Overview: Review of Outbreak Data and Need to Close Immunity Gaps

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Centers for Disease Control and Prevention
I. Review of case-based measles data, 2010-2014

II. Literature review

III. Example China role of adults in measles outbreak
I. Review of case-based measles data, 2010-2014

Purpose:

To evaluate case-based measles data representing all WHO regions and looking at proportion of cases among different age groups, specifically adolescent and adult populations.
Data: Case-based measles surveillance data*
Inclusion criteria: Country-years in 2010-2014
- ≥30 confirmed measles cases per year
  - Confirmed cases = lab-confirmed, epi-linked, or clinically compatible
  - 326 country-years met inclusion criteria

Exclusions:
- Case-based data not available (SEARO all years, EURO 2013-2014)

PAHO data is shown separately

* Reported to WHO HQ, as of September 2015
Age Distribution of Confirmed* Measles Cases by Region, 2010-2014

Note: SEARO case-based data not available; EURO case-based data not available for 2013 and 2014.

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution of Confirmed* Measles Cases by Region, by Year, 2010-2014

AFRO

2010: 7% >=35 years, 13% 25-34, 8% 15-24, 8% 5-14, 8% 0-4, 2% Missing age
2011: 5% >=35 years, 8% 25-34, 8% 15-24, 8% 5-14, 8% 0-4, 2% Missing age
2012: 4% >=35 years, 19% 25-34, 8% 15-24, 8% 5-14, 8% 0-4, 2% Missing age
2013: 4% >=35 years, 2% 25-34, 4% 15-24, 4% 5-14, 4% 0-4, 1% Missing age
2014: 4% >=35 years, 1% 25-34, 4% 15-24, 4% 5-14, 4% 0-4, 1% Missing age

EURO

2010: 4% >=35 years, 8% 25-34, 19% 15-24, 24% 5-14, 16% 0-4, 1% Missing age
2011: 8% >=35 years, 34% 25-34, 39% 15-24, 25% 5-14, 22% 0-4, 1% Missing age
2012: 39% >=35 years, 25% 25-34, 22% 15-24, 16% 5-14, 15% 0-4, 1% Missing age

WPRO

2010: 5% >=35 years, 10% 25-34, 9% 15-24, 7% 5-14, 7% 0-4, 2% Missing age
2011: 9% >=35 years, 14% 25-34, 14% 15-24, 13% 5-14, 13% 0-4, 3% Missing age
2012: 14% >=35 years, 13% 25-34, 13% 15-24, 19% 5-14, 17% 0-4, 3% Missing age

EMRO

2010: 5% >=35 years, 8% 25-34, 7% 15-24, 7% 5-14, 7% 0-4, 2% Missing age
2011: 7% >=35 years, 9% 25-34, 7% 15-24, 7% 5-14, 7% 0-4, 2% Missing age
2012: 7% >=35 years, 7% 25-34, 7% 15-24, 7% 5-14, 7% 0-4, 2% Missing age
2013: 7% >=35 years, 7% 25-34, 7% 15-24, 7% 5-14, 7% 0-4, 2% Missing age
2014: 7% >=35 years, 7% 25-34, 7% 15-24, 7% 5-14, 7% 0-4, 2% Missing age

Note: SEARO case-based data not available; EURO case-based data not available for 2013 and 2014.
*Lab-confirmed, epi-linked, or clinically compatible.
Distribution of confirmed measles cases by age groups, American Region, 2010-2014

N=3,787

Source: Country reports
Distribution of confirmed measles cases by age
The Americas, 2015

Source: Country reports to FGL/IM
### 126,266 Global Measles Cases Among Adolescents and Adults Age ≥15 Years, by Region, 2010-2014

