Introduction and overview of the program; new vaccine pipeline and prioritization process

Monika Naus, MD, MHS, FRCPC, FACPM
BC Centre for Disease Control
December 7, 2011
The New Vaccine Pipeline and Priorization
Conflicts of interest: none to declare
### Vaccine-preventable diseases, Canada
Change in reported number of cases per year

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pre-vaccine</th>
<th>Now</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>9,000</td>
<td>1</td>
<td>-100</td>
</tr>
<tr>
<td>Polio</td>
<td>20,000</td>
<td>0</td>
<td>-100</td>
</tr>
<tr>
<td>Tetanus (deaths)</td>
<td>40-50</td>
<td>0</td>
<td>-100</td>
</tr>
<tr>
<td>Measles*</td>
<td>300,000</td>
<td>8</td>
<td>-99.99</td>
</tr>
<tr>
<td>Mumps*</td>
<td>52,000</td>
<td>32</td>
<td>-99.99</td>
</tr>
<tr>
<td>Rubella*</td>
<td>69,000</td>
<td>9</td>
<td>-99.99</td>
</tr>
<tr>
<td>CRS</td>
<td>2,000</td>
<td>1</td>
<td>-99.95</td>
</tr>
<tr>
<td>Invasive Hib</td>
<td>2,000</td>
<td>30</td>
<td>-98.5</td>
</tr>
<tr>
<td>Pertussis*</td>
<td>25,000</td>
<td>2,718</td>
<td>-89.13</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>477,050</strong></td>
<td><strong>6,271</strong></td>
<td><strong>-99.42%</strong></td>
</tr>
</tbody>
</table>

Based on maximum number cases reported in pre-vaccine era or estimates if not notifiable in past; * 2004 national data Notifiable Diseases On-Line
The Golden Years of New Vaccines: from cost saving to cost effective

- 1992: infant Haemophilus b
- 1992: hepatitis B grade school program (2001 infant)
- 1996: MR campaign + measles 2nd dose
- 1997: acellular pertussis (DPT-P/Hib)

National Immunization Strategy...$300M federal investment

- 2003:
  - meningococcal C conjugate
  - pneumococcal conjugate 7
- 2004: acellular pertussis for adolescents
- 2005: varicella

...$300M federal investment....

- 2008: HPV
Economic benefits of vaccines

- Cost saving: savings in direct medical costs for every $1 spent
  - MMR: $16.24
  - DPT: $6.21
  - Also cost saving: Polio, Hib, Hepatitis B, Varicella

- Cost effective:
  - PCV7: $116,000 per QALY
  - MenC: $39,000 per QALY
  - HPV age 11 female: $24,000 per QALY

Proportion of costs of vaccines for childhood and adolescent series girls, BC, 2009

$806/child for completion of series to adolescence, 2009 dollars

Source: BC Centre for Disease Control, 2008-9 fiscal year data
Price sensitivity of vaccine programs: PCV7 example

Price sensitivity of vaccine programs: Q-HPV example

Post 3 doses; GMT, t = 7 months

Age at Enrollment (Years)

