New vaccines

Nigel Crawford
New *(ish)* Influenza Vaccines

QIV

LAIV
Quadrivalent Influenza Vaccine [QIV]

• 2015
  – Available for the 1\textsuperscript{st} time in Australia
  – Private market only

• Who should have it?
  – Why?
[Victoria & Yamagata]
Myocardial Injury and Bacterial Pneumonia Contribute to the Pathogenesis of Fatal Influenza B Virus Infection

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With No Pathologic Evidence of Bacterial Pneumonia (n = 28)</th>
<th>Patients With Pathologic Evidence of Bacterial Pneumonia (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. females</td>
<td>19 (68)</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Median years-of-age (range)</td>
<td>6.5 (1–34)</td>
<td>20 (0–55)</td>
</tr>
<tr>
<td>No. &lt;18 years of age</td>
<td>26 (93)</td>
<td>8 (47)</td>
</tr>
<tr>
<td>No. with ≥1 high-risk condition</td>
<td>9 (43)</td>
<td>4 (33)</td>
</tr>
<tr>
<td>Median days from illness onset to death (range)</td>
<td>3 (1–22)</td>
<td>4 (2–8)</td>
</tr>
</tbody>
</table>
Quadrivalent Influenza Vaccine 2015

Quadrivalent Influenza Vaccine 2015: MVEC position statement

Quadrivalent influenza vaccine(s) are new to the Australian private pharmaceutical market in 2015. In comparison to the trivalent inactivated influenza vaccine (TIV), the quadrivalent (QIV) includes an additional influenza type B strain.
QIV (inactivated)

• In 2015, the southern hemisphere quadrivalent vaccine includes the following four types:
  – A H1N1/09 pandemic strain
  – A (H3N2) (A/Switzerland/2013)
  – B /Phuket/2013
  – B/Brisbane/2008
QIV

• **Is there additional benefit in having the quadrivalent vaccine?**

• The magnitude of this incremental benefit form the QIV will vary and is not predictable.

• Some studies have shown the proportion of all circulating influenza strains that were of the alternative B lineage (to that included in that season’s TIV) ranged from as little as 0% (in 2000 and 2001) up to a maximum of approximately 30% (in 2008).

• In the United States 2014-15 reports, ~5% of circulating influenza strains that were of the alternative B lineage (Brisbane/2008).
QIV scenarios

• **Second dose of influenza vaccine**

• There is no contraindication to a second dose of influenza vaccine (either TIV or QIV) being administered in the same year.

• It is appropriate to administer two quadrivalent vaccines, a minimum of 4-weeks apart if required [e.g. children < 9 years in the 1st year the vaccine is received or immune suppressed patients (any age > 6-months)].

• **Note: in 2015, the QIV vaccine is not funded under the NIP.**

• It is also appropriate to have a quadrivalent influenza vaccine as a 2nd dose: minimum 4-weeks following a trivalent vaccine.

• We do not believe you need to have two doses of quadrivalent vaccine if you had two doses of trivalent vaccine in previous years, unless you are immunosuppressed.(see MVEC resource)

Live Attenuated Influenza Vaccine [LAIV]

- IIV3
- IIV4
- LAIV3
- LAIV4
Children to be offered annual flu vaccine

"Flu vaccines for all children," BBC News has reported.

The BBC’s story is based on a report by independent expert advisers, who have told the government that all children from the age of two to 17 should have an annual influenza vaccination.

The recommendations of the Joint Committee on Vaccination and Immunisation

Flu vaccine for children will be given via a nasal spray
UK- LAIV program 2013/14

• Joint Committee on Vaccines and Immunisation (JCVI) statement [25 July 2012]
• Cost effectiveness: Direct and indirect effects
• Pilot: Sept 1 2013 -children 2-3 yrs
  – at GP surgery
  – pilot primary schools
• Planned......program extension 2014-16 to potentially include all children aged 2-16 yrs!
LAIV
### LAIV

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Intranasal</td>
<td>• Contraindications:</td>
</tr>
<tr>
<td>• Acceptability</td>
<td>• Immunosuppressed special risk groups</td>
</tr>
<tr>
<td>• Improved coverage</td>
<td>• Children &lt; 2-years</td>
</tr>
<tr>
<td>• Live attenuated</td>
<td>• Increased risk of hospitalisation and</td>
</tr>
<tr>
<td>• Vaccine Efficacy (VE)</td>
<td>wheezing in those &lt; 2-years age</td>
</tr>
<tr>
<td>• Immune memory</td>
<td>• Not yet available in Australia.....</td>
</tr>
</tbody>
</table>
Impact of UK Influenza program

