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

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I HAVE immunity


Princess

The New Vaccine Pipeline and Priorization

Conflicts of interest:

none to declare

Vaccine-preventable diseases, Canada
Change in reported number of cases per year

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

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….

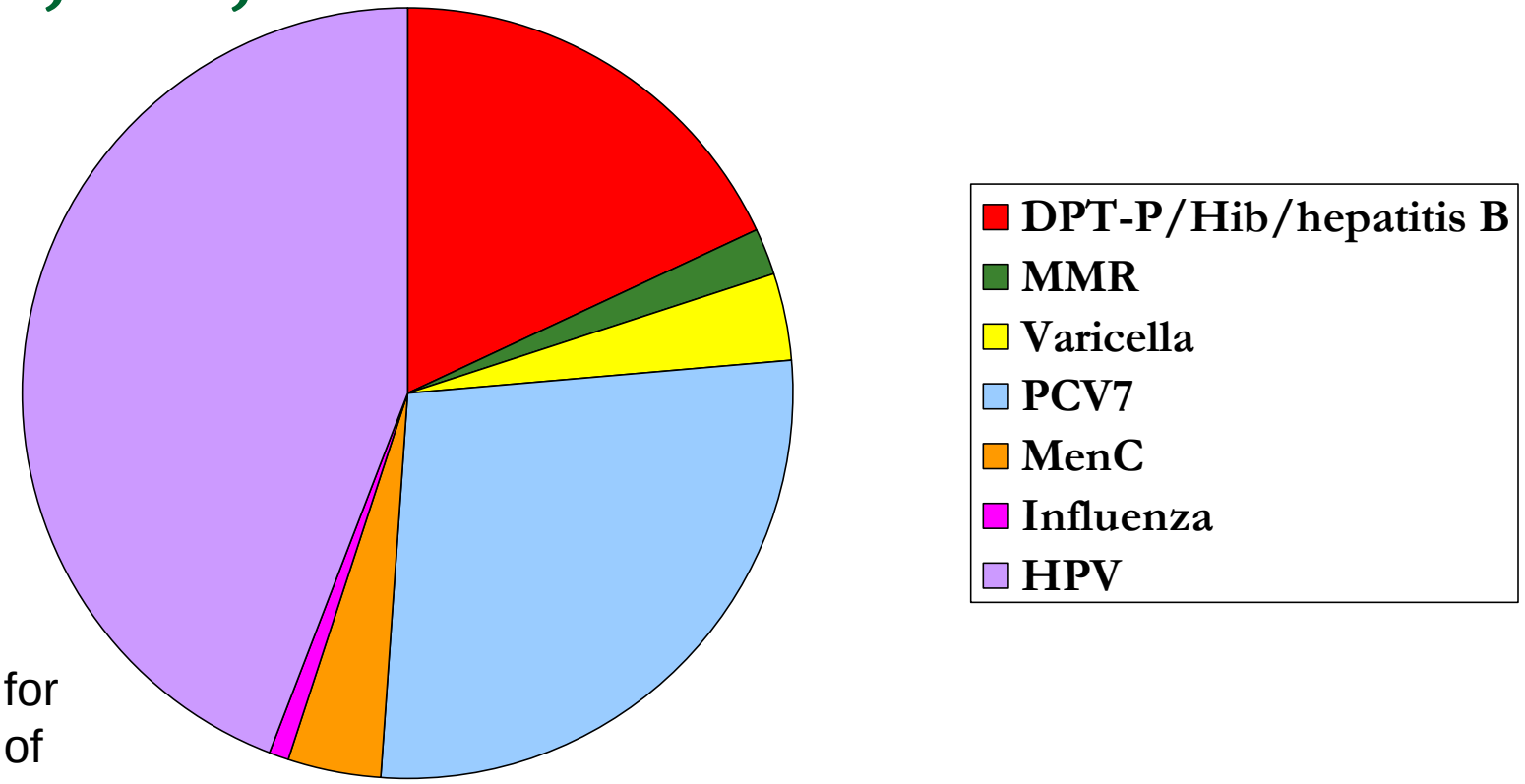
- **2008: HPV**

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

Zhou F, Arch Pediatr Adolesc Med. 2005; CDC, An Ounce of Prevention…What are the Returns? Ed. 2, rev. October 1999; IOM, Vaccines for the 21st Century. A tool for decision making. National Academy Press, 2000; PCV and MCV source: Dr. Philippe deWals; HPV: Pourbohloul B JID 2008; Marra F.

