



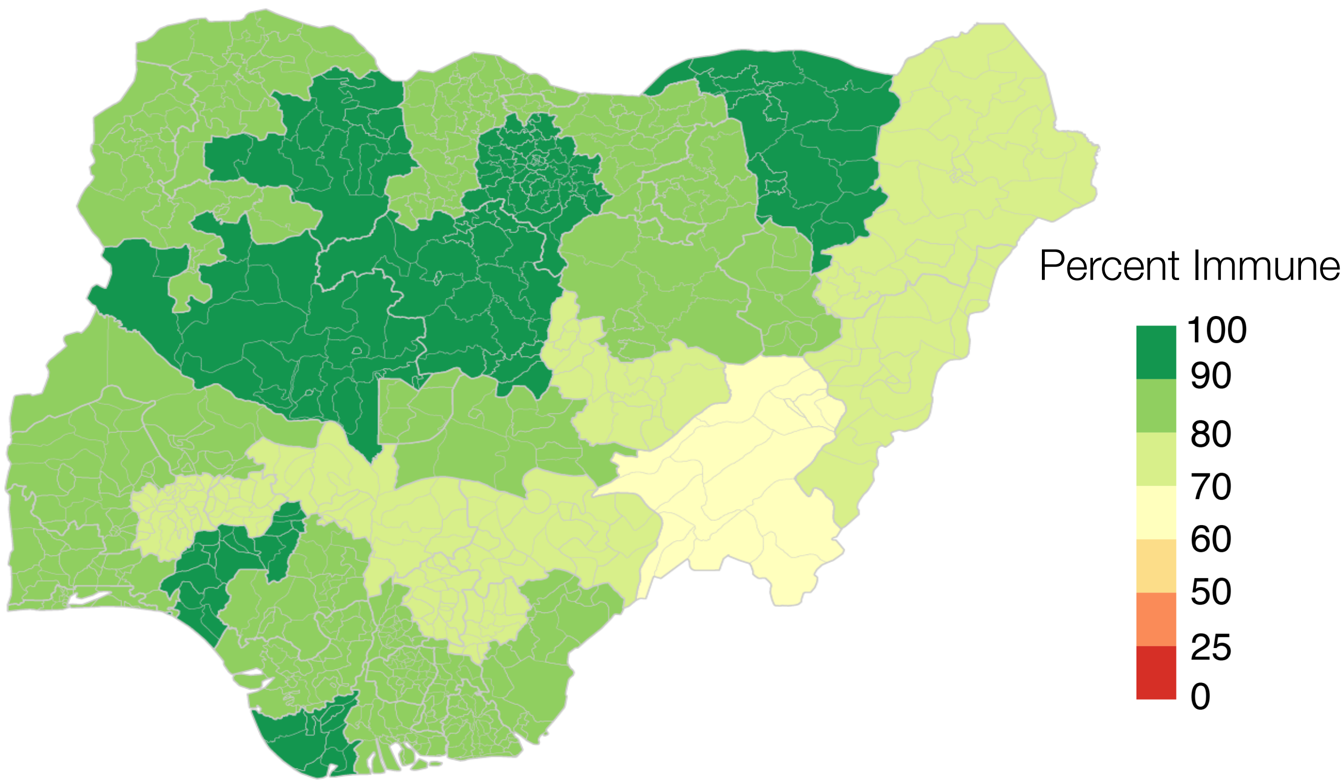
Proportion Immune: 5y old



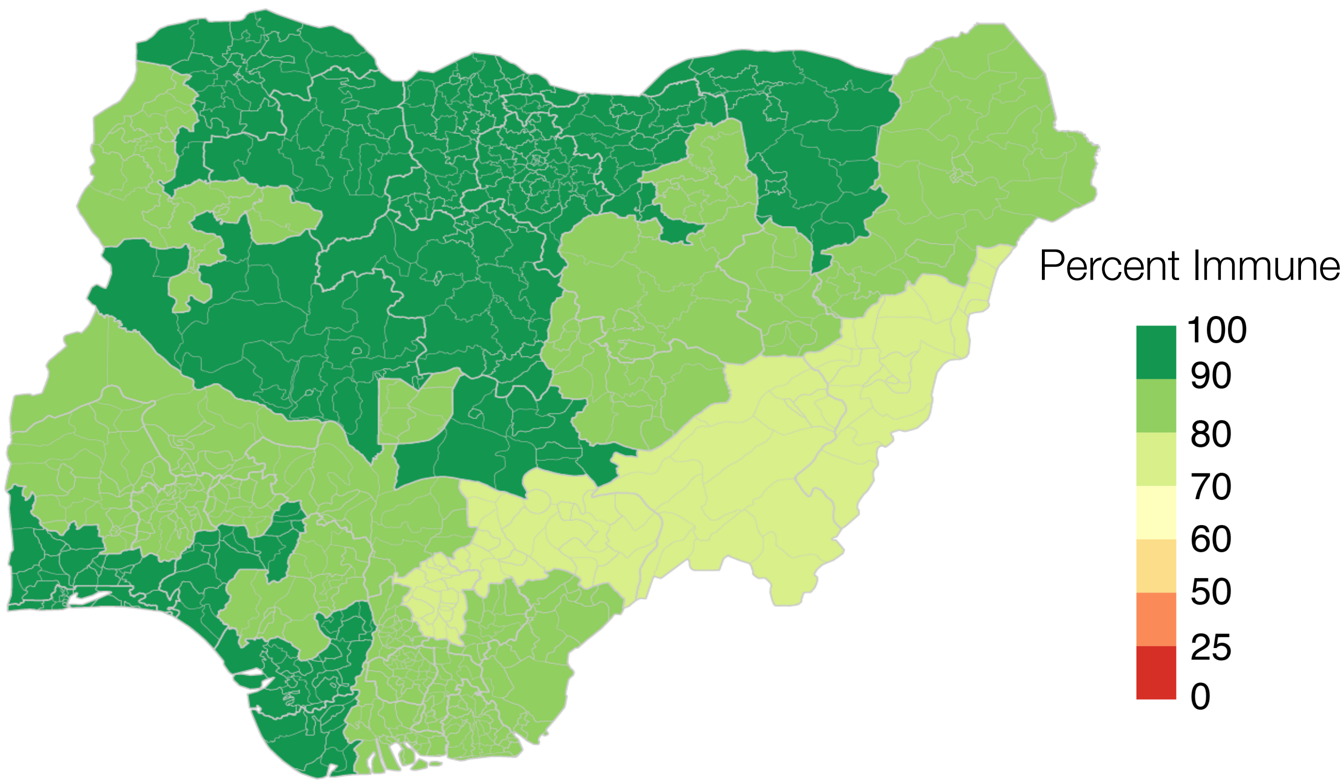
Proportion Immune: 6y old



