WHO efforts to promote next-generation influenza vaccines, with particular focus on low- and middle-income countries

Justin R. Ortiz
WHO Initiative for Vaccine Research

23 August 2016
Outline

- Global Influenza Vaccine Policies and Use
- Mandates to Promote Universal Influenza Vaccine R&D
- Universal Influenza Vaccines and Pandemic Preparedness
- WHO Preferred Product Characteristics for Next-Generation Influenza Vaccines
WHO influenza vaccine policy recommendations aim primarily at protecting vulnerable high risk groups against severe influenza-associated disease and death.

In 2012, WHO updated its Influenza Vaccine Position
For countries considering the initiation or expansion of programmes for seasonal influenza vaccination, WHO recommends that pregnant women have the highest priority.

Additional risk groups: children aged 6–59 months, elderly, individuals with chronic conditions, and healthcare workers.
## 2012 SAGE Influenza Working Group
### Assessment of Risk Groups

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Feasibility of Delivery</th>
<th>Disease Severity</th>
<th>Vaccine Effectiveness</th>
<th>Safety Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women</td>
<td>moderate</td>
<td>high</td>
<td>high</td>
<td>moderate</td>
</tr>
<tr>
<td>Healthcare workers</td>
<td>moderate</td>
<td>low</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td>Children, &lt; 2 years</td>
<td>moderate</td>
<td>high</td>
<td>low</td>
<td>moderate</td>
</tr>
<tr>
<td>Children, 2-5 years</td>
<td>low</td>
<td>moderate</td>
<td>moderate</td>
<td>high</td>
</tr>
<tr>
<td>Elderly</td>
<td>low</td>
<td>high</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>Underlying Health Conditions</td>
<td>low</td>
<td>high</td>
<td>low</td>
<td>high</td>
</tr>
</tbody>
</table>

Adapted from WG report. SAGE also noted indirect benefits of maternal immunization and immunization of school-aged children.
Prioritization of Pregnant Women Relates Burden, VE, and Feasibility of Delivery

- High Burden:
  - elderly
  - underlying conditions

- Feasibility:
  - <2 years
  - pregnant women
  - HCW

- High VE
WHY Prioritize Pregnant Women?

Not a recommendation for all countries to immunize pregnant women but a recommendation to maximize the benefits of influenza vaccines in countries with existing or initiating new influenza vaccination programmes.
IFPMA Survey of Seasonal Influenza vaccine
Doses Distributed by WHO Region

Doses per 1,000 pop

AM
EU
WP
SEA
EM
AF

Palache, et al., Vaccine, Volume 33, Issue 42, 2015, 5598–5605
WHO Member States with Influenza Vaccine Policies in 2014, by WHO Region

- Has national influenza vaccine policy: 59%
- Children: 28%
- Adults with chronic illness: 46%
- Pregnant women: 41%
- Health-care workers: 47%
- Elderly: 45%

Global Average

Ortiz et. al. Vaccine. In press.
Comparison of WHO Member States with and without National Influenza Vaccine Policies in 2014

<table>
<thead>
<tr>
<th></th>
<th>Countries with a national influenza vaccine policy</th>
<th>Countries without a national influenza vaccine policy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Countries</strong></td>
<td>115</td>
<td>79</td>
</tr>
<tr>
<td><strong>Median per capita health expenditure (USD$)</strong></td>
<td>664</td>
<td>82</td>
</tr>
<tr>
<td><strong>World Bank Income Category</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High income</td>
<td>54 (47%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Upper middle income</td>
<td>41 (36%)</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>Lower middle income</td>
<td>19 (17%)</td>
<td>33 (42%)</td>
</tr>
<tr>
<td>Low income</td>
<td>1 (1%)</td>
<td>30 (38%)</td>
</tr>
<tr>
<td>Gavi-eligible</td>
<td>4 (3%)</td>
<td>45 (57%)</td>
</tr>
</tbody>
</table>

Ortiz et. al. Vaccine. In press.
<table>
<thead>
<tr>
<th></th>
<th>Countries with a national influenza vaccine policy n, %</th>
<th>Countries without a national influenza vaccine policy n, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Countries</td>
<td>115 (100%)</td>
<td>79 (100%)</td>
</tr>
<tr>
<td>Birth dose HBV</td>
<td>78 (68%)</td>
<td>29 (37%)</td>
</tr>
<tr>
<td>PCV</td>
<td>80 (70%)</td>
<td>43 (54%)</td>
</tr>
<tr>
<td>HPV</td>
<td>56 (49%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>45 (39%)</td>
<td>30 (38%)</td>
</tr>
<tr>
<td>Functioning NITAG</td>
<td>61 (53%)</td>
<td>17 (22%)</td>
</tr>
<tr>
<td>Eliminated MNT</td>
<td>113 (98%)</td>
<td>57 (72%)</td>
</tr>
<tr>
<td>DTP3 at goal</td>
<td>96 (83%)</td>
<td>33 (42%)</td>
</tr>
</tbody>
</table>