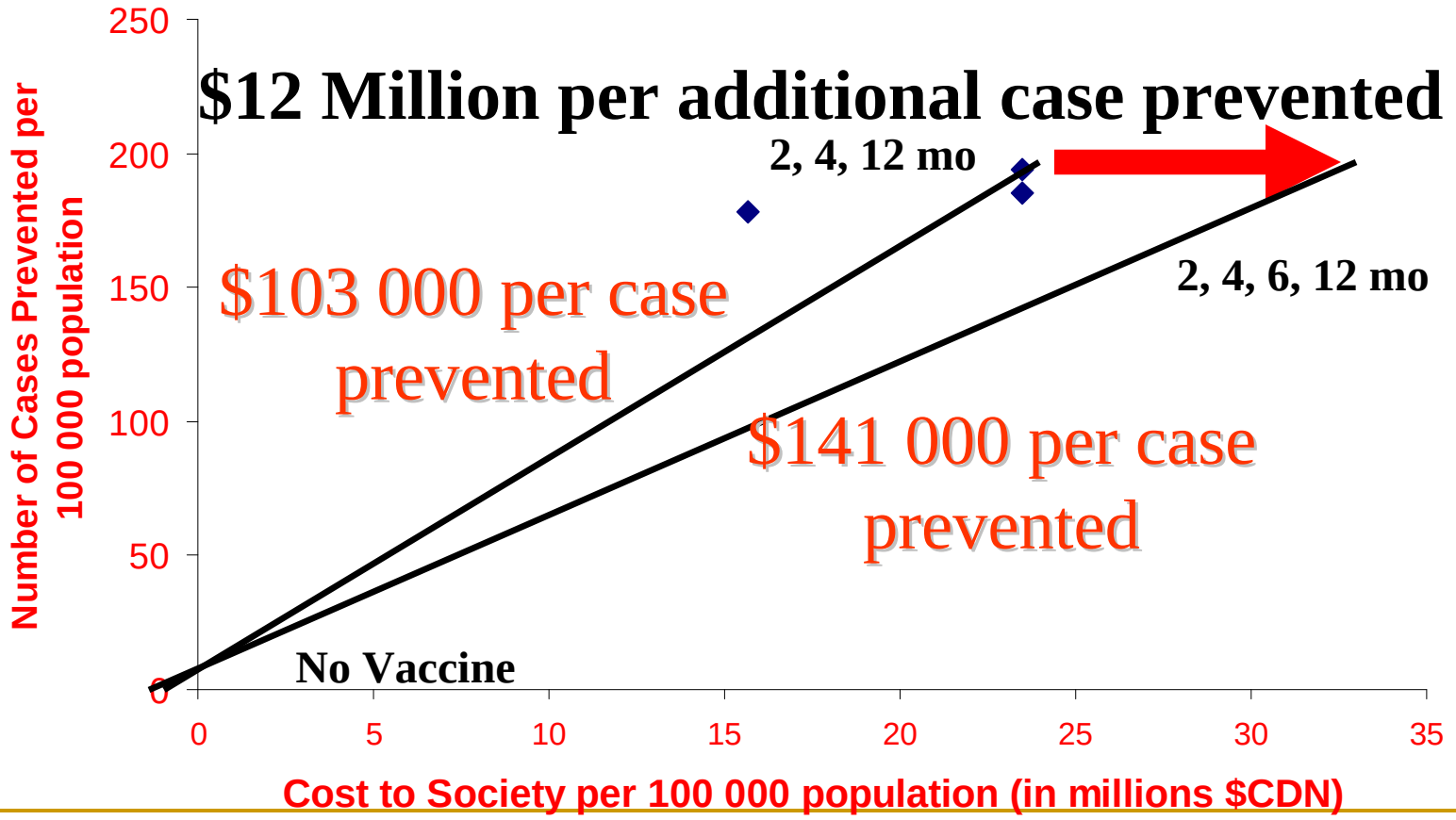
Proportion of costs of vaccines for childhood and adolescent series girls, BC, 2009



