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VACCINE RESOURCE LINE

A QUARTERLY SUMMARY OF PEER-REVIEWED PUBLISHED LITERATURE

Vaccination services for adolescents, adults vary considerably

Huot et al. Adult immunization services: Steps have to be done. Vaccine *2010;28(5):1177-80.*

Current and future vaccination services for adolescents and adults vary considerably depending on the vaccine and the medical clinic involved, according to a survey of medical clinics around the Quebec City region.

Dr. Caroline Huot, Université Laval, Quebec City, and multicentre colleagues carried out a descriptive, cross-sectional study in the spring and summer of 2007 in which they studied adult immunization services provided by 81 medical clinics in the Quebec City region. Approximately 80% of "high" vaccinators (at least 100 doses of a vaccine delivered between June 2006 and May 2007) responded to the questionnaire as did 66% of "low" vaccinators (less than 100 doses during the same interval) for an overall response rate of 70%. "The majority of respondents were doctors [89%]," investigators noted, "and more than half of the clinics [56%] had five doctors or more and one-third [33%] had between two and four doctors."

Results revealed that the majority of medical clinics offered vaccines for influenza, pneumococcus and hepatitis A and B, but that vaccines for diphtheria-tetanus, acellular pertussis and for travellers were felt to be less important. (In the spring of 2007, the human papillomavirus vaccine was already being given in nearly half of the clinics surveyed.) "Vaccines were stored by 95% of clinics," investigators reported, although 20% of high vaccinators and 29% of low vaccinators who stored vaccines did not have a dedicated refrigerator. Ten per cent of high vaccinators and 29% of low vaccinators did not have a maxima-thermometer while up to 91% of medical clinics allowed patients to bring vaccines in from outside the clinic. The authors questioned the practice of allowing patients to purchase a vaccine outside the clinic as it is seldom possible to be sure that the vaccines have been properly stored. "Any break in the cold chain can lead to a reduction in the effectiveness of the immunization product, vaccine failure or side effects," they cautioned.

Two-thirds of the clinics made their services available through evening vaccinations and about one-quarter of the clinics offered vaccination on weekends. Other services, including those provided at home, a nurse vaccinator or dedicated clinics, were very much reduced in the evening and almost non-existent on weekends. As investigators noted, over 90% of clinics who offered vaccination planned to maintain or increase their offer of vaccination services over the next five years. To make up for current shortcomings, strategies to improve vaccine coverage might include a greater range of vaccination hours, increased involvement of nurses in vaccination and better methods for identifying and following up non-vaccinated patients, investigators suggested.

"The goal of this study was to describe the organization of vaccination for adolescents and adults in medical clinics and to explore the determinants of the offer of vaccination services so as to adapt these services to current and future needs," investigators explained. "[It was] warranted by the lack of knowledge on the subject, by the importance of morbidity and mortality caused by vaccine-preventable disease in adults and by the arrival of new vaccines, both recent [HPV] and imminent [herpes zoster] specifically aimed at this population."

Children whose parents refuse varicella vaccination at high risk of infection

Glanz et al. Parental refusal of varicella vaccination and the associated risk of varicella infection in children. Arch Pediatr Adolesc Med *2010;164(1):66-70.*

Children whose parents refuse to have them vaccinated against varicella have a ninefold increased risk of developing the infection, according to a Kaiser Permanente Colorado health plan study.

Dr. Jason Glanz, Kaiser Permanente Colorado (KPCO) Institute for Health Research, Denver, and colleagues examined individual level data on both vaccination and disease status of children enrolled in a managed health care plan for a 10-year period. The KPCO health plan has over 430,000 members who receive full coverage of all recommended pediatric vaccines. The study population included children between the ages of 12 months and 8 years who were members of the health plan between 1998 and 2008.

