Infectious disease dynamics: the public health importance of linking models and data for rubella

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with

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Rubella and Congenital Rubella Syndrome

Friedrich Hoffman, first clinical description, 1740

Rubella

Norman Gregg, a paediatric ophthalmologist made the link to Congenital Rubella Syndrome in 1941
Rubella vaccination: key metrics

**CRS** (Congenital Rubella Syndrome) (brain damage, deafness, blindness in children born to women who were infected during the first trimester)
Rubella vaccination: key metrics

**CRS:** Congenital Rubella Syndrome (brain damage, deafness, blindness in children born to women who were infected during the first trimester)

CRS burden in the absence of vaccination
Rubella vaccination: key metrics

**CRS:** Congenital Rubella Syndrome (brain damage, deafness, blindness in children born to women who were infected during the first trimester)

- **Vaccine coverage**
- **CRS cases per 1000 live births**

Minimum vaccination coverage

CRS burden in the absence of vaccination
These projections ignore the potential role of local extinction in increasing the burden of CRS.
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Rubella vaccination: local extinction and CRS

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Inequities in vaccine coverage may amplify this process.
Nine year biweekly time series from all districts; used to develop a spatial and age-structured epidemiological model.

Human movement was parametrized via fade-outs, as in Peru - and effectively came down to: “people go to big places”.

Vaccination was then introduced.
Rubella vaccination: vaccine heterogeneity


Index of concentration of vaccination in districts with larger populations ('polarity')

Country-wide CRS burden

No districts where CRS burden increased

South Africa

Problems with this approach

• **Spatial scale of movement may be unrealistic**
  • based on **districts** - and based on **rubella dynamics** rather than measures of e.g., costs of travel. Rubella is massively **under-reported**.

• **Vaccine heterogeneity poorly described**
  • based on South Africa **district level** administrative measures of cover.
Measles vaccination: isolation by distance

Travel time, hours to nearest urban centre with >50,000 people

Combine with DHS data to assess the impact of travel time on vaccine cover

Linard et al. 2013. PloS One
Measles vaccination: isolation by distance

Two examples:

**Mali**

**Cameroon**

Travel time (hours)

Vaccine coverage at 12mo
Measles vaccination: isolation by distance

Lower coverage associated with higher inequity

maximum coverage achieved in <5 yr olds
Better models of movement

Two scales of movement modeled for immunizing childhood infections:
• **seasonal variation**
• term-time forcing
• rainfall / agriculture
Better models of movement

Two scales of movement modeled for immunizing childhood infections:

- **seasonal variation**
  - term-time forcing
  - rainfall / agriculture

- **extinction / recolonization**
  - people go to big places
  - occasional signature distance

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### England & Wales

![Map of England & Wales](image1)

![Graph of seasonal variation](image2)

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### Niger

![Map of Niger](image3)

![Graph of seasonality](image4)
Functionally, seasonal variation in transmission will actually be shaped by changes in social networks linked to these two drivers, rather than the drivers themselves.
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Better models of movement

1. True Movements
   - Mobile Phone Tower
   - Observed movement
   - Unobserved movement

2. Call Data Records (for an individual)
<table>
<thead>
<tr>
<th>Caller</th>
<th>Receiver</th>
<th>Location (caller)</th>
<th>Location (receiver)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jane</td>
<td>Bob</td>
<td>Tower 5</td>
<td>Tower 10</td>
<td>Day 2, 23h</td>
</tr>
<tr>
<td>Jane</td>
<td>Sally</td>
<td>Tower 4</td>
<td>Tower 22</td>
<td>Day 3, 3h</td>
</tr>
<tr>
<td>Jane</td>
<td>Bob</td>
<td>Tower 2</td>
<td>Tower 10</td>
<td>Day 3, 12.5h</td>
</tr>
<tr>
<td>Jane</td>
<td>Sam</td>
<td>Tower 4</td>
<td>Tower 32</td>
<td>Day 4, 2.5h</td>
</tr>
<tr>
<td>Jane</td>
<td>Joe</td>
<td>Tower 3</td>
<td>Tower 22</td>
<td>Day 4, 15h</td>
</tr>
<tr>
<td>Jane</td>
<td>Sally</td>
<td>Tower 3</td>
<td>Tower 22</td>
<td>Day 5, 23h</td>
</tr>
<tr>
<td>Jane</td>
<td>Marc</td>
<td>Tower 2</td>
<td>Tower 12</td>
<td>Day 7, 7h</td>
</tr>
<tr>
<td>Jane</td>
<td>Marc</td>
<td>Tower 1</td>
<td>Tower 12</td>
<td>Day 7, 16h</td>
</tr>
</tbody>
</table>

3. Inferred Location
   - Hour
   - Day

4. Location per Day
   - Day
   - Hour

5. Individual Trips Counted
   - Day
Better models of movement

Central Province

Transmission

Travel (M Trips)
Conclusions

Novel data sources

• are necessary for modeling rubella because vaccination must be designed to prevent late age large outbreaks such as have been repeatedly observed for measles; and must be spatially equitable

• are required to better estimate spatial aspects of vaccine heterogeneity

• are required to get a better understanding of the human metapopulation and its movements
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Felicity Cutts

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Campaigns and travel time

Measles

DTP3

Travel time (hours)

Difference in coverage 13 mo and 60 mo
Rubella in Costa Rica

![Graph showing ages and log incidence from 1980 to 2005]

- Ages range from 1980 to 2005.
- Log incidence scale ranges from 0 to 6.

![Graph showing coverage of infants from 1975 to 2005]

- Coverage of infants ranges from 0.0 to 0.8.
- Years range from 1975 to 2005.
Rubella in Costa Rica

Start vaccination of infants, 1975

Log incidence

Coverage of infants

0.0 0.4 0.8

Rubella in Costa Rica

Start vaccination of infants, 1975
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Coverage of infants
Rubella in Costa Rica

Start vaccination of infants, 1975

Metcalf et al. 2011 TPB
Better models of movement
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