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

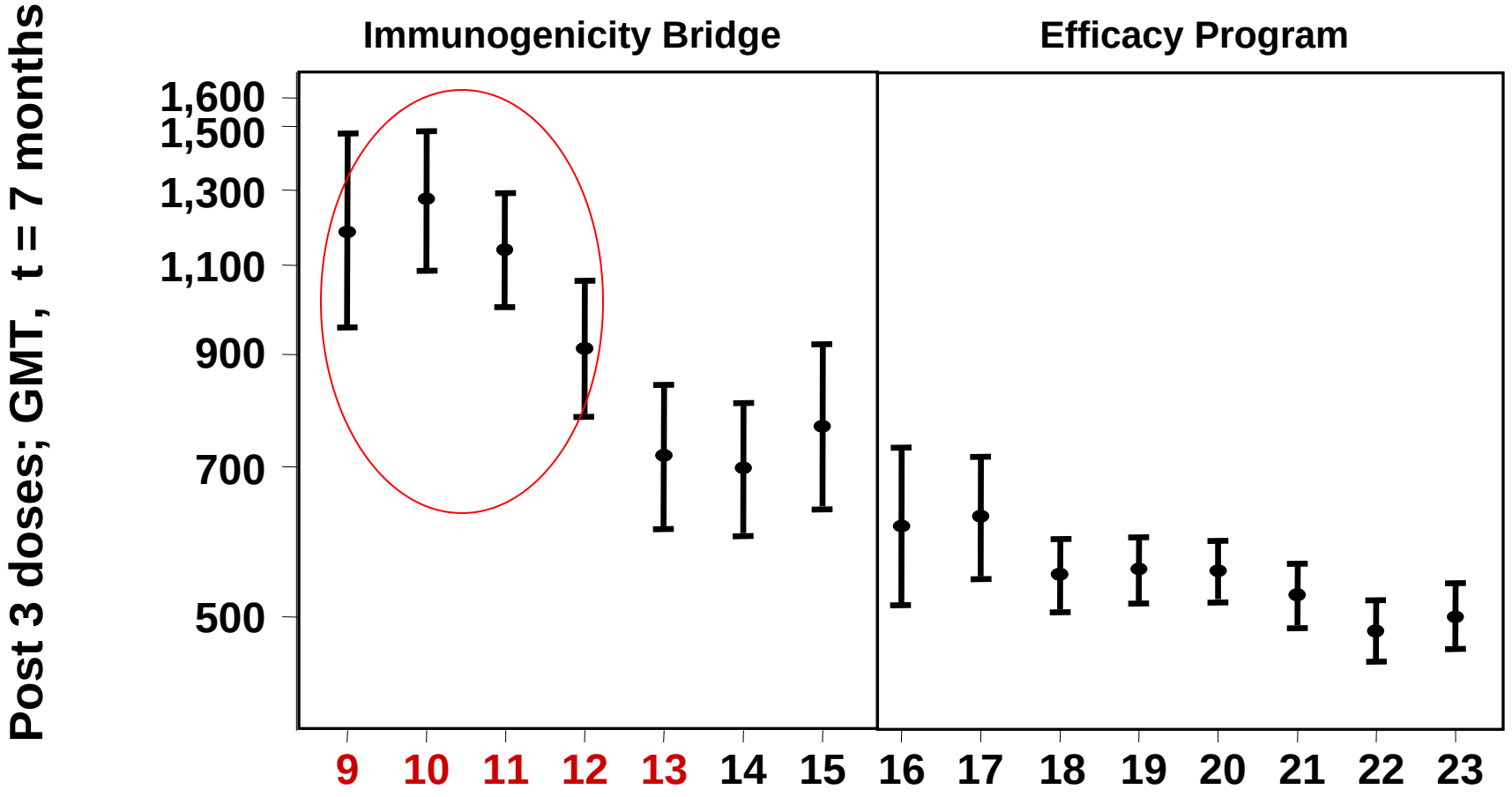
Source: BC Centre for Disease Control, 2008-9 fiscal year data

Price sensitivity of vaccine programs: PCV7 example



Source: De Wals P, Petit G, Morrow A, et al. Institut national de santé publique du Québec

Price sensitivity of vaccine programs: Q-HPV example



MSD, Data on file.