Ortiz et. al. Vaccine. In press.
Summary of Influenza Vaccine Policy and Use

- 59% of WHO Member States have influenza vaccine policies
- Most vaccine policies and use in AMR, EUR, WPR
- Most vaccine policies in wealthy countries -- median per capita health care expenditure is $82 in countries without policies
- Countries with policies
  - have more experience introducing new or under-utilized vaccines
  - have stronger vaccine decision making capacity
  - have stronger immunization systems overall

Ortiz et. al. Vaccine. In press.
The Need for Innovation

- With current evidence, the investment case for seasonal influenza vaccines in LMICs has been difficult to make.
- In these settings, product innovation and more relevant data for vaccine decision making are needed.
- Research must be mindful of:
  - programmatic limitations for vaccine delivery
  - the numerous new and under-utilized vaccines competing for introduction.
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2015 PDVAC Universal Influenza Vaccine Review

- Noted that universal influenza vaccines had a number of scientific and regulatory challenges

- Advised that incremental advancement of influenza vaccines may represent more realistic near-term approach with regards to developing products for use in LMICs

- Advised WHO to develop strategic public health goals and PPCs for improved seasonal influenza vaccines and to provide guidance on data that would be needed to establish improved performance of such vaccines
Global Vaccine Action Plan (GVAP)

- Calls for “progress towards a universal influenza vaccine (protecting against drift and shift variants)”
- Operational definition is the # of trials assessing “clinically the breadth of protection completed and reported”
- Target is “at least one vaccine providing broad spectrum protection against influenza A licensed” by 2020
- Universal influenza vaccines are generally considered to induce broadly protective and long-lasting immune responses, although the parameters of broadly protective and long-lasting are not defined

http://www.who.int/immunization/global_vaccine_action_plan/en/
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Global Action Plan for Influenza Vaccines (GAP) aims to reduce the global shortage of pandemic vaccines.

Lacking significant production capacity, LMICs will have decreased access to pandemic vaccines and may suffer disproportionately.

Improved vaccines that provide broad protection against influenza viruses could enable sustainable production, stockpiling, and rapid deployment in all countries.
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WHO Preferred Product Characteristics Working Group Objectives

1. To define the unmet public health need for next generation influenza vaccines, with an emphasis on low-resource countries

2. To develop a WHO Preferred Product Characteristics (PPC) guidance for next-generation influenza vaccines, with an emphasis on low-resource countries

3. To identify research and activity gaps that must be undertaken in order to address the unmet public health need and to develop next generation influenza vaccines that meet the preferred characteristics
WHO Preferred Product Characteristics

Considers these Topics

1. Indication
2. Target population
3. Safety
4. Co-administration
5. Outcome measure and efficacy
6. Duration of protection
7. Immunogenicity
8. Registration and prequalification
9. Programmatic suitability
Goals of the Preferred Product Characteristics for Next-Generation Influenza Vaccines

To promote research and development of next generation influenza vaccines for use in LMICs, where the burden of severe influenza disease is the highest

- Emphasize the data needs to drive policymaking and use in LMICs
- Promote product development within the risk groups where advancement is most needed given disease burden
- Promote product development that aligns with practical realities of vaccine delivery
Goals of the Preferred Product Characteristics for Next-Generation Influenza Vaccines

What PPC is not doing:

- Not proposing a special LMIC vaccine formulation
- Not producing regulatory guidance or advocating thresholds for licensure
- Not establishing thresholds for policy making
Advisory Group Members

- Joe Bresee, US Centers for Disease Control and Prevention
- Fernando de la Hoz, Colombia National Health Institute
- Kari Johansen, European Centers for Disease Control
- Ruth Karron, Johns Hopkins University
- Anand Krishnan, All India Institute of Medical Sciences
- Shabir Madhi, NICD, South Africa
- Punam Mangtani, London School of Tropical Medicine and Hygiene
- Kathy Neuzil, University of Maryland
- David Spiro, US National Institutes of Health
Procedures and Timelines


- Comments compiled through 7 November 2016 and subsequently revised by WHO


- Revision will be subsequently reviewed by WHO Product Development for Vaccines Advisory Committee (PDVAC) for potential endorsement as a formal WHO document
PPC Advisory Group recommends that standardized clinical endpoints be used in influenza vaccine efficacy studies that are conducted to inform immunization policies in LMICs.

WHO has convened a working group of clinical trialists and influenza clinical experts to propose clinical endpoints that would be of the highest value to inform vaccine decision making.

As with PPC, this is not regulatory guidance, but data preferences for policy makers.

Working group deliberations are ongoing (as will be discussed by Brad Gessner later today).
Thanks!

ortizj@who.int