Simulations of Rubella Vaccination Strategies in China

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References

Background:

- **Rubella**: mild childhood infectious disease
- **Congenital Rubella Syndrome**: severe consequences when pregnant women are infected
- **Vaccination status**: 1969 – now
- **WHO recommendations on Rubella/CRS control**
Background:

WHO recommended that “All countries should assess their rubella situation and, if appropriate, make plans for introduction of rubella vaccination and CRS/rubella surveillance.” (Geneva, 2000)
Warning:

“inadequately implemented childhood vaccination runs the risk of altering rubella transmission dynamics and increasing susceptibility in women of child bearing age, thereby increasing the risk of CRS” (Geneva, 2000)
Background: -China

- Rubella vaccination is not mandatory in the national immunization program. MMR is available in some major cities.
- Resources for vaccination are limited.
- Population structure is changing
- Should China vaccinate for rubella? If so, which strategy?
### Table 2. Seropositivity for rubella antibody, by age group, of persons tested in 20 provinces in the People’s Republic of China, 1979–1980.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No. of persons tested</th>
<th>Percentage of persons seropositive</th>
<th>Geometric mean titer</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>766</td>
<td>34.5</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>644</td>
<td>41.9</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>652</td>
<td>56.9</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>698</td>
<td>63.5</td>
<td>81</td>
</tr>
<tr>
<td>5</td>
<td>723</td>
<td>73.6</td>
<td>83</td>
</tr>
<tr>
<td>6–10</td>
<td>3,422</td>
<td>88.5</td>
<td>71</td>
</tr>
<tr>
<td>11–15</td>
<td>2,399</td>
<td>96.0</td>
<td>55</td>
</tr>
<tr>
<td>16–20</td>
<td>1,918</td>
<td>96.2</td>
<td>41</td>
</tr>
<tr>
<td>21–25</td>
<td>1,624</td>
<td>95.2</td>
<td>38</td>
</tr>
<tr>
<td>26–30</td>
<td>1,525</td>
<td>94.6</td>
<td>37</td>
</tr>
<tr>
<td>31–40</td>
<td>2,287</td>
<td>96.8</td>
<td>41</td>
</tr>
<tr>
<td>Total</td>
<td>16,658</td>
<td>85.6</td>
<td>51</td>
</tr>
</tbody>
</table>
Method:

Use mathematical models and computer simulations to compare various rubella vaccination strategies with consideration of China’s changing population structure

- Construct demographical model
- Add epidemiological model
China Demographic Model

• 58 age groups: 0,1,2,…,49, 50-54, 55-59, …, 75-79, 80-84, 85+

China Demographic Model

• Derived 1965 age distribution from 1987 age distribution data.
• Used the birth/death rate from 1965-1992 as the scaling factor for fertility and death rate.
• Interpolate fertility and death rate between 1992 and 2000 data.
• Used Leslie matrix population model
Leslie population matrix demographic model

\[ n_i = \text{size of population in age group } i \]

\[ m_i = \text{average birth rate of people in age group } i \]

\[ S_i = \text{fraction of those in age group } i \]

\[ \text{who survive to age group } i+1 \]

\[
\begin{bmatrix}
  n_1 \\
  n_2 \\
  n_3 \\
  \vdots \\
  n_k
\end{bmatrix} = 
\begin{bmatrix}
  m_1 & m_2 & m_3 & \cdots & m_k \\
  S_1 & 0 & 0 & \cdots & 0 \\
  0 & S_2 & 0 & \cdots & 0 \\
  0 & 0 & S_3 & \cdots & 0 \\
  0 & 0 & 0 & \cdots & S_{k-1}
\end{bmatrix}
\begin{bmatrix}
  n_1 \\
  n_2 \\
  n_3 \\
  \vdots \\
  n_k
\end{bmatrix}
\]
1990: the model and the data
2000: the model vs. data
Growth rate with the size
The changing age structure of the population:
The epidemiological model:

- **M**: passively immune
- **I**: infective
- **S**: susceptible
- **R**: recovered with immunity
- **E**: exposed (latent)
- **V**: vaccinated
Parameter values:

- average passive immunity period is 6 months (182.5 days)
- average latent period is 10 days
- average infectious period is 12 days
- force of infection values: .20 for 0, .24 for 1-4, .27 for 5-9, .15 for 10-14, .10 for 15-49, .04 for 50-64, .03 for 65+
Seropositivity: the model vs. data (with no vaccination)
Rubella cases: no vaccination

![Graph showing the number of Rubella cases in China from 1966 to 2051 without vaccination.](image)
CRS cases: no vaccination
Why?

• Changing demographics => average age of infection increases => more rubella in pregnant women.
• Average CRS in 2020-2050 is over two times the level in 2005
• Thus maintaining current policy will lead to more CRS
Vaccination Strategies

• Routine vaccination: 1 year old children
• Routine vaccination: 12 year old girls
• Mass campaign: 2-14 year old children
• Mass campaign: 2-14 year old girls
• Mass campaign: 15-40 year old women
• Combinations of above
Rubella cases:
CRS cases:
Increasing age of attack:
Results from simulations:

• Routine vaccination of 1 year old children causes rubella incidence to decrease.
• CRS incidence increases unless 50% or more are vaccinated.
• Rubella and CRS will be eliminated if 80% or more are vaccinated (assuming the current population control policy continues).
Rubella: vaccinate 12 year old girls
CRS: vaccinate 12 years old girls
Observations:

- Routine vaccination of 12 year old girls are effective in reducing CRS cases.
- This strategy will never lead to elimination of rubella.
### Table 1. Comparison of rubella vaccination strategies in China in 2005 to 2051