Vaccines for consideration (1)

Vaccine	NACI recommendation	Likely target population for BC program	Estimated cost of program, per year
Zoster (shingles)	Routine use for immuno-competent older adults	Adults starting at age 60 or 65	$2.4M for vaccine
Meningococcal quadrivalent conjugate vaccine	Children based on epidemiology in the province	Young children and/ or preadolescents/ adolescents	$2M for preadolescent program
Rotavirus	Routine use in infants	Infants under 8 months of age	$1.7M for vaccine
Pneumococcal 13-valent conjugate vaccine	Child catch-up of healthy children up to 59 months old	Infant program is in place since June 2010; target population in BC would be children under 59 months	Est. $2.4M for vaccine alone assuming 30% uptake

Vaccines for consideration (2)

Vaccine	NACI recommendation	Likely target population for BC program	Estimated cost of program, per year
HPV	Pending with respect to male and older female vaccine	Boys in grade 6	$4.6M for vaccine
Varicella (chickenpox)	2nd dose for children under 12	2nd dose most cost effective at grade 6	$1.3M for vaccine
MMRV	May be used in place of separate injection MMR and varicella vaccines	For first dose at 12 months and/ or second dose if varicella 2nd dose is given at 18 months or school entry	Small additional cost or cost neutral
Influenza –adjuvanted and intranasal vaccines	Under development	Older adults for higher immunogenicity vaccines; high risk children for intranasal	Est. $<1M

Vaccines for consideration (3)

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

Vaccines with expected approval

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

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

Summary of analysis of considerations for new vaccines for public funding in British Columbia

Vaccine	Varicella 2nd dose	Hepatitis A	PCV 13	Zoster	Rotavirus	Meningococcal quadrivalent	Meningococcal B	HPV for males	Tdap for contacts of newborns
Burden of Illness	Low at this time, likely to increase in coming decade especially in adolescents	Low overall and declining; periodic outbreaks especially in First Nations communities	3 to 9 cases per year in past 4 years of PCV13 types in children aged 2-4	Sufficient burden after age 60 to warrant consideration; incidence rises after 50 yo	High incidence but low severe outcomes	Low incidence of A,Y,W135 with occurrence at older ages	Sufficient in infants; severity warrants prevention	High for genital warts especially in MSM; anal cancer in males over 15 yo 1.5 per 100,000 in 2006	Insufficient at this time in BC
Vaccine Characteristics	High immunogenicity after 2nd dose; acceptable safety	Highly immunogenic and effective; acceptable safety	High immunogenicity and protection expected based on experience with PCV7	Moderate efficacy; acceptable safety	Excellent efficacy, effectiveness; acceptable safety	Good immunogenicity and effectiveness; acceptable safety	Immunogenic and safety comparable to other vaccines	Excellent efficacy; acceptable safety	
Immunization Strategies	Routine immunization at 1 of three milestones	Infant or adolescent	Physician and PHN immunization of children 2 years to 59 months, 1 dose	Physician, public health and pharmacist immunizers	Physicians and public health	Adolescent (more sensible) or infant/ early childhood	Routine infant immunization	Adolescent prior to sexual debut as for girls, i.e., grade 6	
Cost Effectiveness	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.	Wide range in 17 studies in infants/ children from <$20K to >$100K per QALY; most favourable for infant and high incidence geographic areas	Cost per QALY gained US for 16-35 mos $25,052; 16-59 mos $73,564	Yes; $33,000 per QALY for 65 yo; less than $75,000 per QALY for 75+ (Canadian)	Not at current pricing; exceeds $100,000/QALY; CEA analysis by GSK and Merck is more favourable, as is CEA with societal perspective	Not at current pricing; $113,000/QALY incremental over meningoC in adolescents	UNKNOWN	Not at current pricing; incremental cost/QALY for anogenital endpoints 80% coverage $1M. If high coverage in girls, CEA for males not favourable except in MSM.	Not at current burden of illness; estimated cost to prevent 1 infant hospitalization $500k
Acceptability	Yes; consider potential for use of MMRV if given at 18 mos or 4-6 years	Likely yes; issue of 'stigmatization' but outbreak experience is supportive	Likely yes as prevents 'bacterial meningitis'; uptake may be low as other vaccines not given until end of this age group	YES: for patients YES: for limited providers willing to handle frozen formulation	Yes, for both parents, infants and providers; orally administered	Likely yes because of disease severity	Requires additional injections in infancy which is not favourable for parents and providers	Likely yes but as in girls uptake may be lower in first few years of program	
Feasibility	Yes	Yes, with consideration of schedule of injections especially for infants (6 mo+12 or 18 months)	Yes, but uptake may be relatively low compared to routine infant schedule	Freezer stable formulation would require investment in cold chain infrastructure	Yes; series completion will be higher with 2-dose series as cannot give after 8 mos; MSP billing code required	Yes in adolescence; no if booster doses required in adulthood for sustained protection	Yes, with consideration of schedule of injections	Yes routinely, as for girls; consider 2 dose series. High risk strategy not feasible.	
Ability to Evaluate Program	Impact on burden with administrative data bases	Yes; reportable disease but often asymptomatic in infants and young children. Impact on disease burden may not be seen for some years.	Yes, reportable disease readily diagnosed with isolates from normally sterile site	Impact on burden with administrative data bases; coverage by survey and net doses distributed	Not in current system; sentinel surveillance required	Yes; reportable disease readily diagnosed with isolates from normally sterile site	Yes; reportable disease readily diagnosed with isolates from normally sterile site	Yes, as for girls, using specifically designed and funded study initiatives	
Research Questions	Impact on varicella and shingles incidence longer term; duration of protection	Whether targeted program will result in disease reduction overall	Whether other non vaccine preventable serotypes will emerge over time	Duration of protection	Serotype specific incidence; whether use in infants will shift burden to older ages	Duration of protection	Efficacy, effectiveness, safety in large scale use	Effectiveness, duration of protection, factors influencing uptake	