MSD, Data on file.
# Vaccines for consideration (1)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>NACI recommendation</th>
<th>Likely target population for BC program</th>
<th>Estimated cost of program, per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoster (shingles)</td>
<td>Routine use for immuno-competent older adults</td>
<td>Adults starting at age 60 or 65</td>
<td>$2.4M for vaccine</td>
</tr>
<tr>
<td>Meningococcal quadrivalent conjugate vaccine</td>
<td>Children based on epidemiology in the province</td>
<td>Young children and/ or preadolescents/ adolescents</td>
<td>$2M for preadolescent program</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Routine use in infants</td>
<td>Infants under 8 months of age</td>
<td>$1.7M for vaccine</td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate vaccine</td>
<td>Child catch-up of healthy children up to 59 months old</td>
<td>Infant program is in place since June 2010; target population in BC would be children under 59 months</td>
<td>Est. $2.4M for vaccine alone assuming 30% uptake</td>
</tr>
<tr>
<td>Vaccine</td>
<td>NACI recommendation</td>
<td>Likely target population for BC program</td>
<td>Estimated cost of program, per year</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>----------------------------------------------------------</td>
<td>---------------------------------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>HPV</td>
<td>Pending with respect to male and older female vaccine</td>
<td>Boys in grade 6</td>
<td>$4.6M for vaccine</td>
</tr>
<tr>
<td>Varicella (chickenpox)</td>
<td>2nd dose for children under 12</td>
<td>2nd dose most cost effective at grade 6</td>
<td>$1.3M for vaccine</td>
</tr>
<tr>
<td>MMRV</td>
<td>May be used in place of separate injection MMR and varicella vaccines</td>
<td>For first dose at 12 months and/ or second dose if varicella 2nd dose is given at 18 months or school entry</td>
<td>Small additional cost or cost neutral</td>
</tr>
<tr>
<td>Influenza -adjuvanted and intranasal vaccines</td>
<td>Under development</td>
<td>Older adults for higher immunogenicity vaccines; high risk children for intranasal</td>
<td>Est. $&lt;1M</td>
</tr>
</tbody>
</table>
## Vaccines for consideration (3)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>NACI recommendation</th>
<th>Likely target population for BC program</th>
<th>Estimated cost of program, per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A vaccine</td>
<td>High risk strategy...no universal recommendation</td>
<td>Infants or children, perhaps targeted to First Nations on and off reserve, possibly limited to VIHA</td>
<td>$130K for infant/ K for vaccine</td>
</tr>
<tr>
<td>Tdap for adults</td>
<td>Adults once in lifetime; consideration of cocooning for parents/ care givers of newborns</td>
<td>Adults with focus on women of reproductive age and/ or postpartum; adults of any age in need of a Td booster</td>
<td>$1M if replace Td for adults with Tdap</td>
</tr>
</tbody>
</table>
## Vaccines with expected approval

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Likely target population for BC program</th>
<th>Estimated cost of program, per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningococcal B</td>
<td>Infants / young children</td>
<td>$2.5M for vaccine alone, based on group C vaccine pricing</td>
</tr>
<tr>
<td>Pneumococcal 13 valent conjugate for adult indications</td>
<td>Older adults</td>
<td>$1.5M for vaccine alone for single cohort of 65 year olds at 70% uptake</td>
</tr>
<tr>
<td>Influenza vaccines - enhanced immunogenicity</td>
<td>Older adults, some high risk</td>
<td>Est. $3M but not additive to those above listed for influenza as would replace those above</td>
</tr>
<tr>
<td>Heptavalent vaccine</td>
<td>Infants</td>
<td>$0.3M</td>
</tr>
</tbody>
</table>
## Analytic Framework Components

| Burden of Illness                          | • Disease (infectious agent, mode of transmission, etc.)  
|                                         | • Epidemiology in Canada, risk groups  
| Vaccine characteristics                   | • Efficacy, effectiveness (short and long term)  
|                                         | • Safety: short-term, long term  
| Immunization strategies                   | • Schedules  
|                                         | • Age group/ risk group  
|                                         | • Modes of delivery (physician, public health, school-based)  
| Cost effectiveness                        | • Vaccine related  
|                                         | • Disease related  
|                                         | • Perspective (health care system, societal, individual)  
| Acceptability and feasibility             | • Public  
|                                         | • Health care professionals  
|                                         | • Political  
| Ability to evaluate program               | • Vaccine effectiveness  
|                                         | • Adverse events  
|                                         | • Vaccine coverage  
|                                         | • Disease  
| Research questions                        | • Fundamental  
|                                         | • Intervention  
|                                         | • Program delivery  
| Other considerations                      | • Equity, ethics, legal, political  
| Overall recommendation                    | • Should the vaccine be publicly funded and if so, for whom?  