The national childhood flu immunisation programme 2014/15

Information for healthcare practitioners
UK LAIV program

- In 2013/14 flu vaccine was offered to all 2-3 year old children
  - and those aged 4-10 years
    - 7 different geographical pilot areas
- In 2014/15 flu vaccine was offered to all 2-4 year old children
  + secondary school aged children [Years 7 & 8] in different geographical pilot areas
LAIV UK Uptake

Figure 17. Total cumulative uptake of LAIV in pilot sites by year group, England, 2013-14

Impact on disease


Direct impact was defined as reduction in cumulative incidence based on residence in pilot relative to non-pilot areas in 4-11 year-olds.

Low influenza activity overall

A consistent, though not statistically significant, decrease in cumulative disease incidence

- Exception was older age groups (>12-years)

Nil safety concerns/ flags
Figure 15: Cumulative weekly influenza vaccine uptake by target group in England

2014/15 season indicated by bold lines,
2013/14 season indicated by fainter dashed lines.  
Collections for 4yrs started in 2014/15

Vaccine uptake (%) vs Week number

- 2yrs
- 3yrs
- 4yrs
## Flu vaccine uptake rates 2012/13 – 2014/15

<table>
<thead>
<tr>
<th>Category</th>
<th>2014/15</th>
<th>2013/14</th>
<th>2012/2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients aged 65 years or older</td>
<td>72.8%</td>
<td>73.2%</td>
<td>73.4%</td>
</tr>
<tr>
<td>Patients aged six months to under 65 years in risk groups (excluding pregnant women without other risk factors)</td>
<td>50.3%</td>
<td>52.3%</td>
<td>51.3%</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>44.1%</td>
<td>39.8%</td>
<td>40.3%</td>
</tr>
<tr>
<td>Health care workers</td>
<td>54.9%</td>
<td>54.8%</td>
<td>45.6%</td>
</tr>
<tr>
<td>Carers</td>
<td>45.1%</td>
<td>44.8%</td>
<td>46.3%</td>
</tr>
<tr>
<td>Children aged two years old (including those in risk groups)</td>
<td>38.5%</td>
<td>42.6%</td>
<td>N/A</td>
</tr>
<tr>
<td>Children aged three years old (including those in risk groups)</td>
<td>41.3%</td>
<td>39.5%</td>
<td>N/A</td>
</tr>
<tr>
<td>Children aged four years old (including those in risk groups)</td>
<td>32.9%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
United States

- Specific CDC recommendation re LAIV

Starting in 2014-2015, CDC recommends use of the nasal spray vaccine for healthy* children 2 years through 8 years of age when it is immediately available and if the child has no contraindications or precautions to that vaccine. If the nasal spray vaccine is not immediately available and the flu shot is, vaccination should not be delayed and a flu shot should be given. For more information about the new

http://www.cdc.gov/flu/about/qa/nasalspray.htm?mobile=nocontent
LAIV not effective against influenza A H1N1 viruses in children 2 through 8 years during the 2013-’14 influenza season

New observational data from the U.S. Flu Vaccine Effectiveness Network and two additional studies conducted during the 2013-’14 influenza season unexpectedly showed that the live attenuated influenza vaccine (LAIV) was not effective against the influenza A H1N1 pandemic strain (H1N1 pdm09) virus when compared with inactivated influenza vaccine (IIV) in children 2 through 8 years of age. Specifically, children 2 through 8 years immunized with LAIV were not protected against H1N1 pdm09.

The data were presented at the Oct. 29 meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention (CDC).

the same H1N1 vaccine virus was used for production of 2013-’14 vaccine.

• Based on previous study results, however, LAIV is predicted to provide protection against influenza A (H3N2) and influenza B viruses that are related to those contained in the vaccine and may offer better cross-protection against drifted strains of influenza viruses than IIV.

• Very limited and early U.S. surveillance data for the 2014-’15 influenza season show a predominance of influenza A (H3N2) and influenza B viruses.

• Given the unpredictable nature of influenza each season, any
LAIV: VE against H1N1

• “Comprehensive investigations into potential explanations are ongoing. They do believe that there are differences by lot that might be explained by H1N1 strain potency loss. A/California LAIV is more susceptible to thermal degradation due to a unique HA stalk sequence, and those results are in press. The sequence is not present in seasonal influenza LAIV strains, which were used for the clinical trials of IIV versus LA”

http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html
## Optimal strategy?