<table>
<thead>
<tr>
<th>Region</th>
<th>Total</th>
<th>AFRO</th>
<th>EMRO</th>
<th>EURO</th>
<th>WPRO</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>3,107</td>
<td>6,660</td>
<td>5,266</td>
<td>10,124</td>
<td>17,536</td>
</tr>
<tr>
<td>25-34</td>
<td></td>
<td></td>
<td></td>
<td>224</td>
<td>225</td>
</tr>
<tr>
<td>35-44</td>
<td></td>
<td></td>
<td></td>
<td>3,574</td>
<td>3,546</td>
</tr>
<tr>
<td>45-54</td>
<td></td>
<td></td>
<td></td>
<td>879</td>
<td>1,444</td>
</tr>
<tr>
<td>55+</td>
<td></td>
<td></td>
<td></td>
<td>753</td>
<td>236</td>
</tr>
<tr>
<td>Total</td>
<td>126,266</td>
<td>42,328</td>
<td>14,058</td>
<td>32,205</td>
<td>31,754</td>
</tr>
</tbody>
</table>

*Note: SEARO case-based data not available; EURO case-based data not available for 2013 and 2014. Lab-confirmed, epi-linked, or clinically compatible.*
### 126,266 Global Measles Cases Among Adolescents and Adults Age ≥15 Years, by Year, 2010-2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>126,266</td>
<td>42,328</td>
<td>68,578</td>
<td>10,815</td>
<td>3,107</td>
<td>126,266</td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td>12,920</td>
<td>24,518</td>
<td>15,712</td>
<td>719</td>
<td>3,053</td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td>31,148</td>
<td>719</td>
<td>10,650</td>
<td>397</td>
<td>1,114</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td>15,851</td>
<td>357</td>
<td>1,114</td>
<td>3,315</td>
<td>2,449</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td>7,036</td>
<td>467</td>
<td>1,819</td>
<td>50</td>
<td>120</td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td>10,684</td>
<td>167</td>
<td>329</td>
<td>1,974</td>
<td>55+</td>
</tr>
</tbody>
</table>

**Note:** SEARO case-based data not available; EURO case-based data not available for 2013 and 2014.

*Lab-confirmed, epi-linked, or clinically compatible.*
Measles Incidence and Proportion of Confirmed* Cases ≥15 Years, 2010-2014

Note: Each dot is 1 country
*Lab-confirmed, epi-linked, or clinically compatible.
Measles Incidence and Proportion of Confirmed* Cases ≥15 Years, by Region, 2010-2014

Note: Each dot is 1 country. *Lab-confirmed, epi-linked, or clinically compatible.
Proportion of Confirmed* Cases Among Adults ≥15 Years of Age, Among Countries in Each Region with the Highest Proportions of Adult Cases, 2010-2014

*Lab-confirmed, epi-linked, or clinically compatible.
Proportion of Confirmed* Cases Among Adults ≥15 Years of Age, Among Countries in Each Region with the Largest Numbers of Cases, 2010-2014

*Lab-confirmed, epi-linked, or clinically compatible.
Case-based data for select countries 2010-2014 are shown in Appendix at end of this presentation
II. Literature review

Purpose:

To review the published literature for reports of measles outbreaks involving adolescents/adults and describe the impact of this age group on sustaining measles transmission
Published: 1 Jan 2010 – 31 Mar 2016

Excluded

- < 50 cases
  - These are limited or contained outbreaks
- < 25% in people 15+ years of age (N=14)
  - These are mostly in high risk sub-populations with minimal spillover into the general population.
  - 6/11 had more than 50% of cases under 5 years of age

Includes 25 reports of adult outbreaks
Adolescent & adult outbreaks from the literature

- Pie chart showing proportion articles from WHO regions
- No examples found
  - Eastern Mediterranean
  - Southeast Asia
What did these outbreaks look like?