Ref: Erickson L, deWals P, Farand L. Vaccine 2005(23): 2468-74
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Varicella 2nd dose</th>
<th>Hepatitis A</th>
<th>PCV 13</th>
<th>Zoster</th>
<th>Rotavirus</th>
<th>Meningococcal equivalent</th>
<th>Meningococcal B</th>
<th>HPV for males</th>
<th>Tdap for contacts of newborns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burden of Illness</td>
<td>Low at this time, likely to increase in coming decades especially in adolescents</td>
<td>Low overall and declining periodic outbreaks especially in First Nations communities</td>
<td>3 to 9 cases per year in past 4 years of PCV13 type in children aged 2–4 years</td>
<td>Sufficient burden after age 60 to warrant consideration, incidence rises after age 50</td>
<td>High incidence but low severe outcomes</td>
<td>Low incidence of A, C, W 135 with occurrence at older ages</td>
<td>Sufficient in infants; severity warrants prevention</td>
<td>High for genital tract especially in MSM, mild cancer in males over 15 yo 1.5% per 100,000 in 2004</td>
<td>Significant at this time in BC</td>
</tr>
<tr>
<td>Vaccine Characteristics</td>
<td>High immunogenicity after 2nd dose, acceptable safety</td>
<td>High immunogenicity and protection expected based on experience with PCV7</td>
<td>Moderate efficacy, acceptable safety</td>
<td>Excellent efficacy, effectiveness, acceptable safety</td>
<td>Good immunogenicity and effectiveness, acceptable safety</td>
<td>Immunogenicity and safety comparable to other vaccines</td>
<td>Excellent efficacy, acceptable safety</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunization Strategies</td>
<td>Routine immunization at 1 of three doses</td>
<td>Infant or adolescent</td>
<td>Physician and PHN immunization of children 2 years to 59 months, 1 dose</td>
<td>Physician, public health and pharmacists immunizes</td>
<td>Physicians and public health</td>
<td>Adolescent (more sensible) or infant’s early childhood</td>
<td>Routine infant immunization</td>
<td>Adolescent prior to sexual debut as for girls, i.e., grade 6</td>
<td>Not at current burden of illness; estimated cost to prevent 1 infant hospitalization $50,000</td>
</tr>
<tr>
<td>Cost Effectiveness</td>
<td>Yes especially for K or grade school CEE per QALY gained $1,000K, $4,18K and $262K for 13 month, 4 years and grade 4, respectively.</td>
<td>Wide range in 1 studies in infants children from &lt;$200K to $1,000K per QALY, most favorable for infant and high incidence geographic areas.</td>
<td>Cost per QALY gained US $16.35 mos $25,051, 16-59 mos $73,044</td>
<td>Yes, $33,000 per QALY for 65 yo, less than $75,000 per QALY for 75+(Canadian)</td>
<td>Not at current pricing exceeds $100,000 QALY; CEA analysis by CEM and Nork is more favorable, as is CEA with societal perspective</td>
<td>Not at current pricing, incremental cost QALY for marginal endpoints 20% coverage $13.4M, if high coverage in girl, CEA for males not favorable except in MSM</td>
<td>UNOWN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acceptability</td>
<td>Yes, consider potential for use of MMRV if given at 18 mos or 4-4 years</td>
<td>Likely yes; issue of &quot;infrasaturation&quot; but curbs cure rate is supportive</td>
<td>Likely yes as prevents &quot;kennel meningitis&quot;; uptake may be below other vaccines not given until end of this age group</td>
<td>YES, for patients YES, for limited providers willing to handle feasible formulation</td>
<td>Likely yes because of disease severity</td>
<td>Requires additional injections in infancy which is not favorable for parents and providers</td>
<td>Likely yes but as in girls uptake may be lower in first few years of program</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feasibility</td>
<td>Yes</td>
<td>Yes, with considerations of schedule of injections especially for infants (6 mos or 12-15 months)</td>
<td>Yes, but uptake may be relatively low compared to routine infant schedule</td>
<td>Feasible strategy would require investment in cold chain infrastructure</td>
<td>YES, series completion will be higher with 2-dose series as cannot give more than 3 doses</td>
<td>YES in adolescence, no if booster doses required in adulthood for sustained protection</td>
<td>YES, with consideration of schedule of injections</td>
<td>YES routienly, as for girls consider 2-dose series. High risk strategy not feasible</td>
<td></td>
</tr>
<tr>
<td>Ability to Evaluate Program</td>
<td>Impact on burden with administrative databases</td>
<td>YES, reportable disease but often asymptomatic in infants and young children. Impact on disease burden may not be seen for some years</td>
<td>YES, reportable disease readily diagnosed with isolates from normally sterile site</td>
<td>Impact on burden with administrative databases, coverage by survey and per dose distributed</td>
<td>Not in current system; sentinel surveillance required</td>
<td>YES, reportable disease readily diagnosed with isolates from normally sterile site</td>
<td>YES, reportable disease readily diagnosed with isolates from normally sterile site</td>
<td>YES, as for girls, using specifically designed and funded study initiatives</td>
<td></td>
</tr>
<tr>
<td>Research Questions</td>
<td>Impact on varicella and changes incidence age</td>
<td>Whether targeted program will result in disease reduction overall</td>
<td>Whether vaccine prevalence will emerge over time</td>
<td>Duration of protection</td>
<td>Serotype specific, whether use in infants will shift burden to older ages</td>
<td>Duration of protection</td>
<td>Efficacy, effectiveness, safety in large scale use</td>
<td>Effectiveness, duration of protection, factors influencing uptake</td>
<td></td>
</tr>
</tbody>
</table>