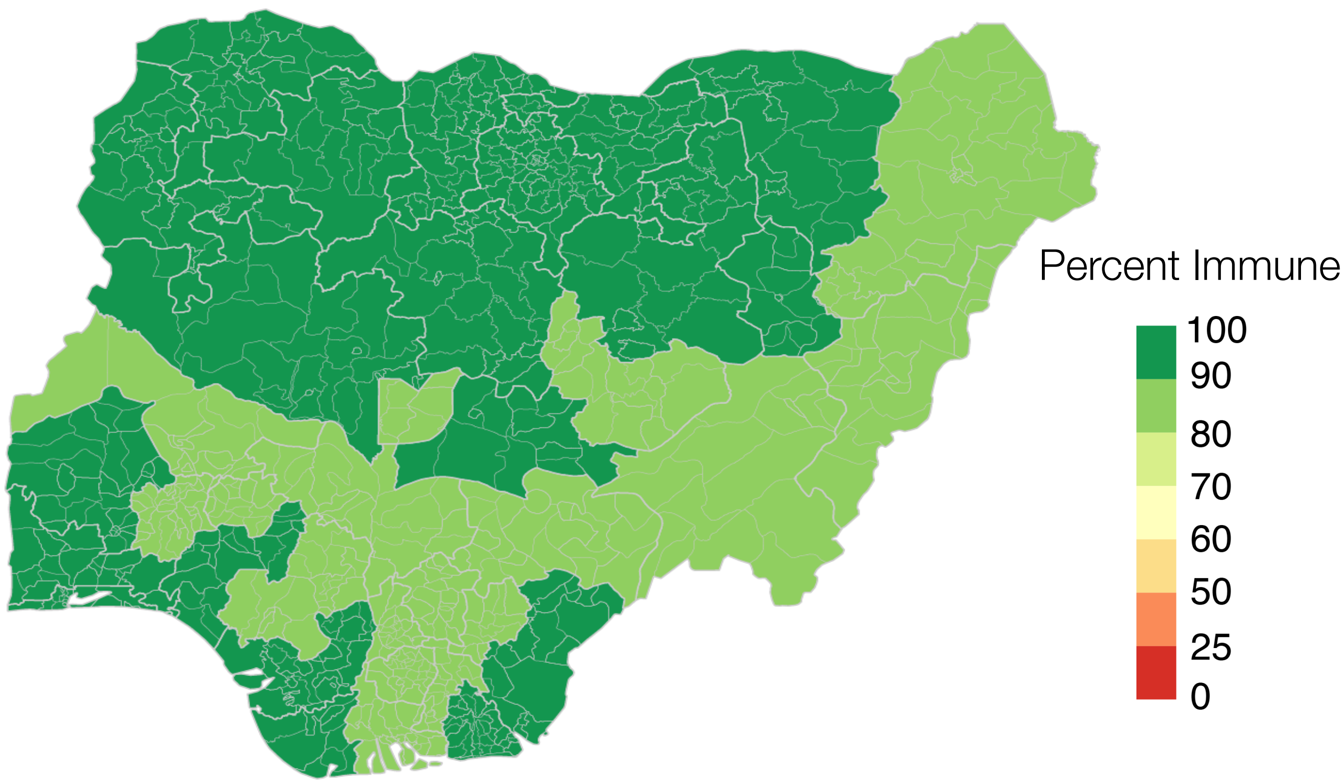
Proportion Immune: 7y old



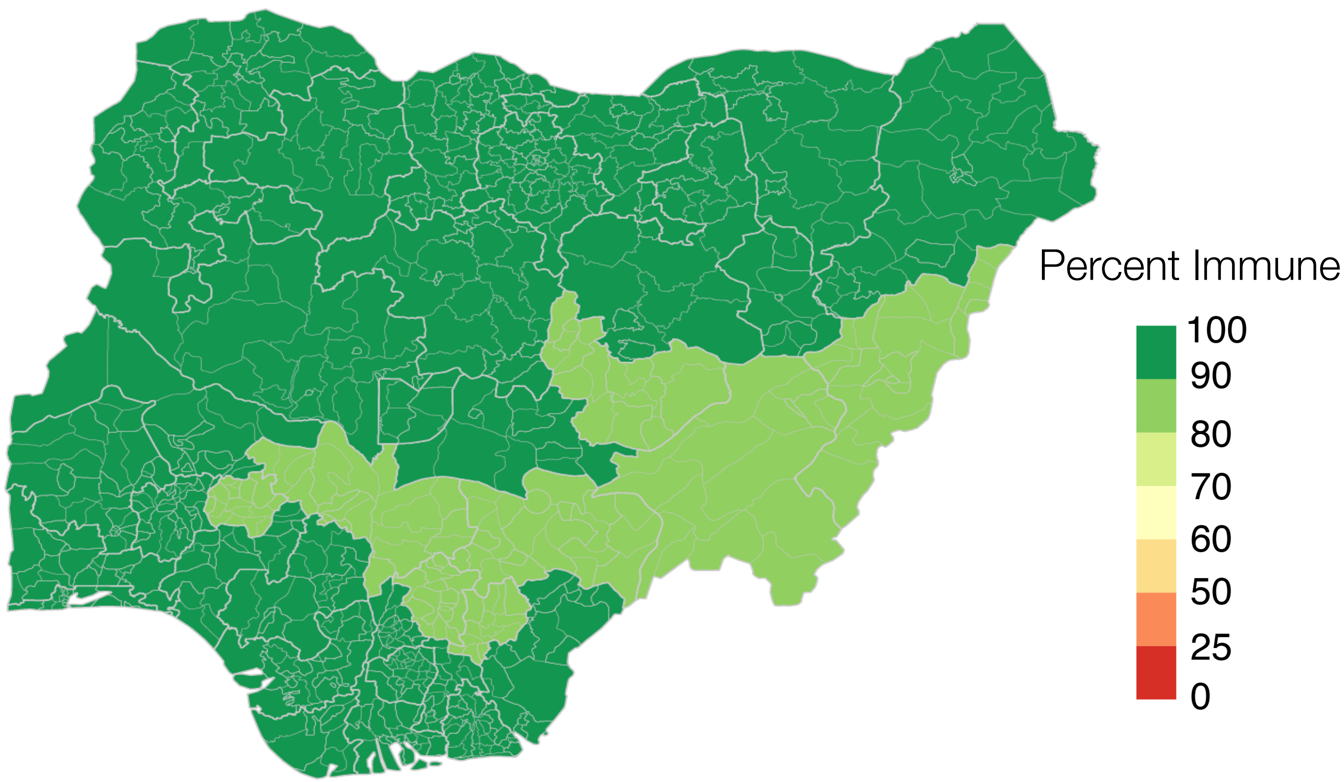
Proportion Immune: 8y old



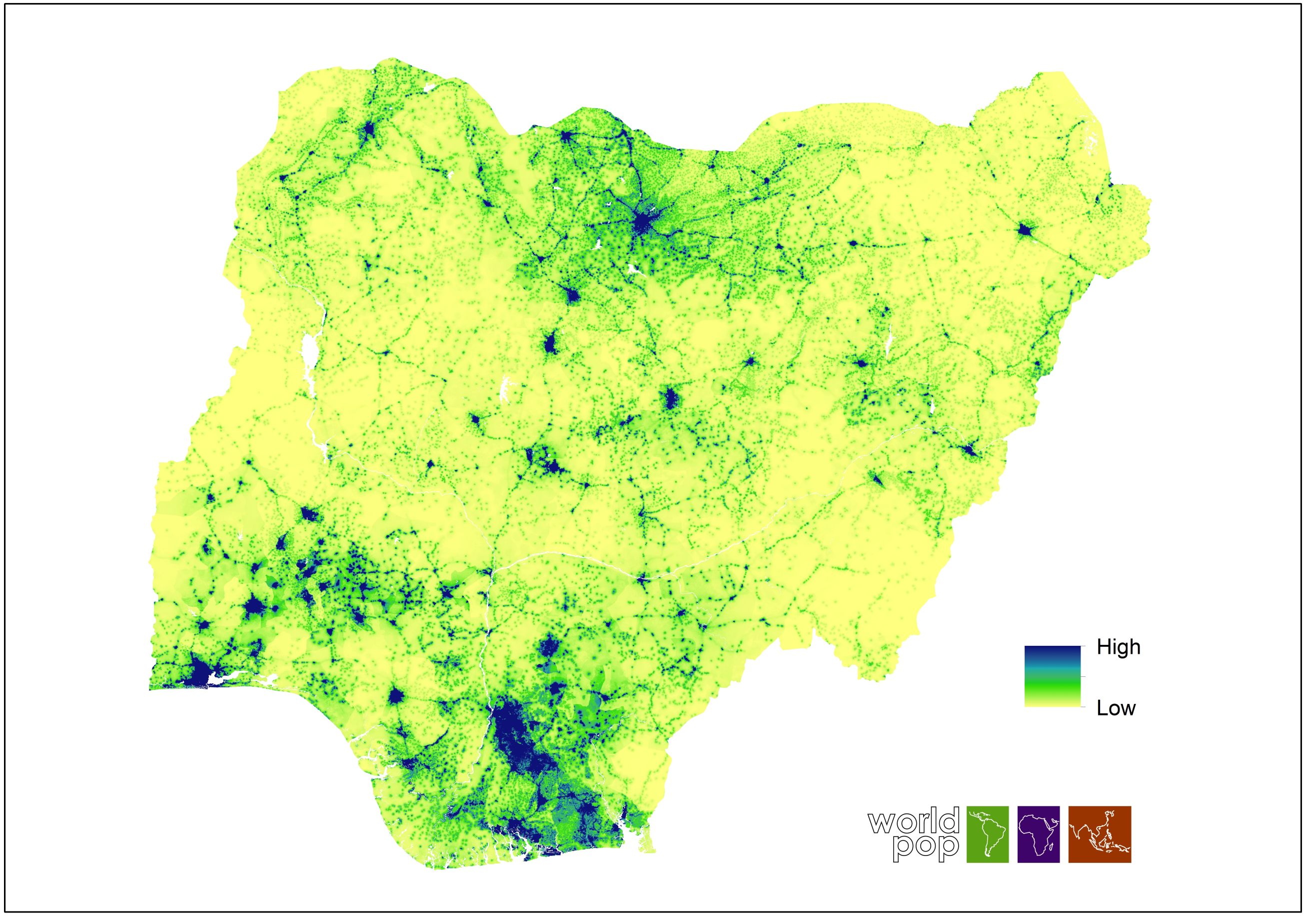