### Case Distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>13%</td>
</tr>
<tr>
<td>1 - 5 years</td>
<td>17%</td>
</tr>
<tr>
<td>5 - 14 years</td>
<td>22%</td>
</tr>
<tr>
<td>15 - 19 years</td>
<td>12%</td>
</tr>
<tr>
<td>20 + years</td>
<td>39%</td>
</tr>
</tbody>
</table>

### Outbreak Descriptions

- 15% too young to vaccinate
- Primary case averaged 22 years
- Median age of cases 11.8 years
- Unknown Vaccination Status 39%
  - Of those where reported
- Unvaccinated Cases 64%
  - Of those where status known, 64% were unvaccinated
Outbreak reports may mention…

- Areas or groups with low vaccination coverage
  - Often minority groups described by
    - Ethnicity (6), Religion (3), Philosophy (2)
  - Sometimes described by geography or health care linked
    - migration status (7), area of residence (2)
    - health worker (3), health care associated transmission (5)
  - These groups are associated with disease in younger people

- Historically low vaccination coverage with measles containing vaccines
  - These populations are associated with disease in older people

( ) denotes # articles where group was mentioned in description of outbreak
Sub-groups within a single outbreak can have distinct age distributions

Age distributions can change over the course of an outbreak (example 1)

Did the older ages sustain the outbreak?

- This review shows summary characteristics of outbreaks with more than 25% of cases over 15 years of age.
- Indicates only that these individuals were affected.
- Does not necessarily mean that adolescents or adults are:
  - The reason the outbreak occurred
  - The primary source of transmission
- 2 examples of outbreaks for discussion.
Example: Malawi 2010
Vaccination history affect on outbreak cases

Vaccine induced immunity by age
# of doses 0= black, 1= gray, 2=white

Example: Malawi 2010
Nation-wide campaigns <15 years ended the outbreak

Figure 1. Weekly distribution of measles cases and time when the reactive vaccination campaigns were implemented and districts where outbreak-response immunizations were conducted by the MoH and MSF.

**Black** arrows indicate campaigns implemented by MoH/MSF.

**Gray** arrows indicate campaigns implemented by MoH only.


Note: Malawi has 28 districts; by July all were affected by outbreak.
Example: Somali Refugees of famine 2011

Required vaccination of adults to end the outbreak.

Figure 1. Reported measles cases and cumulative median age, by week of rash onset, Dadaab, Kenya, June–Nov.2011 (n = 1370).

**Gray arrow** = national measles vaccination targeting children 6–59 M.

**White arrow** = out-break response immunization targeting refugees 15–30 Y.

During week 14, prior to a sudden influx of new arrivals and this outbreak, a campaign targeted children 9 M to 14 Y of age in the camps and surrounding communities.

Adults Sustained

Was vaccination of adults necessary to control the outbreak?

Examples of outbreaks* where lower age SIAs were effective at controlling the outbreak
<duration of outbreak shown in blue>

- Tanzania 2006/7 (SIA up to 15 Y) <7 months>
- Vietnam 2008-2010 (SIA up to 10 Y) <16 months>
- Somalis displaced in Ethiopia 2011 (SIA up to 15 Y) <4 months>
- Malawi 2010 (SIA up to 15 Y) (3 prior sub-national campaigns) <9 months>
- South Africa 2009-2010 (SIA up to 15 Y) (2 prior sub-national up to 19Y <90% coverage) <20 months>
- Namibia 2009-2010 (2 subnational SIAs 6-59 M) <18 months>
- Botswana 2009-2010 (no SIA necessary SIA 11/2009 9-59 M – at beginning of cases) <5 months>
- Mongolia 2001 (no SIA necessary SIA 10/2000 9M-8Y) <6 months> PMID: 17642531 not in analysis

*according to search criteria
Resources


Resources (continued…)


III. Example: China
Role of adults in measles outbreak

Paper in press

Example of a comprehensive assessment of measles transmission patterns during measles outbreak

