Rotavirus and PCV: Case study of the appropriateness of vaccines

Rebecca Freeman Grais

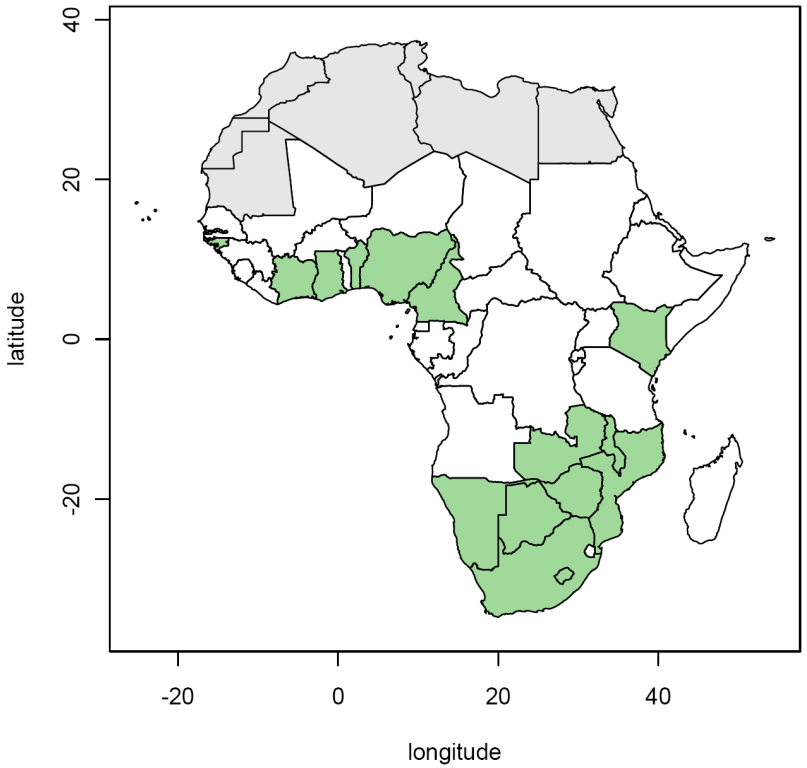
January 28, 2009

Background

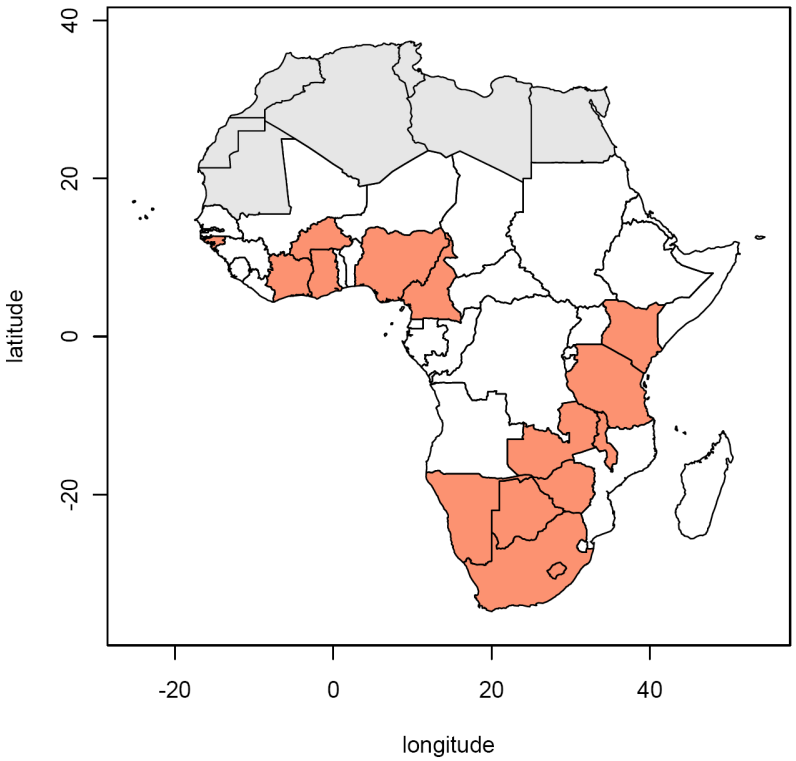
- Epicentre, epidemiological research branch of Médecins Sans Frontières
- Two examples of issues where appropriateness of vaccines plays a role
  - Rotavirus and mass pneumococcal vaccination
    1. Burden and appropriateness of vaccine to provide operational guidance

Systematic review of rotavirus burden and circulating strains in Sub-Saharan Africa

41 studies with burden data



39 studies with strain data



Sanchez-Padilla E, Grais RF, Guerin PJ, Steele AD, Burny ME, Luquero FJ. Burden of disease and circulating serotypes of rotavirus infection in sub-Saharan Africa: systematic review and meta-analysis. Lancet Infect Dis. 2009 Sep;9(9):567-76.