Proportion Immune: 9y old



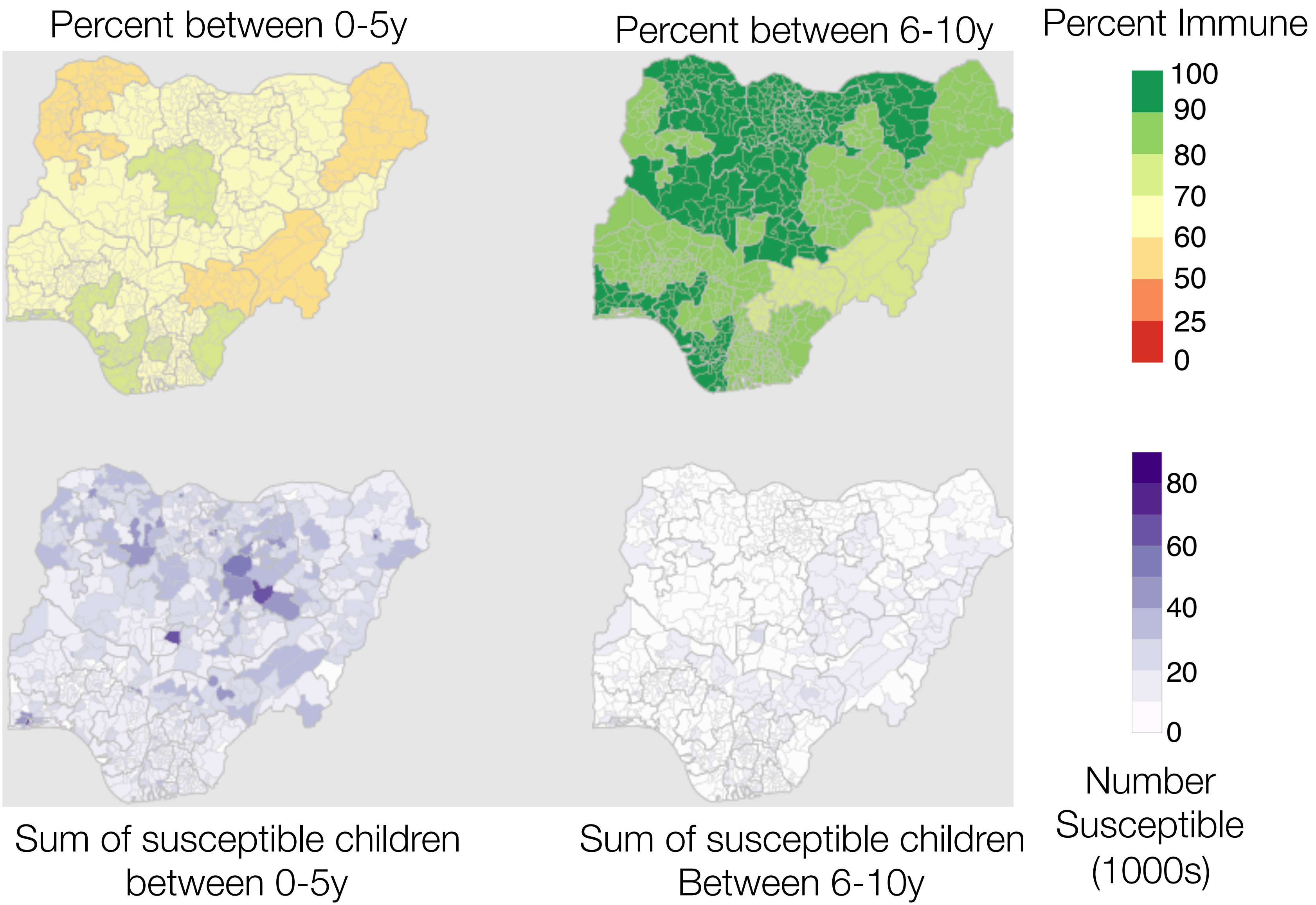
Proportion Immune: 10y old



Population Density: 0-59m