Task group summary to CD Policy Committee May 17 2011

Summary of recommended new vaccines for public funding in British Columbia

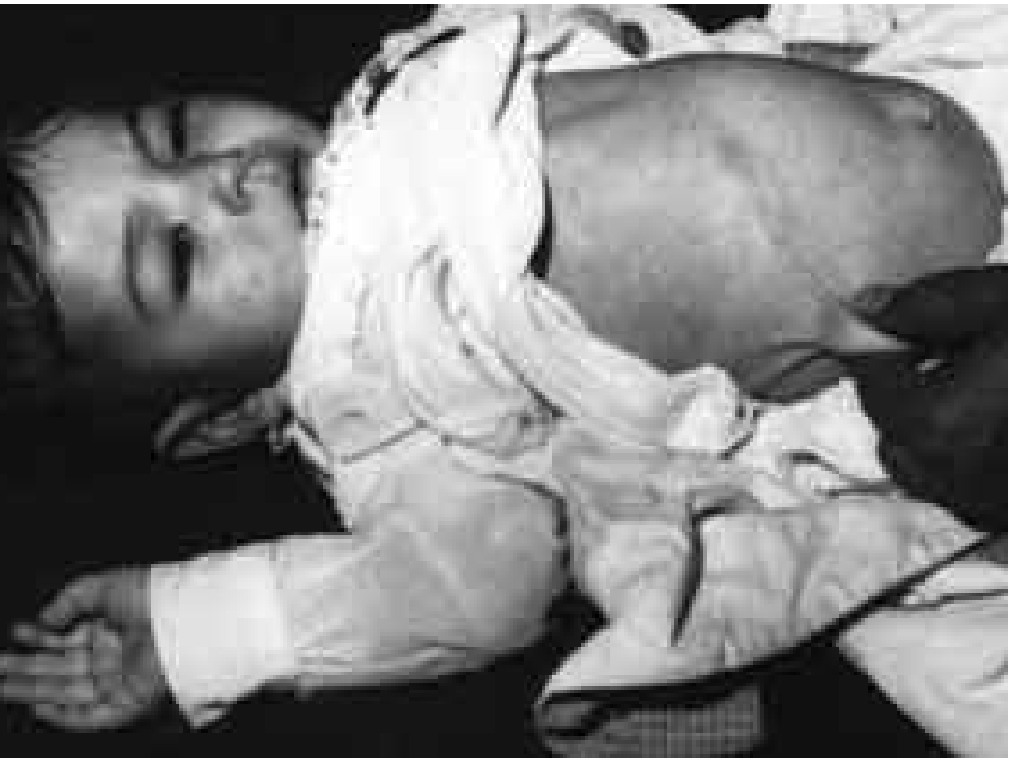
Vaccine	PCV 13 catch-up for 3+4 year olds	HPV catch-up for females 18-26 years old	Varicella 2nd dose ★	Hepatitis A for FN: routine infant, VIHA K entry permissive for <19 ★	Zoster	Rotavirus ★
Burden of Illness	3 to 9 cases per year in past 4 years of PCV13 types in children aged 2-4	Sufficient burden for cervical cancer and dysplastic lesions	Low at this time including outbreaks; likely to increase in coming decade especially in adolescents	Low overall and declining, periodic outbreaks especially in First Nations communities	Sufficient burden after age 60 to warrant consideration; incidence rises after 50 yo	High incidence but low severe outcomes
Vaccine Characteristics	High immunogenicity and protection expected based on experience with PCV7	Excellent efficacy; high safety profile	High immunogenicity after 2nd dose; acceptable safety	Highly immunogenic and effective; high safety profile	Moderate efficacy; acceptable safety	Excellent efficacy, effectiveness; acceptable safety
Immunization Strategies	Physician and PHN immunization of children 2 years to 59 months, 1 dose	Adolescent and early adulthood prior to infection with oncogenic HPV strains	Routine immunization at 1 of three milestones: 18 month, K, grade 6	Infant or adolescent	Physician, public health and pharmacist immunizers	Physicians and public health
Cost Effectiveness	Cost per QALY gained US for 16-35 mos $25,052; 16-59 mos $73,564	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.	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.	CEA results range from <$20K to >$100K per QALY; likely cost effective in infants Cost effectiveness lower in adolescence because of acquisition of hepatitis A	Yes; $33,000 per QALY for 65 yo; less than $75,000 per QALY for 75+ (Canadian)	At current pricing of Rotarix this program is now cost effective in at least two Canadian CEAs with health care system perspective only i.e., not societal