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant (0- &lt; 2 years)</td>
<td>Adjuvanted inactivated influenza vaccine (IIV)</td>
</tr>
<tr>
<td>Childhood (2- &lt;9 years)</td>
<td>LAIV</td>
</tr>
<tr>
<td>9 years +</td>
<td>IIV</td>
</tr>
</tbody>
</table>
# LAIV Summary

<table>
<thead>
<tr>
<th>Positives</th>
<th>Negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Delivery method/acceptability</td>
<td>• Relatively low coverage in the UK</td>
</tr>
<tr>
<td>o Satisfactory safety profile</td>
<td>• LAIV VE requires ongoing review</td>
</tr>
<tr>
<td>o Single dose</td>
<td>o ? strain specific</td>
</tr>
<tr>
<td>• Systematic data collection in the Northern</td>
<td>o ? in older children</td>
</tr>
<tr>
<td>hemisphere</td>
<td>o ?? herd protection (indirect cost effectiveness)</td>
</tr>
</tbody>
</table>

## What next?
- Availability in Australia.....  
- Review target age groups/ contraindications
New vaccines

Nigel Crawford
GLOBAL HEALTH

Designing Tomorrow’s Vaccines

Gary J. Nabel, M.D., Ph.D.


Interactive slide
Figure 1. Timelines for Vaccine Development and Licensure of Commercial Vaccines.
New vaccines

1. Updates from Europe
   - ESPID Conference May 2015
     • 4CMenB (Bexsero)

2. New vaccines
   - Example Ebola
   - Role of GAVI
New vaccine

• What is the disease?
  – What is the clinical disease/ severity?

• Who?/ Where?
  – Epidemiology

• Vaccine?
  – Phase(s) clinical trial development
  – Vaccine efficacy/ vaccine effectiveness
  – Cost Effectiveness
  – Inclusion in immunisation program(s)?
    • International priorities (GAVI)
Group B Meningococcal (MenB) vaccines explained

Jim Buttery
SAEFVIC
Monash Children’s Hospital
Monash University
Figure 1. Notification rates of confirmed invasive meningococcal disease, by year and serogroup (excluding non-groupable isolates), Australia, 1999–2012*

* Data source: National Notifiable Diseases Surveillance System

MenCCV: Meningococcal C conjugate vaccine
Britain Will Be First To Offer Nationwide Meningitis B Vaccination Program

By Jim Algar, Tech Times | March 31, 1:20 AM

Britain has announced that it will be the first country to vaccinate all babies against the potentially fatal meningitis B.

The program, which will begin later this year, comes after long negotiations between the British government and drug manufacturers over costs, according to Health Secretary Jeremy Hunt.

The UK announced an agreement with drug company GSK over the costs of the vaccine for MenB. The nationwide
UK meningococcal disease

• Very proactive charities
Cumulative cases of laboratory-confirmed invasive meningococcal group W disease by epidemiological year in England, to end-January 2015
Men ACWY vaccine

Teenagers are to be offered a vaccination to prevent meningitis W (Men W) disease.

Cases of meningitis and septicaemia caused by meningococcal group W bacteria are rising due to a particularly deadly strain of the Men W bacteria.

Men W can be prevented by a single injection into the upper arm with the Men ACWY vaccine which protects against four different.
MenACWY (conjugate vaccine) UK

• All 14-18 year olds (children in school years 10-13) will be offered the Men ACWY vaccine as part of the routine NHS vaccination programme

• Teenagers who have already received the Men C vaccine will also be offered the Men ACWY vaccine
Ebola

Historical

• EBOV was identified in 1976 in Central Africa with two simultaneous outbreaks in Sudan and Zaire (now Democratic Republic of the Congo)

• The ‘gold standard’ animal disease models for EBOV are the rhesus and cynomolagus macaque, which can be infected with non-adapted virus strains.

Transmission

• The current outbreak in West Africa commenced in March 2014

• The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission.

http://www.who.int/mediacentre/factsheets/fs103/en/
Ebola virus disease

Clinical

- Previously known as ‘haemorrhagic fever’
- Acute onset; typically 8–10 days after exposure (range 2–21 days)
- Virus present in high quantity in blood, body fluids, and excreta of symptomatic EVD-infected patients

- > 20,000 cases
- Mortality rate 50%
- High mortality in health care workers
  - ~ 800 infected
- Protective equipment
Ebola