Of a cohort of 86,993 children who were enrolled in KPCO for a minimum of six months, investigators identified 343 children, mean age 3.9 years, who had been diagnosed with varicella during the 10-year study interval. "Varicella vaccine refusal was strongly associated with medical record-verified varicella illness [odds ratio 8.6] and the percentage of attributable risk in the vaccine refuser population was 99.4%," investigators indicated. Numerically, all seven of the unvaccinated varicella cases were attributed to vaccine refusal, indicating that 4.7% of the varicella cases in the total population were associated with vaccine refusal.

As investigators pointed out, routine varicella immunization has led to substantial health care and societal cost savings. Prior to universal varicella immunization, varicella illness was responsible

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for more than $330 million in health care costs per year and more than $1.5 billion in societal costs. "Since licensure, universal two-dose immunization has reduced varicella-associated health care costs by 97% and societal costs by 98%," the authors observed. It is "therefore likely," they added, that parents who refuse to have their children vaccinated against varicella place an added economic burden on the nation's health care system and society as a whole.

"Parents who refuse varicella immunization place their children at risk for varicella infection requiring medical care when compared with fully vaccinated children," investigators concluded. "If the number of vaccine-refusing parents continues to increase across the US, it is likely that the incidence of severe varicella-associated complications will also increase over time."

Most health care workers agree with mandatory influenza vaccination

Douville et al. Health care worker knowledge, attitudes, and beliefs regarding mandatory influenza vaccination. Arch Pediatr Adolesc Med *2010;164(1):33-7.*

The majority of health care workers polled about their views regarding mandatory influenza vaccination agreed with a policy that would mandate them to receive the influenza vaccine, according to an American survey.

Lauren Douville, Center for Practical Bioethics, Kansas City, Missouri, and multicentre colleagues surveyed a random sample of health care workers consisting of physicians, nurses and other employees at a large tertiary care children's hospital in the US. The sample included 40% of all physicians, 18% of all nurses and 18% of all other employees working at the hospital. Out of 946 surveys distributed to employees, the authors received a total of 574 responses, almost equally answered by physicians, nurses and other health care workers.

"Most employees [70%] either strongly agreed or agreed that the hospital should mandate influenza immunization," investigators reported, "and nearly everyone, 363 of 391 [94%] who favoured mandatory immunization, had been immunized themselves." A total of 15% of the surveyed respondents opposed mandatory immunization even though over half of them (55.6%) had been immunized against influenza. Survey results showed that those who favoured mandated influenza vaccination were more likely to believe that it was safe for both adults and children than those who did not. Over half of those who were in favour of the mandate (51%) also indicated that they were at high risk of contracting influenza.

Employees who opposed the mandate were more likely to report that they opposed mandatory routine childhood immunization in general, while only 29% of the antimandate group believed they were at high risk of contracting influenza. As investigators pointed out, their data suggest that employees who oppose mandated vaccination fall into two groups; one group who simply misunderstands the facts about influenza or the vaccine; and a second group who understands the facts but who feel that decisions about immunization—either their own or for children—should be up to the individual. Educational efforts targeting health care workers' fears and misconceptions about influenza vaccines may therefore help decrease the reservoir of unimmunized health care workers, the authors suggested. Failing that, "Hospitals mandate many things to prevent nosocomial infections: equipment is sterilized, frequent handwashing is enforced, isolation procedures are used for patients with contagious illness and evidence of noninfection or immunity is routinely collected with tuberculin skin testing and serologic response to vaccines for employees," they stated.

Although all of these interventions are expensive for hospitals and possibly burdensome for health care workers, "A health care worker who refuses to comply with such hospital policies would not be well tolerated. It should be no different for influenza immunization," they concluded.

