A B S T R A C T

Background: This paper uses a straightforward method of quantifying the benefits and risks of immunization, illustrated by universal immunization programs in British Columbia against invasive *Haemophilus influenzae* type b disease (Hib), measles, rubella, and paralytic poliomyelitis.

Methods: Data were extracted from provincial communicable disease and vaccine adverse event surveillance systems. Average disease incidence was compared before and after implementing universal immunization programs. Estimates of prevented deaths and serious disease complications were calculated and compared with expected numbers of serious vaccine-associated adverse events (VAAEs).

Results: Average incidence of reported cases decreased 90 to 100% over a 5-year period after implementing universal programs. These benefits were sustained or strengthened over time. Rates of reported serious VAAEs were low.

Discussion: The remarkable success of immunization has created a paradox. Despite a low absolute risk of serious VAAEs, the relative risk of some VAAEs can exceed risk of disease in the province.

A B R É G É

Contexte : L'étude emploie une méthode simple pour quantifier les avantages et les risques de l'immunisation, tels qu'illustrés par les programmes de vaccination systématiques de la Colombie-Britannique contre l'infection invasive à Hib (hémophilus influenzae B), la rougeole, la rubéole et la poliomyélite paralytique.

Méthode : Nous avons extrait des données des systèmes provinciaux de surveillance des maladies transmissibles et des réactions adverses aux vaccins, puis comparé l'incidence moyenne des maladies avant et après la mise en œuvre de programmes de vaccination systématiques. Nous avons ensuite estimé les décès et les complications graves évités, que nous avons comparés avec le nombre attendu de réactions adverses vaccinales (RAV) graves.

Résultats : L'incidence moyenne de cas déclarés a diminué dans une proportion de 90 à 100 % sur cinq ans après la mise en œuvre des programmes systématiques. Ces avantages se sont maintenus ou renforcés avec le temps. Les taux déclarés de RAV graves étaient faibles.

Question à débattre : Le succès remarquable de la vaccination entraîne un paradoxe : bien que le risque absolu de RAV grave soit faible, le risque relatif de certaines RAV peut dépasser le risque de la maladie dans la province.

Comparing Benefits and Risks of Immunization

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Success of immunization programs depends on sustained public acceptance that individual and collective benefits of immunization outweigh the risks. The benefits and safety of immunization are questioned by some persons or groups who are generally opposed to immunization.¹⁻⁵ Parents must evaluate conflicting claims and counter-claims about immunization.⁶ Health professionals' role in informing parents about the benefits and risks of immunization is increasingly challenging.^{6,7}

Misunderstanding of the benefits and safety of immunization is fueled by two converging trends, leading some parents to believe that the risk of immunization exceeds the risk of disease. First, the incidence in Canada of many vaccine-preventable diseases has decreased to such low levels that some parents question the need to immunize their children.^{2,8,9} This attitude may be reinforced by a minority of parents whose children have not been immunized, yet who have indirectly benefited from disease protection afforded by high levels of vaccination-derived population immunity^{10,11} – a phenomenon known as “herd immunity”.¹² Some persons also believe that the decline in vaccine-preventable diseases is more related to other factors, such as improved public sanitation, better nutrition or accessible, high-quality health care.^{5,13}

Second, there is increased awareness of vaccine-associated adverse events (VAAEs)

or instances when immunization has failed to prevent disease.¹⁴ Since vaccines are neither 100% effective, nor 100% safe,^{5,9,15} incidents of break-through disease in immunized persons and reports of VAAEs are expected and reasons for continued disease surveillance and monitoring of VAAEs.⁹ At the same time, public awareness of VAAEs has been heightened by improved post-market monitoring and reporting of VAAEs,^{16,17} and media accounts¹⁸ or publications^{19,20} of perceived vaccine risks. Since illness in children is often first recognized or diagnosed at an age when immunizations are also routinely administered, a temporal association of immunization to initial recognition of childhood disease is inevitable.²¹

To further evaluate these trends, this study outlines a straightforward method of quantitatively comparing the benefits and risks of immunization. A population-based analysis was undertaken, using communicable disease and VAAE surveillance data that are routinely collected in British Columbia and other Canadian provinces and territories. Four universal childhood immunization programs in British Columbia were considered: measles, rubella, paralytic poliomyelitis and invasive *Haemophilus influenzae* type b (Hib).