Proportion of Children Immune

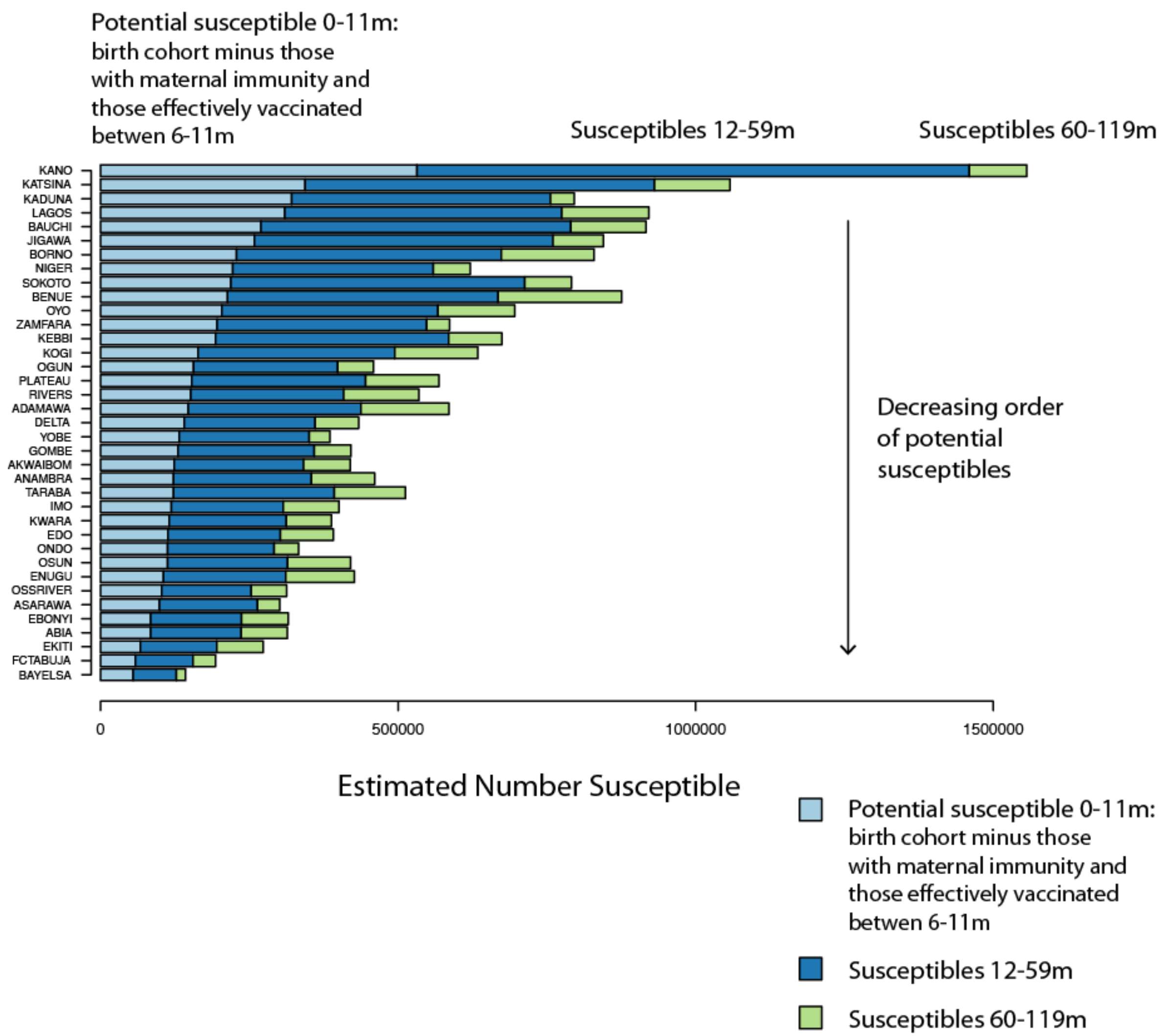


Density of Susceptible Children

Operational Interpretation

- Maps provide useful visual display of variation but are difficult to translate directly into an operational prioritization
- Locations must be ranked in priority relative to some operational objective, e.g.:
  - Total number of susceptibles
  - Marginal benefit of wide-age campaigns
  - Cost-effectiveness of wide-age campaigns