<table>
<thead>
<tr>
<th>mass:</th>
<th>mass:</th>
<th>mass:</th>
<th>routine:</th>
<th>routine:</th>
<th>total CRS</th>
<th>CRS</th>
<th># of routine</th>
<th># of mass</th>
<th>total # of</th>
<th># of vaccinations</th>
</tr>
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<tbody>
<tr>
<td>2-14 yr</td>
<td>2-14 yr</td>
<td>15-40</td>
<td>1 yr old</td>
<td>12 yr</td>
<td>2005-2051</td>
<td>2051</td>
<td>vaccinations</td>
<td>vaccinations</td>
<td>vaccinations</td>
<td>prevented</td>
</tr>
<tr>
<td>girls</td>
<td>boys</td>
<td>women</td>
<td>children</td>
<td>girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>90%</td>
<td>90%</td>
<td>60%</td>
<td>90%</td>
<td>2,578</td>
<td>0</td>
<td>596,350,829</td>
<td>395,198,054</td>
<td>991,548,883</td>
<td>2,622</td>
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</tr>
<tr>
<td>90%</td>
<td>60%</td>
<td>90%</td>
<td>90%</td>
<td>5,515</td>
<td>0</td>
<td>596,350,830</td>
<td>277,610,095</td>
<td>873,960,925</td>
<td>2,329</td>
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<td>90%</td>
<td>90%</td>
<td>90%</td>
<td>90%</td>
<td>5,923</td>
<td>0</td>
<td>596,350,828</td>
<td>227,438,932</td>
<td>823,789,760</td>
<td>2,198</td>
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<tr>
<td>70%</td>
<td>90%</td>
<td>90%</td>
<td>8,173</td>
<td>0</td>
<td>596,350,828</td>
<td>195,718,976</td>
<td>792,069,804</td>
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<td>90%</td>
<td>90%</td>
<td>12,613</td>
<td>0</td>
<td>596,350,830</td>
<td>109,850,973</td>
<td>706,201,803</td>
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<td>90%</td>
<td>20,757</td>
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<td>1,657</td>
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<tr>
<td>80%</td>
<td>27,308</td>
<td>1</td>
<td>530,089,627</td>
<td>0</td>
<td>530,089,627</td>
<td>1,500</td>
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<tr>
<td>70%</td>
<td>100,970</td>
<td>2,247</td>
<td>463,828,423</td>
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<td>463,828,423</td>
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<tr>
<td>90%</td>
<td>117,601</td>
<td>1,722</td>
<td>308,049,970</td>
<td>0</td>
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<td>1,171</td>
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<tr>
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<td>147,426</td>
<td>2,837</td>
<td>273,822,196</td>
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<td>273,822,196</td>
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<tr>
<td>60%</td>
<td>276,978</td>
<td>8,139</td>
<td>397,567,219</td>
<td>0</td>
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<td>3,831</td>
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<tr>
<td>90%</td>
<td>302,672</td>
<td>11,015</td>
<td>0</td>
<td>109,850,973</td>
<td>109,850,973</td>
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<tr>
<td>90%</td>
<td>327,554</td>
<td>10,656</td>
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<td>227,438,932</td>
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<tr>
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<td>345,807</td>
<td>11,386</td>
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<td>223,678,829</td>
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<td>6,403</td>
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<tr>
<td>50%</td>
<td>358,881</td>
<td>11,387</td>
<td>0</td>
<td>139,799,268</td>
<td>139,799,268</td>
<td>6,395</td>
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<tr>
<td>50%</td>
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<td>12,453</td>
<td>331,306,016</td>
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<tr>
<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
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</tr>
<tr>
<td>10%</td>
<td>399,712</td>
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<td>66,261,203</td>
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<tr>
<td>40%</td>
<td>406,976</td>
<td>13,910</td>
<td>265,044,813</td>
<td>0</td>
<td>265,044,813</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td>413,971</td>
<td>13,143</td>
<td>132,522,406</td>
<td>0</td>
<td>132,522,406</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>30%</td>
<td>419,181</td>
<td>13,701</td>
<td>198,783,609</td>
<td>0</td>
<td>198,783,609</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Results from simulations:

• If the achievable vaccination rate is not high, vaccinating 12 year old girls reduces CRS cases by direct protection.

• If the achievable vaccination rate is high, vaccinating 1 year old children is a better strategy that leads to elimination of the disease.

• The threshold for switching is about 80%
Rubella: 2005 Mass campaign + …

CHINA RUBELLA CASES 1966-2051

vaccinating women 15-40 year in 2005

with no vaccination
10%
30%
50%
70%

70% women plus 90% 1 year old thereafter

yearly incidence

time in years
CRS: 2005 mass campaign + ...
Rubella: Campaign vaccination of 2-14 yr olds in 2005
CRS: Campaign vaccination of 2-14 yr olds in 2005

CHINA CRS CASES 1966-2051

vaccinating 2-14 years old in 2005

with no vaccination

80% 2-14 yr old

80% 2-14 yr old plus 90% 1 year old thereafter

yearly incidence

time in years


0 5000 10000 15000
Observations:

• A mass campaign of vaccinating 15-40 year old women can reduce CRS cases during the following 10-20 years.

• A mass campaign of vaccinating 2-14 year old children only can lead to large oscillations in CRS cases with peaks above the no-vaccination levels.
Conclusion (1):

The changes in demographic structure are altering rubella transmission dynamics. “No vaccination” or “Low coverage infant vaccination” are not good strategies for China.
Conclusion (2):

The best strategy seems to be a combination of initial mass vaccination to provide good short term direct protection plus routine vaccination of at least 80% of 1 year old children to move towards elimination of rubella in China.