Acceptability	Likely yes as prevents 'bacterial meningitis'; uptake may be low as other vaccines not given until end of this age group	Likely higher than for school girl program but coverage rates may be low because of distributed delivery system	Yes; consider potential for use of MMRV for 2nd dose (18 mos or 4-6 years)	Likely yes; issue of 'stigmatization' but outbreak experience is supportive and less of an issue if not given in school	YES: for patients YES: for limited providers willing to handle frozen formulation	Yes, for both parents, infants and providers; orally administered
Feasibility	Uptake may be relatively low compared to routine infant schedule. Targeted reminder campaign such as personal mailing recommended for optimal uptake.	Yes but require multiple providers and settings including physicians, pharmacy, student health services; targeting those with lower probability of prior infection not feasible	Yes; see cell above	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.	Freezer stable formulation would require investment in cold chain infrastructure; Pharmacare consideration but subject to 'Fair' Pharmacare i.e., means based co-funding	Yes; series completion will be higher with 2-dose series as cannot give after 8 mos; MSP billing code required
Ability to Evaluate Program	Yes, reportable disease readily diagnosed with isolates from normally sterile site	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	Impact on burden with administrative data bases	Yes; reportable disease but often asymptomatic in infants and young children. Impact on disease burden may not be seen for some years.	Impact on burden with administrative data bases; coverage by survey and net doses distributed	Not in current system; sentinel surveillance required
Research Questions	Whether other non vaccine preventable serotypes will emerge over time	Effectiveness, duration of protection, factors influencing uptake	Impact on varicella and shingles incidence longer term; duration of protection	Whether targeted program will result in disease reduction overall	Duration of protection	Serotype specific incidence; whether use in infants will shift burden to older ages