Sub-National Prioritization



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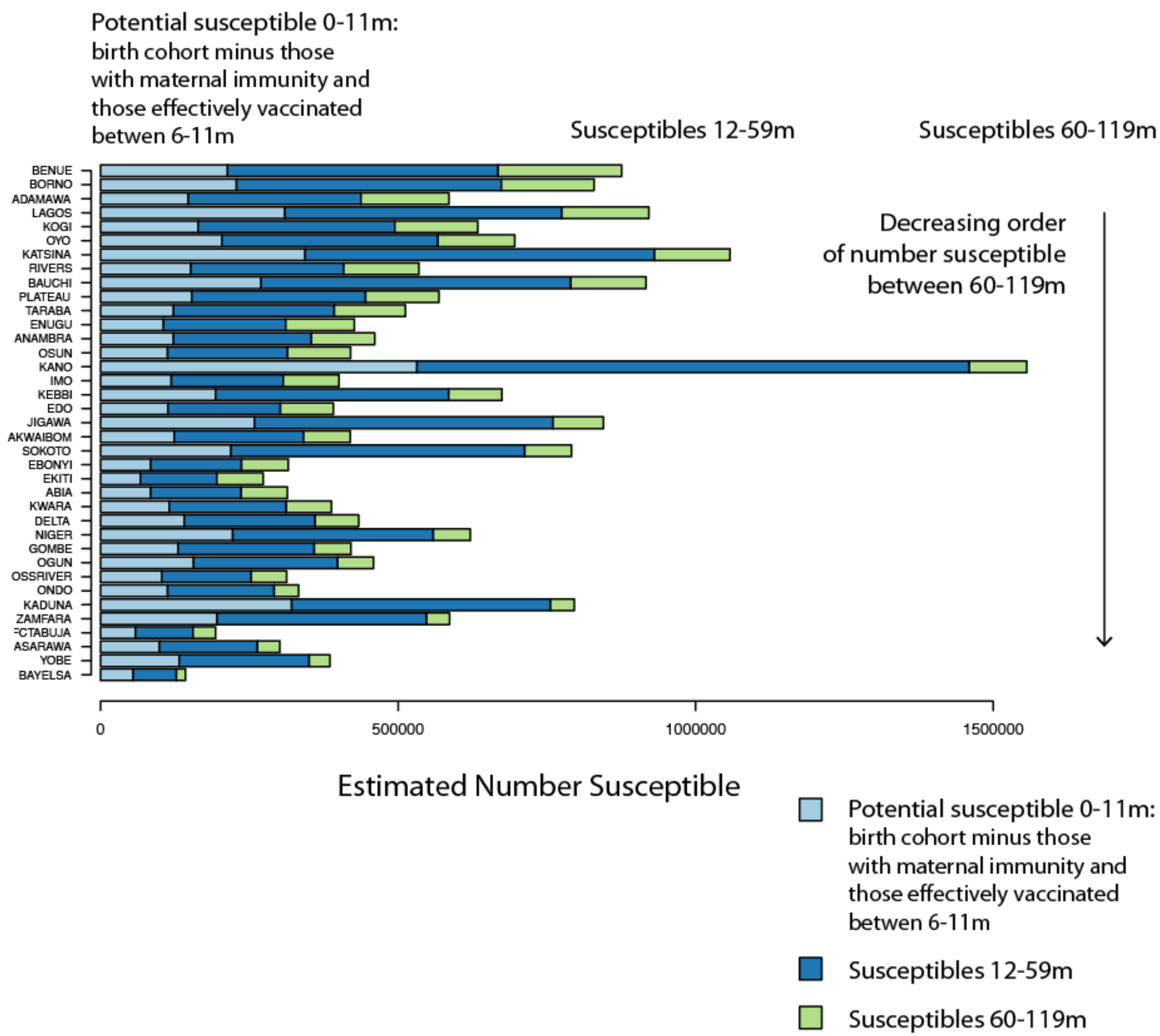