Task group summary to CD Policy Committee May 17 2011
### Summary of recommended new vaccines for public funding in British Columbia

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>PCV 13 catch-up for 3-4 year olds</th>
<th>HPV catch-up for females 18-26 years old</th>
<th>Varicella 2nd dose</th>
<th>Hepatitis A for FN: routine infant, VIHA K entry, permissive for &lt;19</th>
<th>Zoster</th>
<th>Rotavirus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Burden of Illness</strong></td>
<td>3 to 9 cases per year in past 4 years of PCV13 types in children aged 2-4</td>
<td>Sufficient burden for cervical cancer and dysplastic lesions</td>
<td>Low at this time including outbreaks; likely to increase in coming decade especially in adolescents</td>
<td>Low overall and declining periodic outbreaks especially in First Nations communities</td>
<td>Sufficient burden after age 60 to warrant consideration; incidence rises after 50 yo</td>
<td>High incidence but low severe outcomes</td>
</tr>
<tr>
<td><strong>Vaccine Characteristics</strong></td>
<td>High immunogenicity and protection expected based on experience with PCV7</td>
<td>Excellent efficacy, high safety profile</td>
<td>High immunogenicity after 2nd dose, acceptable safety</td>
<td>Highly immunogenic and effective, high safety profile</td>
<td>Moderate efficacy; acceptable safety</td>
<td>Excellent efficacy, effectiveness; acceptable safety</td>
</tr>
<tr>
<td><strong>Immunization Strategies</strong></td>
<td>Physician and PHN immunization of children 2 years to 59 months, 1 dose</td>
<td>Adolescent and early adulthood prior to infection with oncogenic HPV strains</td>
<td>Routine immunization at 1 of three milestones: 18 month, K, grade 6</td>
<td>Infant or adolescent</td>
<td>Physician, public health and pharmacist immunizers</td>
<td>Physicians and public health</td>
</tr>
<tr>
<td><strong>Cost Effectiveness</strong></td>
<td>Cost per QALY gained US for 18-35 mos $25,052; 16-59 mos $73,564</td>
<td>Published literature suggests cost/QALY for age group including 26 up to $150K; BC analysis ICER for 18-26 is $60-70K/QALY; better if genital warts protection included</td>
<td>Yes especially for K or grade school; CER per QALY gained $106K, $41K and $28K for 12 month, 4-6 years and grade 4, respectively.</td>
<td>CEA results range from &lt;120K to &gt;$100K per QALY; likely cost effective in infants</td>
<td>Cost effectiveness lower in adolescence because of acquisition of hepatitis A</td>
<td>Yes, $33,000 per QALY for 65 yo; less than $75,000 per QALY for 75+ (Canadian)</td>
</tr>
<tr>
<td><strong>Acceptability</strong></td>
<td>Likely yes as prevents ‘bacterial meningitis’, uptake may be low as other vaccines not given until end of this age group</td>
<td>Likely higher than for school girl program but coverage rates may be low because of distributed delivery system</td>
<td>Yes; consider potential for use of MMRV for 2nd dose (18 months) 4-6 years</td>
<td>Likely yes; issue of ‘stigmatization’ but outbreak experience is supportive and less of an issue if not given in school</td>
<td>YES: for patients</td>
<td>YES: for limited providers willing to handle frozen formulation</td>
</tr>
<tr>
<td><strong>Feasibility</strong></td>
<td>Uptake may be relatively low compared to routine infant schedule Targeted reminder campaign such as personal mailing recommended for optimal uptake.</td>
<td>Yes but require multiple providers and settings including physicians, pharmacy, student health services; targeting those with lower probability of prior infection not feasible</td>
<td>Yes, see cell above</td>
<td>Yes, with consideration of schedule of infant injections especially for infants (6 mo-18 months) and catch-up on VIHA for K entry because of repeat outbreaks. Under 19 program will likely have low uptake</td>
<td>Freezer stable formulation would require investment in cold chain infrastructure, Pharmacare consideration but subject to ‘Fair Pharmacare i.e., means based co-funding</td>
<td>Yes, series completion will be higher with 2-dose series as cannot give after 8 mos; NGP billing code required</td>
</tr>
<tr>
<td><strong>Ability to Evaluate Program</strong></td>
<td>Yes, reportable disease readily diagnosed with isolates from normally stool site</td>
<td>Coverage assessment requires survey; effectiveness can be evaluated using specifically designed and funded study initiatives and linked data bases; capture of vaccination data into registry requires additional effort</td>
<td>Impact on burden with administrative data bases</td>
<td>Yes, reportable disease but often asymptomatic in infants and young children. Impact on disease burden may not be seen for some years.</td>
<td>Impact on burden with administrative data bases; coverage by survey and net doses distributed</td>
<td>Not in current system; sentinel surveillance required</td>
</tr>
<tr>
<td><strong>Research Questions</strong></td>
<td>Whether other non vaccine preventable serotypes will emerge over time</td>
<td>Effectiveness, duration of protection, factors influencing uptake</td>
<td>Impact on varicella and shingles incidence longer term, duration of protection</td>
<td>Whether targeted program will result in disease reduction overall</td>
<td>Duration of protection</td>
<td>Serotype specific incidence; whether use in infants will shift burden to older ages</td>
</tr>
</tbody>
</table>
Recommended for introduction as soon as possible: January 1, 2012