Task group summary to CD Policy Committee July 12 2011

Recommended for introduction as soon as possible: January 1, 2012

- Rotavirus
- Varicella 2nd dose
- Hepatitis A

Rotavirus



Child dehydrated due to rotavirus infection

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

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

Rotarix in 'oral' syringe
DO NOT INJECT

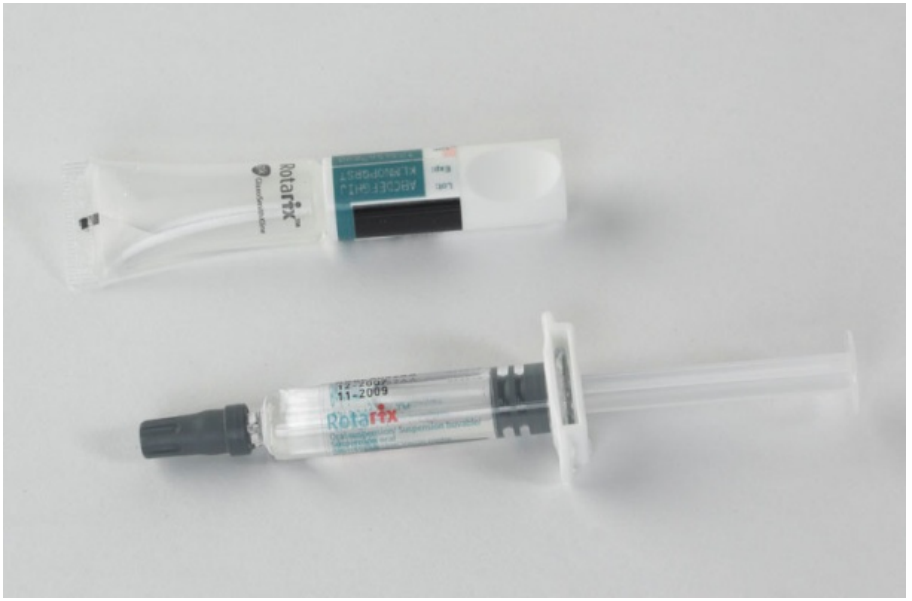
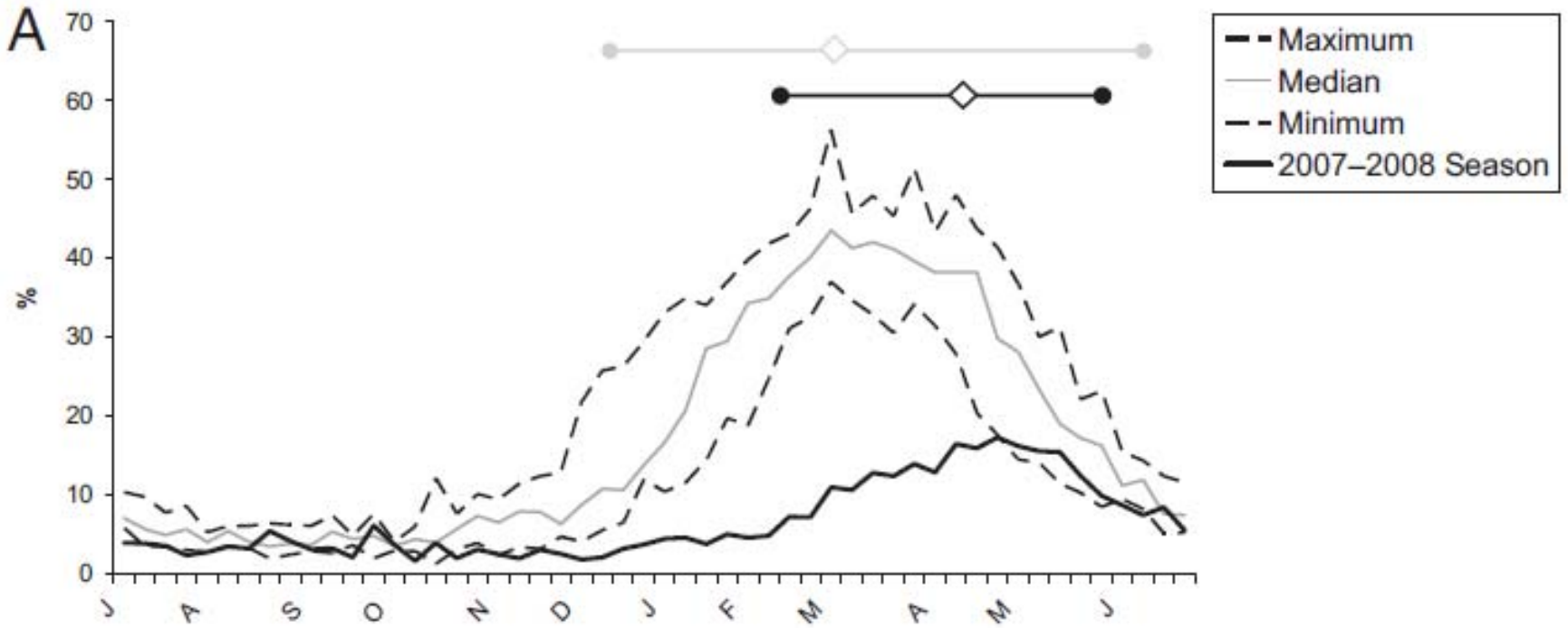