Significant reduction in rotavirus hospitalizations and costs following introduction of vaccines

Chang et al. Reduction in hospitalizations for diarrhea and rotavirus infections in New York state following introduction of rotavirus vaccine. Vaccine *2010;28(3):754-8.*
Vesikari et al. RotaTeq, a pentavalent rotavirus vaccine: efficacy and safety among infants in Europe. Vaccine *2009;28(2):345-51.*

New York hospitals are reporting a significant reduction in rotavirus (RV) hospitalizations and related costs following the introduction of the RV vaccine in both eligible younger children as well as in unimmunized older children. Dr. Hwa-Gan Chang, New York State Department of Health, and multicentre colleagues assessed the effect of RV vaccination in children under the age of 19 years in 10 sentinel New York hospitals as well as all state-wide hospitals. The inquiry focused on children under the age of 2 years in particular who were most likely to have been immunized.

Prior to the introduction of the first RV vaccine (2003-2006), the annual incidence of RV-associated hospitalizations was 13 per 10,000. Following the introduction of both vaccines (oral pentavalent in February 2006, attenuated oral in April 2008), the incidence of RV-associated hospitalization had dropped to 2.5 per 10,000 in 2008. "A marked reduction in the number of diarrhea-associated hospitalizations [40% decrease] and RV-coded hospitalizations [85% decrease] was observed in calendar year 2008 compared with the average of calendar year 2003-2006," investigators added. In children between the ages of 12 and 23 months, who were most likely to be immunized, there was an 86% reduction in RV hospitalizations between the pre- and post-vaccination intervals examined at the 10 sentinel hospitals involved in the survey and an 83% reduction in state-wide hospitals. In addition, there was at least a 70% reduction in hospitalizations in 2008 in both sentinel and state-wide hospitals in older children compared with the average reported in pre-vaccination years.

"These decreases in hospitalizations were associated with reductions in hospital costs," investigators noted. For example, total hospital costs among children between one and 23 months at the 10 sentinel hospitals included in the survey was $0.7 million for RV in 2008 compared to an average of $3.3 million for the same period between 2003 and 2006. "At all hospitals state-wide, there was a $10 million reduction from the $13.7 million average per year from 2003-2006 to $3.7 million in 2008 for RV hospitalizations in the same age groups," investigators reported, "and overall, for ages 1 month through 18 years, there was a $13 million reduction—from $19 million to $6 million—in hospital costs for RV."

A post-hoc analysis of the REST (Rotavirus Efficacy and Safety Trial) European data set indicates that the oral pentavalent vaccine (RotaTeq) had "excellent" clinical efficacy against severe disease and reduced disease severity among those who became infected. Nearly 70,000 infants were enrolled in REST and all received their first oral dose of either the vaccine or placebo at six to 12 weeks of age, followed by two more doses at four- to 10-week intervals up to 32 weeks of age.

In the Finnish cohort reported in the post-hoc analysis (n=2686), the vaccine was 98.3% effective against severe RV gastroenteritis (GE) due to any serotype during the first two

seasons post-vaccination and 68% effective against RVGE of any severity due to any serotype during the same follow-up interval. The combined rate of hospitalizations as well as emergency department visits due to any RVGE from any serotype was reduced by 94.5% for up to two years after vaccination, investigators observed, and there were no statistically significant differences between infants who received the vaccine and placebo controls for any of the safety end points.

"These results indicate that [the oral pentavalent RV vaccine] in Europe provided a high level of protection against RVGE of any severity, and particularly against severe RVGE up to two years, and was well tolerated," investigators concluded. "These data hold great promise for the potential public health impact of [the oral pentavalent RV vaccine] for infants and children in Europe with widespread use."

Protection against influenza-related hospitalization and death for frail elderly despite incompletely matched vaccine

Dean et al. Incompletely matched influenza vaccine still provides protection in frail elderly. Vaccine *2010;28(3):864-7.*

Despite an incompletely matched vaccine, a high degree of protection against pneumonia- and influenza-related hospitalizations and death from all causes has been demonstrated in frail elderly patients during several outbreaks in Australia.