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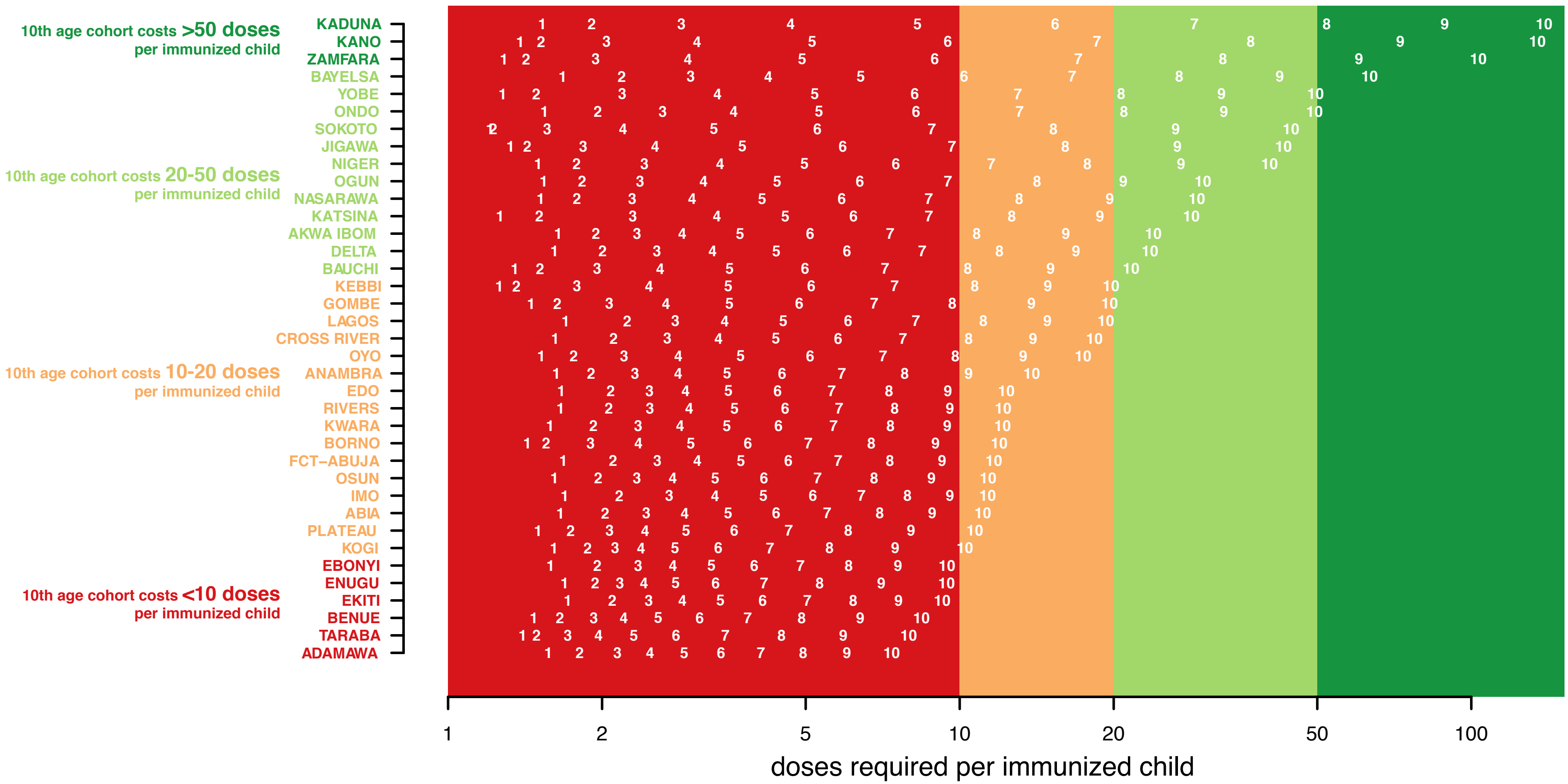

Conclusions

- Age specific records are a powerful source of information about both historical dynamics and current risk
- Need to develop new tools for inference using age-specific records
  - And account for novel sources of uncertainty: e.g. age-specific disease severity and reporting
- Potential for adaptive strategies for interventions targeted to local needs

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