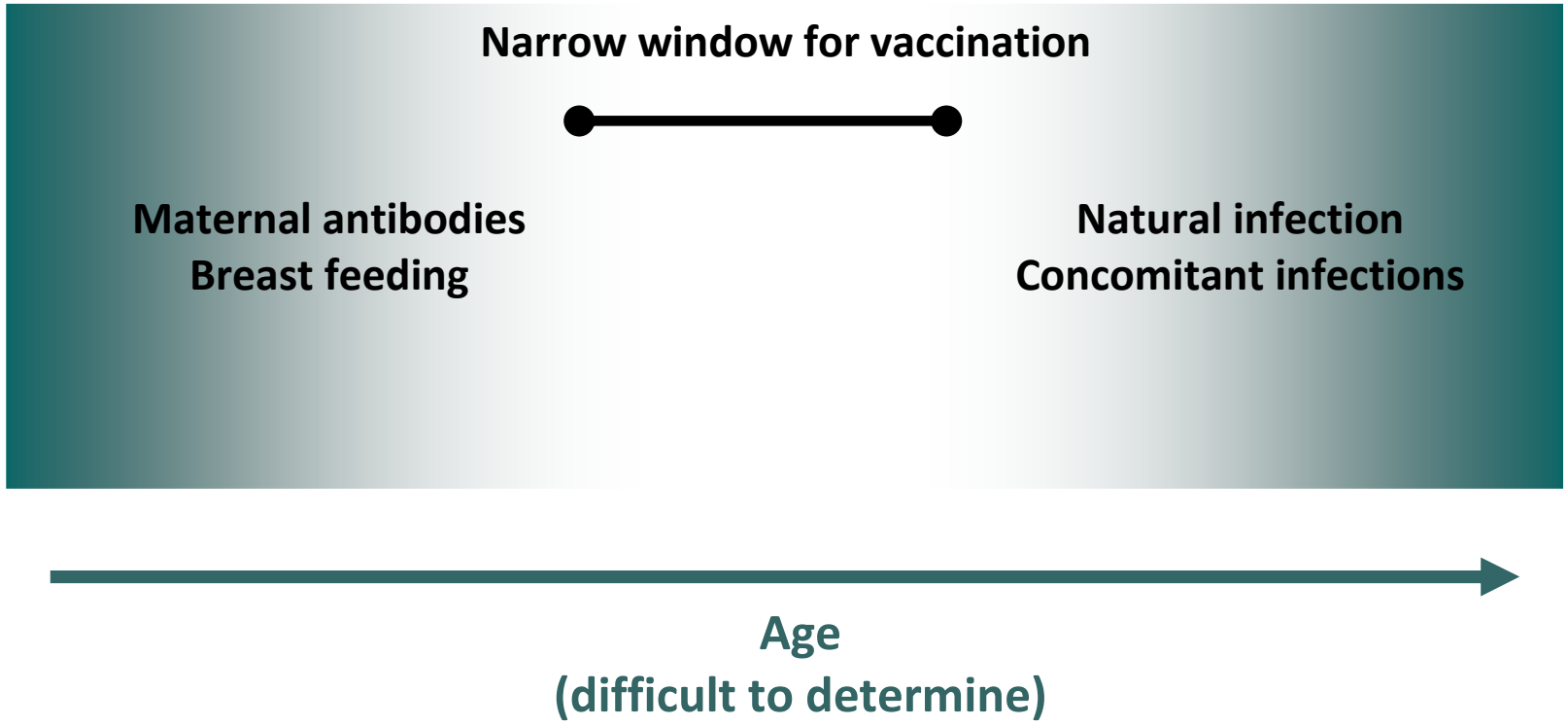
Systematic review of **burden** and circulating strains in Sub-Saharan Africa

- Proportion of rotavirus diarrhea (14 countries)
  - 0.6% for hospitalized children under 2 in Mozambique
  - 56% for patients under 5 (outpatient Nigeria).
  - highest in hospitalized children under 1
  - lowest in community based studies including children below age 3
- 300,000 children under five die of rotavirus infection.
  - higher than the most recent WHO estimate
  - number of studies low (6)
  - Geographic variability in rotavirus mortality rates which ranged between 6.2 to 300.4 deaths per 100,000 children under 5

Systematic review of burden and **circulating strains** in Sub-Saharan Africa

- High heterogeneity in circulating strains
  - RT-PCR used in the majority of studies but many strains remained un-typed
  - most common genotypes (G1-G4, P[8]) worldwide are underrepresented and uncommon serotypes are more prevalent
  - The G8 serotype fourth most common genotype, whereas outside of Africa it has seldom been detected
- WH0 prequalified vaccines: proven efficacy mainly against the G1-G4 and G9 (represent only 57% of the circulating strains)
- New P-G strains could emerge as the result of mixed rotavirus infections that account for up to 8% of the samples

Additional Challenges (I)



Additional Challenges (II)