Graciously shared by Dr. Ma Chao, lead epidemiologist at China CDC
**Table 1** Age distribution and MCV vaccination status of the 280 measles cases in an outbreak, KL County, Inner Mongolia Autonomous Region, China, 2013-2014.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total case No.</th>
<th>Incidence (per 100,000)</th>
<th>No. of cases by MCV history</th>
<th>% of vaccinated</th>
<th>Description of eligibility for MCV doses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>0 doses</td>
<td>1 dose</td>
<td>2 doses</td>
</tr>
<tr>
<td>0-4 Years</td>
<td>55</td>
<td>614.3</td>
<td>614.3</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>0-7 Months</td>
<td>22</td>
<td>2318.2</td>
<td>2318.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8-23 Months</td>
<td>24</td>
<td>938.2</td>
<td>938.2</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>2-4 Years</td>
<td>9</td>
<td>165.2</td>
<td>165.2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5-9 Years</td>
<td>3</td>
<td>28.5</td>
<td>28.5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>10-14 Years</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15-19 Years</td>
<td>2</td>
<td>23.6</td>
<td>23.6</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>20-24 Years</td>
<td>11</td>
<td>100.2</td>
<td>100.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25-29 Years</td>
<td>20</td>
<td>137.6</td>
<td>137.6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>30-34 Years</td>
<td>57</td>
<td>437.5</td>
<td>437.5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>35-39 Years</td>
<td>62</td>
<td>388.2</td>
<td>388.2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>40-44 Years</td>
<td>44</td>
<td>269.5</td>
<td>269.5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>45-49 Years</td>
<td>19</td>
<td>120.1</td>
<td>120.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>≥50 Years</td>
<td>7</td>
<td>16.2</td>
<td>16.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>167.5</td>
<td>145</td>
<td>16</td>
<td>8</td>
</tr>
</tbody>
</table>

Note: [1] 8-17 month old children are eligible for 1 dose MCV, and 18-23 month old children are eligible for 2 doses; [2] 5-6 year old children are eligible for both 2010 and 2012 SIA, 7-9 year old children are eligible for both 2010 SIA; [3] since 1986 China used lyophilized MV, and before that liquid MV was used.
Figure 1 Weekly distribution of outbreak-associated measles cases by date of rash onset, KL County, Inner Mongolia Autonomous Region, China, 2013-2014.
Figure 2 Timeline demonstrating chain of measles transmission in the 83 cases, by date of rash onset and transmission setting, KL County, Inner Mongolia Autonomous Region, China, 2013-2014.
Why we have measles in older ages - illustration: SIAs China, Tianjin (2005 - 2013)

Black Arrows show province SIAs
2008 = 8 M - 14Y
2010 = 8 - 59 M
Red line = Observed cases
Gray line = Model of expected cases
Observe more cases in older populations in 2010 & more dramatically in 2013. This is because the SIAs have protected the younger children.

This example is based on SIAs, but the same can occur with routine immunizations with introduction, or with improvements in coverage.

Thank You
Jennifer Kriss
Jennifer Knapp
Katrina Kretsinger
Susan Reef
Mark Papania
David Sniadack
Appendix of country-specific case-based data
Age Distribution and Incidence of Confirmed* Cases by Year, Romania, 2010-2012

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Italy, 2011-2012

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Australia, 2010-2014

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Jordan, 2013

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Japan, 2010-2014

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Germany, 2010-2012

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, United Kingdom, 2010-2012

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Austria, 2011

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Namibia, 2010-2014

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Malawi, 2010

*Lab-confirmed, epi-linked, or clinically compatible.
Age Distribution and Incidence of Confirmed* Cases by Year, Philippines, 2010-2014

*Lab-confirmed, epi-linked, or clinically compatible.
Figure 2. Attack rate and proportion of confirmed measles cases by age group, Ceará, 2014 & 2015*

Source: SESA/COPROM/NUVEP/SINAN. * Updated on: 11/24/2015
Age distributions can change over the course of an outbreak (example 2)

Age distribution of measles cases, by month and region, Vietnam, Oct 2008-Jan 2010