METHODS

All four diseases were reportable under the provincial Health Act. Public health units report cases to the British Columbia Centre for Disease Control (BCCDC), which maintains a provincial registry of reportable communicable disease.

Average incidence rates for a 5-year period immediately before and after introduction of measles, rubella, and Hib immunization programs were calculated. A 5-year period was utilized to minimize bias

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of year-to-year variability in disease incidence. For poliomyelitis, a 10-year pre-immunization average rate was utilized to conservatively adjust for outbreaks that occurred in British Columbia in the five years prior to introduction of a poliomyelitis immunization program. Estimates of the number of cases prevented in 1999 were derived from the difference between actual number of reported cases and the expected number of cases, calculated from pre-immunization program rates and using the 1999 provincial population.²² Estimates of prevented disease-specific morbidity and mortality were calculated using published rates of disease-associated complications.⁸

Average incidence rates for four VAAEs (anaphylaxis, seizure, encephalitis/meningitis and encephalopathy) were calculated, using VAAE data submitted from British Columbia to the Canadian Vaccine-Associated Adverse Events Surveillance System (CVAAESS) and birth cohort data from British Columbia Vital Statistics between 1990-1997.^{22,23} We chose to examine these four VAAEs because their clinical severity is of greatest concern and they are more likely to be reported.²⁴

Since most vaccines given to children are manufactured as combination vaccines, we used the most conservative method to estimate the number of VAAEs attributable to each individual vaccine component: a reported VAAE was counted as an adverse event for each individual vaccine component included in a combined vaccine. For example, a VAAE reported following administration of measles-rubella combined vaccine would be counted as a VAAE for each of measles and rubella vaccine components.

We also made a conservative assumption that all of these vaccines were administered to children (i.e., no adults) and that vaccines were administered in accordance with the recommended BC Ministry of Health childhood immunization schedule between 1990-1997.²⁵ Adjustment was made to reflect different recommended schedules for oral polio vaccine (used in British Columbia until 1996) and inactivated polio vaccine, as well as implementation of a second routine dose and childhood catch-up of measles and rubella-containing

TABLE I
Change in Incidence of Reported Disease Following Implementation of Immunization Program in British Columbia

Vaccine-Preventable Disease	Average Pre-immunization Incidence Rate per 100,000	Average Post-immunization Incidence Rate per 100,000	% Reduction in Incidence
Invasive Hib	3.0 (1987-1991)*	0.3 (1992-1996)	90%
Measles	70.0 (1976-1980)	5.0 (1981-1985)	93%
Rubella	50.0 (1965-1969)	0.5 (1970-1974)	99%
Paralytic poliomyelitis	7.0 (1947-1956)	0.0 (1957-1961)	100%

* (1987-1991) – indicates range of years included in analysis

TABLE II
Reported Disease Prevented by Immunization in British Columbia in 1999

Vaccine-Preventable Disease	Expected Number (Rate per 100,000) of Reported Cases based on Pre-vaccine Era Rate	Actual Number (Rate per 100,000) of Reported Cases in 1999	% Reduction of Reported Disease
Invasive Hib	120 (3)	4 (0.1)	96.7%
Measles	2800 (70)	11 (0.3)	99.3%
Rubella	2000 (50)	3 (0.1)	99.9%
Paralytic poliomyelitis	280 (7)	0 (0)	100%

TABLE III
Disease Complications Prevented by Immunization in British Columbia in 1999

Vaccine-Preventable Disease	Reported Cases Prevented	Disease Complication (risk if infected)*	Disease Complications Prevented
Invasive Hib	116	<ul style="list-style-type: none"> death (5%) meningitis (55-65%) deafness (15-20%) other serious neurologic effects (10-15%) 	<ul style="list-style-type: none"> 6 64-75 17-23 12-17
Measles	2,789	<ul style="list-style-type: none"> death (0.03%) encephalitis (0.1%) pneumonia/otitis media (10%) congenital rubella (0.05% births)† 	<ul style="list-style-type: none"> 1 3 279 21 280
Rubella	1,997		
Paralytic Poliomyelitis	280		

* Health Canada. *Canadian Immunization Guide*, 5th Edition. Ottawa: Canadian Medical Association, 1998.