- Region of Maradi, Niger (OMS case definition)
  - Survey of 2940 children (April 2009):
  - diarrhea period prevalence was 36.8% (95CI: 33.7 – 40.0)
  - Highest in children 6 – 18 m
- Among those who sought medical consultation,
  - 80.4% (95%CI: 76.8-84.1) received ORS
  - 6.1% (95%CI: 3.1-8.7) received intravenous rehydration
- Surveillance of childhood diarrhea in health centers and posts rather than hospitals
  - Select bacteriology
  - Rotavirus RDT (50% in pilot phase, October)
  - Rotavirus genotyping

Additional Challenges (III)

- Compliance within a tight-time frame (DTP3)
- Volume in already strained cold chain
- Some formulations may be more adapted than others

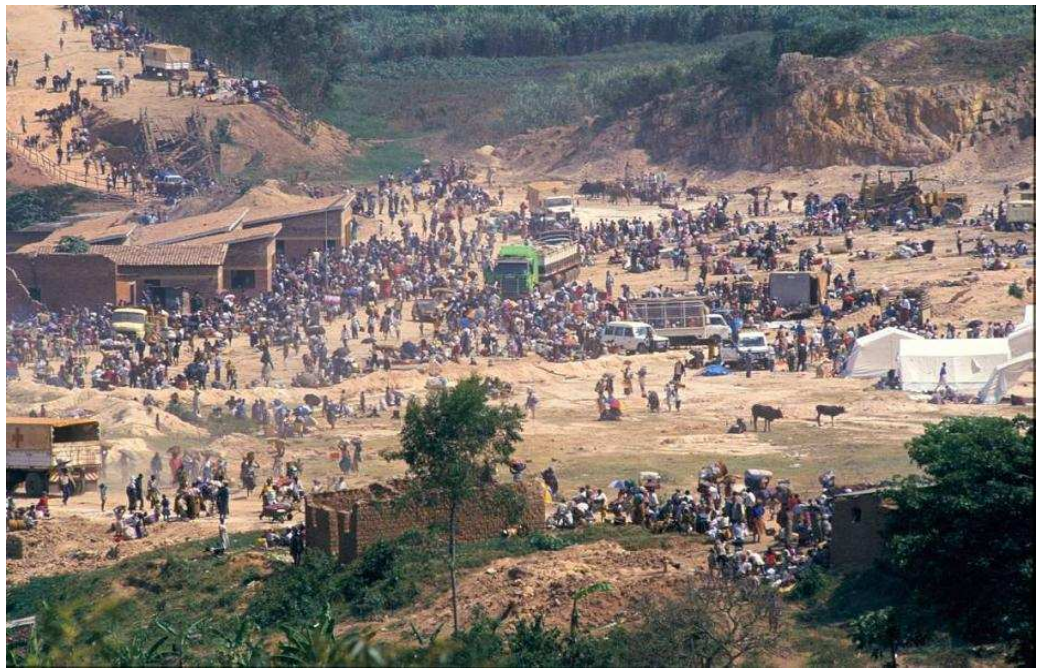
Photo: JHU, Dr. Hai-Quan Mao

Mass pneumococcal vaccination in crisis-effected populations

- Mass vaccination preferred mode of delivery in crises as a supplement to routine
  - Currently measles (MCV), occasionally yellow fever
- The pneumococcal conjugate vaccine (PCV) may be one of the most important new vaccines to address burden
- Concept phase for randomized effectiveness trial
  - optimal dosage
  - age groups
  - vaccine – PCV -7, 10, 13
  - endpoints

Mass PCV in crisis-effected populations: dose

- Single dose of PCV could be coupled with MCV and other mass-delivered interventions
- 2 doses “feasible”, 3 doses not feasible
- Limited data for a single dose



Sierra Leone

Mass PCV in crisis-effected populations: age and vaccine

- Age groups
  - Current: children 1 to 24 months old targeted during PCV implementation
  - Possible benefits by extending target age group to as much as 15 years of age
- Vaccine
  - PCV-10 replaces PCV-7
  - PCV-13
  - Choice dependent upon procurement and recent/new evidence

Mass PCV in crisis-effected populations: endpoints

- Mortality is preferred endpoint, but
  - formidable sample size challenges
  - all-cause mortality possible, pneumonia-attributable mortality less so
  - compromise of verbal autopsy-driven classification into acute infection-related or other.
- Clinical pneumonia non-specific
- Radiological pneumonia with mortality as secondary outcome along with
  - carriage and immunogenicity through nested studies (important for age groups)
  - incidence of hospital admission
  - prescription of antibiotic courses

Appropriateness of vaccines and research challenges

- Vaccine characteristics
  - Heat-stable
  - Low space requirements
  - Low dosage
  - Efficacy in range of immune profiles (ex., malnourished)
  - Needle-free delivery
- Research
  - Ethical and study design challenges

See for example: Deen & Clemens *Nature Reviews Drug Discovery* **5**, 932–940 (November 2006)