Dr. Anna Dean, The Children's Hospital, Westmead, Australia, and multicentre colleagues estimated influenza vaccine efficacy against laboratory-confirmed influenza, influenza-like illness, hospitalization and death using data pooled from five influenza outbreaks in 2007. During that year, a cluster-randomized controlled trial was being carried out in 16 aged care facilities (ACF) in the greater Sydney area, including year-round active surveillance for influenza-like illness combined with rapid testing procedures.

Vaccination coverage among ACF residents ranged from 59% to 100% whereas it was "consistently low" among staff at between 11% and 33%, study authors observed. Some 288 residents (83%) of the cohort exposed to influenza infection during the five outbreaks were vaccinated prior to the 2007 season. During these five outbreaks, investigators identified 63 cases of influenza-like illness, with attack rates ranging from 12% to 25%—17% among those who had been vaccinated and 24% among those who had not.

Some 54 cases of influenza infection in residents were confirmed by laboratory testing. Attack rates in this group ranged from 9% to 24%, with 14% among vaccinated residents and 24% among those who had not been vaccinated. Fourteen residents required hospitalization for pneumonia- or influenza-related illness and 14 residents died.

As the authors pointed out, influenza accounts for many pneumonia- and influenza-related deaths in the elderly, as well as a substantial proportion of winter deaths from all causes. In this particular study, vaccine efficacy against pneumonia- and influenza-related hospitalizations was 82% while efficacy against death from all causes was 75%. "These estimates are for effectiveness during the outbreak only and would be expected to alter as deaths and hospitalizations from outside the outbreak period were included," investigators cautioned.

Nevertheless, given the high mortality in this frail, vulnerable population, the point estimate of 75% protection in their study warrants reporting, despite the confidence limit passing zero, they stated. They added that despite the incomplete vaccine match, "The strong protection shown is encouraging and provides additional support for influenza vaccination policies targeting the frail elderly."

High HPV transmission rates seen in new couples

Burchell et al. Human papillomavirus infections among couples in new sexual relationships. Epidemiology *2010;21(1):31-7.*

Burchell et al. Influence of partner's infection status on prevalent human papillomavirus among persons with a new sex partner. Sex Transm Dis *2010;37(1):34-40.*

Very high transmission rates of human papillomavirus (HPV) infections occur among couples in new sexual relations, according to a recent analysis of the HITCH (HPV Infection and Transmission among Couples through Heterosexual Activity) cohort study. Project coordinator Ann Burchell, PhD, Division of Cancer Epidemiology, MUHC-McGill University, Montreal, Quebec, and multicentre colleagues analyzed cross-sectional enrolment data from HITCH, an ongoing longitudinal investigation initiated in May 2005. The 263 couples included in this analysis had been sexually active together for a median of 4.2 months and all but three couples had engaged in vaginal sex. The mean frequency of vaginal sex was 4.8 times a week, but only 9% of the couples never used condoms.

"HPV was highly prevalent in the 263 couples, with at least one partner having at least one HPV type in 64% of couples," the authors reported. Both partners were HPV-positive in 48% of the couples; among this group, 87% were concordant for one or more HPV type. HPV 16 was the most common type detected, occurring in 22% of couples. Among couples in which HPV was present in at least one partner, nearly two-thirds (64%) were concordant for at least one HPV type; in these couples, the mean number of types present was 3.4. Interestingly, the proportion of HPV infections for which both partners were infected varied little by oncogenic risk, at 43% for high-risk oncogenic types and 39% for low-risk oncogenic types. Also of note, the proportion of infections shared by both partners was higher among couples who had engaged in vaginal sex for longer periods of time, peaking at 68% among those who had had vaginal sex for five to six months. "Detection of one or more HPV types was observed in 64% of recently formed sexual partnerships and the same type was detected in both partners at 41% of couples—far more frequent than expected by chance," the authors reported, "and these data are consistent with HPV being highly transmissible."