- Rotavirus
- Varicella 2nd dose
- Hepatitis A
Rotavirus

Most common cause of viral gastroenteritis with vomiting and diarrhea in children; most likely to result in dehydration and hospitalization

Global morbidity associated with fatalities, which are now rare in Canada

Easily spread in the home, daycare, and health care settings

Preventable by two orally administered vaccines

Child dehydrated due to rotavirus infection

Image courtesy of World Health Organization, photo credit Dr. D. Mahalanabis
Rotavirus vaccines

- Rotarix (GSK): human rotavirus, live, attenuated
  - 2 dose regimen
- RotaTeq (Merck): Pentavalent vaccine containing 5 human-bovine (WC3) reassortants
  - 3-dose regimen

Dosing: 2, 4 +/- 6 months

Complete series by 8 months

Efficacy trials done for approval
Effectiveness demonstrated in several countries
Evidence of protection through 3 rotavirus seasons (mainly winter/spring in Canada)
No reduction in efficacy by breastfeeding
Contraindications: anaphylaxis, intussusception/predisposition, immunocompromise including SCIDS
Impact of rotavirus vaccination on rotavirus laboratory identification in USA

Program start 2006. 2007-8 season: onset delayed by 15 wks, peak by 6 wks, duration 14 wks compared to 26; 67% decline in number, seen in all regions of USA

Tate JE, et al. Pediatrics 2009; 124(2)
Varicella vaccine: 2\textsuperscript{nd} dose

- 1\textsuperscript{st} and 2\textsuperscript{nd} vaccine failure contribute to ‘breakthrough’
  - 1\textsuperscript{st} failure shown by gpELISA and FAMA Ab
  - 2\textsuperscript{nd} failure shown by outbreak epidemiologic studies; increased risk with time since vaccination
  - Annual rates of disease, cases / 1,000 PY:
    - 1.6 cases within 1 year
    - 9 cases at 5 years
    - 58.2 cases at 9 years after vaccination
  - No effect of age at 1\textsuperscript{st} dose (12-14, 15-17, and 18-23 months of age)

Varicella 2\textsuperscript{nd} dose

Starting January 1, 2012 in BC:

- 2\textsuperscript{nd} dose at kindergarten entry; 1\textsuperscript{st} dose remains at 1\textsuperscript{st} birthday
- MMR 2\textsuperscript{nd} dose moving from 18 months to school entry: holiday for ~ 3 years
- MMRV will be introduced for 2\textsuperscript{nd} dose in ~ 2015

Child on 5\textsuperscript{th} day of illness with chickenpox
Hepatitis A trends in BC

- Declining rates of hepatitis A in past decade in BC
  - Vaccination of high risk individuals: IDU, MSM, hepatitis B/C/chronic liver disease, others

- BC outbreaks in last 15 years:
  - 1995-96: at least 35 cases among FN people in the Duncan area
  - 1999: 23 cases (incl. 18 FN) in Northern Interior Health Region
  - 2000: 19 cases, mostly FN children, in Quesnel
  - 2004: 8 cases secondary to 3 travel-related cases in a religious community in NHA
  - 2010-11: over 85 cases among FN people in Cowichan-VIHA

- Low uptake of vaccine
Hepatitis A vaccine for aboriginal children

- Routine infant vaccination starting January 1, 2012
  - 2 doses at 6 and 18 months
- Kindergarten catch-up program
- Opportunistic offering of hepatitis A vaccine to aboriginal individuals under 19 years old
- On and off reserve
- Self-identified ‘aboriginal’ ethnicity