Public Health response

The Next Epidemic

Lessons from Ebola

The ongoing Ebola epidemic in Guinea, Sierra Leone, and Liberia is a huge tragedy. The impact on the 22 million people who live in those countries goes far beyond the Ebola deaths. The health systems and the economies of the three countries have been largely shut down during the outbreak. The world has a lot of work to do to make sure the case rate drops to zero—in the week leading up to March 1, 2015, there were 132 new confirmed cases reported. It will also need to make sure a good health care system is built and enough food and other basics are available. Without catch-up vaccination for the children who have not gotten vaccines during the epidemic, for example, the increase in measles deaths alone could outnumber the deaths from Ebola.
Ebola vaccines

• Rapid clinical trial progression
  – 1-month to ethics and recruitment in the UK
  – Oxford Jenner Institute
  – Vaccine candidates (Biodefense)

• Stakeholders/ competing trials
Guineau Ebola vaccine trial

Geneva, 1st April 2015

The VSV-ZEBOV experimental vaccine triggers the production of Ebola virus neutralising antibodies

The first results of the phase I clinical trial at Geneva University Hospitals (HUG) show that the VSV-ZEBOV vaccine candidate triggers the production of antibodies capable of neutralising the Ebola virus. These results – published today as a world first in the New England Journal of Medicine – are based on a total of 158 volunteers in Europe and Africa. Most of the observed side effects were mild to moderate (fever and muscle pain for one or two days), but around 20% of the volunteers reported mild to moderate joint pain for a couple of weeks. The vaccine was able to disseminate through the body and was detected in vesicles on the hands or feet of some of the volunteers. The phase III clinical trials recently launched in West Africa will determine whether the immune response triggered by this vaccine is able to protect the population against the Ebola virus, and if large-scale vaccination campaigns are feasible.
Guinean Ebola vaccine trial

ring vaccination strategy

• based on the approach used in the 1970s to eradicate smallpox

• Involves the identification of a newly diagnosed and laboratory-confirmed case of Ebola virus disease — “patient zero” — and the tracing of people who have been in contact with that patient.

• “ring”, generally made up of 50 to 100 individuals.

Ebola crisis: No useful data likely from vaccine trials as virus stamped out of West Africa, WHO says

Updated 13 May 2015, 6:06am

With Ebola nearly stamped out in West Africa, vaccine trials will probably fail to provide enough useful data on how well they protect people against the deadly virus, the World Health Organisation (WHO) says.

Liberia was declared free from Ebola by the government and the WHO on Saturday after 42 days without a new case of the virus, which has killed more than 4,700 people there during a year-long epidemic.

Guinea reported seven cases last week while Sierra Leone had two, Dr Marie-Paule Kieny, WHO

PHOTO: Ebola has killed more than 11,000 people since December 2013. (Supplied: Helena Humphrey)
Vaccine investment strategy

Through the Vaccine Investment Strategy the Vaccine Alliance determines which vaccines are made available to countries through Gavi’s vaccine support programmes. A new strategy is developed every five years when Gavi takes stock of available and expected vaccines and sets new priorities through in depth analysis and widespread consultations. In 2013, Gavi developed a new vaccine investment strategy for the period 2014-2018.
Gavi-supported vaccination programmes: an overview

- Pentavalent
- Hepatitis B
- Hib
- Yellow fever
- Measles 2nd dose
- Pneumococcal
- Meningitis A
- Rotavirus
- Measles rubella
- Japanese encephalitis
- Cholera
- HPV
- Ebola


Refers to the first Gavi-supported introduction of each vaccine.
## 2013 vaccines considered:

<table>
<thead>
<tr>
<th>Existing vaccines not supported by GAVI</th>
<th>‘Pipeline’ vaccines</th>
<th>Potential expansion of GAVI vaccine support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera</td>
<td>Malaria</td>
<td>DTP (booster)</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Dengue</td>
<td>Hepatitis B (birth dose)</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>Enterovirus 71</td>
<td>Measles (additional campaigns)</td>
</tr>
<tr>
<td>Influenza</td>
<td></td>
<td>Meningococcal (additional serotypes)</td>
</tr>
<tr>
<td>Mumps</td>
<td></td>
<td>Yellow Fever (additional campaigns)</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabies</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Budget 2015: Foreign aid to Africa cut by 70pc; contributions to Indonesia nearly halved

By political reporter Johanna Nicholson
Updated 26 May 2015, 5:26pm

Australia's foreign aid to Africa has been cut by 70 per cent and the contribution to Indonesia nearly halved, the latest budget has revealed.

Foreign aid contributions will be reduced by a further $3.7 billion over the next three years.
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W: www.mvec.vic.edu.au