† Based on estimated CRS rate of 4.6 per 10,000 births in pre-rubella vaccine era (see text)

TABLE IV
Expected Number and Rate of Serious VAAEs in British Columbia in 1999

Vaccine	Expected Number of Serious VAAEs (Rate per 100,000 Immunizations Administered)			
	Anaphylaxis	Seizure	Meningitis/Encephalitis	Encephalopathy
Hib	<1 (0.2)	34 (20)	<1 (0.1)	<1 (0.4)
Measles	<1 (0.5)	22 (27)	0 (0)	0 (0)
Rubella	<1 (0.5)	22 (27)	0 (0)	0 (0)
OPV/IPV*	<1 (4.3)	35 (17)	<1 (<0.1)	<1 (0.4)

* For simplicity, rate calculated without distinguishing between Inactivated Polio Virus (IPV) vaccine or live, attenuated Oral Polio Virus (OPV) vaccine. IPV used in British Columbia 1957-1962 and 1996 to present; while OPV used from 1961-96

vaccine in 1996. We assumed 90% uptake among eligible children, based on published periodic surveys of vaccine uptake in British Columbia at 2 years of age.²⁶

The preceding assumptions were necessary because there was no central, electronic immunization registry in British Columbia to collect immunization utilization data during the study period.

RESULTS

Significant reductions in disease incidence were consistently observed when average incidence of reported disease before and after implementing each of these universal childhood immunization programs was compared (Table I and Figure 1). The average rate of reported Hib disease plummeted by 90% in the 5-year period following implementation of universal infant Hib immunization, with even more impressive reductions noted for measles (93%) and rubella (99%). Not a single case of paralytic poliomyelitis caused by wild virus infection was reported in the 5-year period following that program's implementation.

Table II depicts the estimated percent reduction of reported cases for 1999 by comparing actual numbers of reported dis-

ease in 1999 with expected numbers, based on pre-vaccine era rates of reported disease. The polio immunization program has sustained elimination of paralytic poliomyelitis from British Columbia, and by 1999, the disease prevention impact for the other three diseases had surpassed levels observed in the period immediately following program implementation. For 1999, there were over 99% fewer reported cases of measles and rubella and almost 97% fewer reports of invasive Hib disease than expected had respective immunization programs not been deployed.

Reduced reported disease attributable to immunization in 1999 was translated into estimates of reduced disease-associated morbidity and death (Table III). In 1999 alone, immunization prevented an estimated 6 deaths and 64 to 75 cases of meningitis from invasive Hib; 1 death and 3 cases of encephalitis from measles; 21 cases of congenital rubella; and 280 cases of paralytic poliomyelitis.

The burden of vaccine-prevented disease for 1999 is in marked contrast to the comparatively lower risk of serious VAAEs, summarized in Table IV. Less than one reported case of anaphylaxis, encephalitis/meningitis, or encephalopathy would be expected in association with province-wide

immunization programs against any of the four diseases studied, over an entire year. However, 22 seizures would be expected to be temporally associated with the administration of about 83,000 doses of measles and rubella-containing vaccine in 1999. Administration of approximately 166,000 doses of Hib and 212,000 doses of polio vaccination in 1999 would be expected to be temporally associated with 34 and 35 reports of seizures respectively.

It is noteworthy that incidence rates for these four diseases in 1999 in British Columbia are of the same order of magnitude or less (range: 0-0.3 per 100,000, from Table II) than rates of reported serious VAAEs examined in this study (range: 0-27 per 100,000, from Table IV).