Image courtesy of GSK

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: 2nd dose

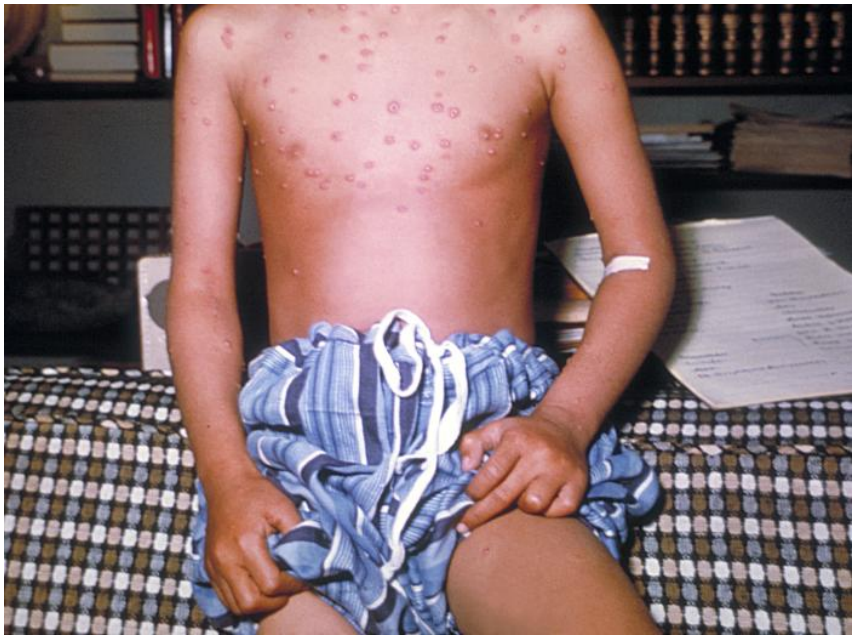
- 1° and 2° vaccine failure contribute to 'breakthrough'
  - 1° failure shown by gpELISA and FAMA Ab
  - 2° failure shown by outbreak epidemiologic studies; increased risk with time since vaccination annual rates of disease, cases / 1,000 PY:
    - 1.6 cases within 1 year
    - 9 cases at 5 years
  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

Chaves S, NEJM 2007; NACI statement http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-8/index-eng.php

Varicella 2nd dose

Starting January 1, 2012 in BC:

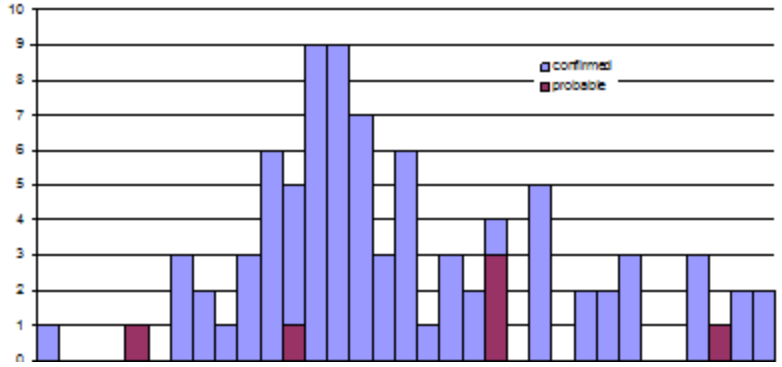
- 2nd dose at kindergarten entry; 1st dose remains at 1st birthday
- MMR 2nd dose moving from 18 months to school entry: holiday for ~ 3 years
- MMRV will be introduced for 2nd dose in ~ 2015



Child on 5th 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