Using the same cohort, the investigators also reported that the current partner's HPV status was the most important risk factor for prevalent HPV infections. In this analysis, one or more HPV types were detected in identical numbers of women and men (56%) but couples were not necessarily concordant for the same HPV type. "Ignoring type, in 48% [of couples], both partners were HPV-positive," they added. Regarding specifically vaccine-preventable HPV types 6, 11, 16 and 18, the authors detected HPV 16 in 17.9% of women and 16.4% of men, HPV 18 in 4.9% of women and 3.8% of men, HPV 6 in 3.8% of women and 6.5% of men, and HPV 11 in 0.4% of women and 0% in men.

"Genital HPV infection was very common among persons with a new sex partner, the strongest risk factor [being] the presence of infection in one's current sexual partner which resulted in an over fiftyfold increase in the prevalence of type-specific infection," the authors stated. As already documented, HPV prevalence was also higher with increasing lifetime partners. The authors also found that frequent condom use was protective in men, especially if the partner was HPV-infected, but was significantly less protective among women with an infected partner.

"Our study is the first to document HPV prevalence in young adult heterosexual couples that are newly-forming," investigators concluded, "and these findings underscore the very high sexual transmissibility of HPV infection and should assist policymakers in devising strategies to supplement the preventive effect of prophylactic HPV vaccination."

Switching to acellular pertussis vaccine cost-saving for Canada

Iskedjian et al. Economic impact of the introduction of an acellular pertussis vaccine in Canada: a 6-year analysis. Vaccine *2010;28(3):714-23.*

Switching to an acellular pertussis vaccine from the whole cell vaccine as Canada did in the late 1990s has proven to be both cost-saving from a societal perspective and cost-effective from a Ministry of Health (MoH) perspective.

Michael Iskedjian, BPharm, MSc, Pharm*Ideas* Research and Consulting, Oakville, Ontario, and multicentre colleagues determined the economic impact of replacing the whole cell pertussis vaccine with an acellular vaccine for immunization of Canadian children against pertussis using actual epidemiologic data. "In the base case analyses, we assumed that the coverage rate would be 95% for both vaccines despite the possibility that coverage for the whole cell vaccines and the acellular vaccines may differ," the authors noted.

Analyses revealed that more than 166,000 cases of pertussis were avoided following the introduction of the acellular vaccine and approximately 700 hospital admissions were probably averted over the six-year interval analyzed. "From the MoH perspective, the change in vaccines resulted in an incremental cost of CAD$108.39 per pertussis case avoided or $129.15 per discounted pertussis case avoided for the six-year period," investigators added. From a societal perspective, there was a savings of $30,639,159 over the same six years. "These savings were a result of a decrease in productivity and leisure time loss for the management of pertussis cases," study authors noted, "and the net savings were $183.70 per pertussis case avoided [and] $218.89 per discounted pertussis case avoided."

As the authors also observed, the acellular pertussis vaccine is clearly more efficacious than the whole cell vaccine as the number of actual pertussis cases dropped by 166,787 from the pre-acellular vaccine era to the post-acellular era. Indeed, the acellular vaccine reduced the incidence rate of pertussis by 57.5% and the incidence rate of hospitalizations by 59.2% compared to the whole vaccine era.

"The net impact of switching to the acellular vaccine was a large reduction in the number of pertussis cases and this, in turn, had a ripple effect since it decreased the associated resource utilization," investigators observed. In addition to pertussis cases avoided, there were over 42,000 fewer visits to physicians due to pertussis at a saving of $1.5 million and some 700 hospital beds were made available.

The whole cell vaccine did reduce the incidence of pertussis but it was associated with high rates of adverse reactions. As a result, all Canadian provinces and territories switched from the whole cell vaccine to an acellular vaccine between July 1997 and April 1998. □

UPCOMING EVENTS

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4th Regional Conference of the International Society of Travel Medicine
March 9-12, 2010 / Miami, Florida
www.istm.org

7th International Symposium on Pneumococci and Pneumococcal Diseases
March 14-18, 2010 / Tel Aviv, Israel
www2.kenes.com/isppd/pages/home.aspx

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