DISCUSSION

This study provides impressive evidence of the disease prevention impact of these four universal childhood immunization programs. Invasive Hib disease in children has been virtually eliminated in British Columbia within 7 years of introducing a universal immunization program with conjugate Hib vaccine in 1992. Similarly, since implementing universal measles, mumps and rubella (MMR) immunization in 1981, and adding a second MMR to the routine childhood immunization schedule in 1996 (supplemented by a measles-rubella catch-up of school-aged children), indigenous measles transmission in the province hovers near elimination.²⁶ A mere 2 cases of measles in 1998 and 11 cases in 1999 were reported in British Columbia.^{27,28} Recent measles cases, including an outbreak in 2000 in a north-east British Columbia community that had a low acceptance rate of immunization, have occurred almost exclusively in under-immunized or unimmunized persons. (personal communication: D. MacDonald, 2000)

Co-incident with plummeting rubella incidence, congenital rubella syndrome (CRS) has been virtually eliminated from British Columbia; no CRS was reported in BC in 1999. (personal communication: D. Scheifele, 2000) Although CRS has only been under formal surveillance in Canada since 1996,²⁹ an estimated 21 cases of CRS

would have been expected in British Columbia in 1999, based on an estimated rate of CRS of 4.6 per 10,000 births in the pre-rubella vaccine era.³⁰ Poliomyelitis is an even more dramatic success story, with this disease at the brink of global eradication in 2000.³¹

Such dramatic reductions in disease incidence rates that have been consistently observed within such short periods after implementing universal childhood immunization programs for these four diseases, can only be attributable to immunization. Over these short time periods, there was no significant change in public sanitation, nutrition, health care or other socioeconomic factor in British Columbia. Coherent with this conclusion is the continued high incidence of chicken pox, for which there was no universal childhood immunization program.³²

The overwhelming success of immunization in disease prevention has created a paradox.^{10,33} Although the risk of a serious VAAE is very low, the relative risk of any of these four diseases in British Columbia in 1999 may be even lower. However, the clinical significance of higher relative risk for a serious VAAE is arguably marginal, when the absolute risk of serious VAAEs is as low as this analysis indicates. Moreover, the most common serious VAAE examined in this study was seizures. Most seizures associated with immunization occur in conjunction with fever and do not cause or aggravate any permanent neurologic disorder.³⁴ In fact, this analysis affirms the high degree of safety of these vaccines.

The apparent paradox should also be interpreted in context with other factors. The potential re-emergence of disease warrants continued attention to maintaining high immunization acceptance, illustrated by dramatic resurgences of pertussis in Japan, Sweden and the United Kingdom in the 1970s, after disruptions to pertussis immunization programs in those countries.³⁵ Low risk for these diseases in British Columbia does not reflect the risk elsewhere, to which an individual may travel or from which a person may visit. In addition, persons with medical contraindications to immunization are highly dependent on herd immunity for personal protection.

Several biases affect this study, although many are conservatively oriented and tend to minimize immunization benefits while maximizing associated risk. For example, cases of disease in the post-vaccination era are more likely to be diagnosed and reported than during the pre-vaccination period, due to improved laboratory diagnostic testing,³⁶ increasing use of standardized disease case definitions, and systematic electronic case reporting to public health authorities.³⁷ Similarly, VAAEs are much more likely to have been reported since 1987, when a national VAAE surveillance system was implemented in Canada.²³

Reported VAAEs were over-counted as a result of attributing a VAAE to each vaccine component contained in combined vaccine products. This likely helped counterbalance the under-reporting associated with passive VAAE monitoring systems, although underreporting may have been minimized by our focus on serious VAAEs.^{9,24,38} To enhance the sensitivity of VAAE reporting, the only criterion for reporting an adverse health event as a VAAE is that it occur within a specified time following immunization. Causality based on temporal association alone cannot be inferred.^{14,21,39,40} For example, the rate of encephalitis or encephalopathy occurring within 30 days of measles immunization was found to be lower than that noted for severe neurological disorders of unknown etiology in unimmunized children of the same age group, suggesting that chance temporal association rather than cause and effect, accounted for some if not most of these events.⁴¹

Overall, this study affirms the remarkable effectiveness of four universal childhood immunization programs and a high degree of safety associated with immunization. This population-based analysis is easily adaptable to other jurisdictions, using routinely collected data from provincial/territorial communicable disease and VAAE surveillance systems. It can provide meaningful, practical information for health professionals and parents.

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