Follow-up report on PIDAC-I recommendations for Ontario’s adult pertussis vaccine program

Provincial Infectious Diseases Advisory Committee

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This document was prepared for the Provincial Infectious Diseases Advisory Committee on Immunization (PIDAC-I). PIDAC-I is a multidisciplinary scientific advisory body who provide evidence-based advice to the Ontario Agency for Health Protection and Promotion (Public Health Ontario) regarding immunization. PIDAC-I’s work is guided by the best available evidence and updated as required.

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Background

Following its September 21, 2011 meeting, the Provincial Infectious Diseases Advisory Committee on Immunization (PIDAC-I) recommended: “that every adult should be eligible for a dose of adult pertussis vaccine and that it should not be contingent on the lack of receipt of the adolescent vaccine”. This recommendation was forwarded to Dr. Arlene King, Chief Medical Officer of Health on December 5, 2011. On May 4, 2012, Dr. King responded with a request for a scientific report summarizing the best available evidence supporting the PIDAC-I recommendation regarding the eligibility criteria. The objective of this document is to review the evidence pertaining to pertussis vaccination in adults, including information on waning immunity, and to make recommendations on its use in Ontario.
Methods

An environmental scan of pertussis immunization policies was completed and the product monographs for the two acellular pertussis vaccine combination products authorized for use in adolescents/adults in Canada (diphtheria, tetanus, acellular pertussis [Tdap] vaccine) were reviewed; there is no monovalent pertussis vaccine available in Canada. In addition, the literature was reviewed to identify studies on the duration of antibody persistence following vaccination of adolescents and adults with acellular pertussis vaccines, and studies on the safety and immunogenicity of acellular pertussis vaccines in adults age 65 years and older. The evidence was presented to PIDAC-I at its meeting on August 15, 2012. The committee discussed the evidence and reaffirmed its original recommendation. A detailed presentation and discussion of the epidemiology of pertussis in Ontario was previously made to PIDAC-I on September 21, 2011; therefore, only select pertussis epidemiological data is re-presented in this report.

This report is organized into two sections: (a) duration of protection following the use of acellular pertussis vaccines administered in adolescents and adults and (b) the burden of pertussis, and the safety and immunogenicity of acellular pertussis vaccines, in adults greater than 65 years of age.
Results

A. Duration of protection associated with acellular pertussis vaccine administration in adolescents and adults

Since 2003 in Ontario, adolescents aged 14 to 16 (with eligibility up to age 18) are eligible to receive Tdap vaccine as an adolescent pertussis booster through the publicly-funded program. In 2013, ten years will have elapsed since the first cohort was vaccinated with an adolescent booster dose. Effective August 2011, Ontario adults aged 19 to 64 years of age became eligible to receive one lifetime, publicly-funded dose of Tdap vaccine, if the vaccine had not previously been administered in adolescence.

1. Pertussis Vaccine Recommendations from National Advisory Bodies

Since 2003, the National Advisory Committee on Immunization (NACI) (1) has recommended that:

- “All preadolescents and adolescents who have not received a dose of acellular vaccine should receive a single dose of the adolescent/adult formulation of acellular pertussis vaccine”.
- “For adults who have not previously received a dose of acellular vaccine, it is recommended that a single diphtheria-tetanus (Td) booster dose be replaced by the combined diphtheria-tetanus-acellular pertussis (dTap) vaccine”.

It would be desirable if the language in the NACI recommendation for adults was clarified. A current member of NACI has indicated that the wording of the pertussis recommendation for adults will be revised with the forthcoming edition of the Canadian Immunization Guide. The new language will indicate that “adults who have not previously received a dose of acellular vaccine in adulthood”, are recommended to be vaccinated with Tdap vaccine. This change in language supports the PIDAC-I recommendation that all adults, including those who have previously received a dose of Tdap vaccine in adolescence, be eligible for an adult dose of the vaccine.

The language of the pertussis vaccine recommendations from the Advisory Committee on Immunization Practices (ACIP) in the United States (US) is similar to those of Canada. Since 2005, ACIP has recommended a booster dose of Tdap vaccine for all adolescents aged 11 through 18 years and for adults aged 19 through 64 who have not yet received a dose (2). In February 2012, ACIP recommended Tdap vaccination of adults aged 65 years and older (3). Since 2005 ACIP has also recommended that adults who have or who anticipate having close contact with an infant aged under the age of 12 months (e.g. parents, grandparents, child-care providers, and healthcare providers) should receive a single dose if they have not previously received Tdap vaccine (2).

2. Environmental scan of adult pertussis vaccine policies

A review of the publicly funded immunization schedules within Canada found that 9 provinces and territories, including Ontario, publicly fund a dose of Tdap vaccine in adults. However the specific eligibility criteria used by these jurisdictions are often imprecise. However, there are exceptions. Nova Scotia indicates that all adults “who have not received a dose of pertussis vaccine in adulthood should receive a single dose of Tdap” (4). Quebec’s schedule indicates the use of Tdap vaccine at age 14-16 years with an asterisk that denotes “a dose of this vaccine is also indicated for all adults” (5). The adult immunization schedule for the Northwest Territories recommends one dose of “Tdap instead of Td at least once in their lifetime” (6). When looking at
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3. Tdap vaccines authorized for use in Canada

There are two Tdap vaccine products that are authorized for use in Canada, Adacel® (Sanofi Pasteur) and Boostrix® (GlaxoSmithKline). Adacel® vaccine contains five pertussis antigens: pertussis toxin (2.5 µg), filamentous hemagglutinin (5 µg), pertactin (3 µg), and fimbriae types 2 and 3 (5 µg each) (9). Boostrix® vaccine contains three antigens: pertussis toxin (8 µg), filamentous hemagglutinin (8 µg), and pertactin (2.5 µg) (10). Both vaccines use aluminum phosphate as an adjuvant.

4. Vaccine efficacy and vaccine effectiveness

The estimated vaccine efficacy of acellular pertussis vaccines is generally quoted to be approximately 85% (11). Efficacy of Tdap vaccine among adolescents and adults is estimated to be higher. The Acellular Pertussis Vaccine Trial (APERT) demonstrated a vaccine efficacy of 92% (95% Confidence Interval (CI) 32.0%-99.0%) over two years (12). In contrast, vaccine effectiveness estimates among adolescents range from 66 to 78% (13,14). It is important to note that all of these studies examined adolescents and adults who would have received whole-cell pertussis vaccines in infancy and childhood. Waning of immunity following pertussis vaccination has been well-described (15,16). Data from recent pertussis outbreaks in the US states of California and Washington have suggested that children and adolescents who were immunized exclusively with acellular pertussis vaccines have more pronounced waning of immunity than was originally ascribed to acellular pertussis vaccines (17,18). In the Washington State pertussis outbreak, incidence rates have been observed to be highest among infants under one year of age who have yet to receive the full primary series and children aged 10, 13 and 14 years, in keeping with early waning of immunity from acellular vaccines (17). This data mirrors national trends in the US with respect to this age group suggesting that there is a cohort of increased susceptibility owing to the receipt of exclusively acellular pertussis vaccine products (17). Further data on waning of immunity comes from the California pertussis outbreak. A case-control study comparing children aged 4-12 years who had received five doses of DTaP found that the risk of pertussis increased by 42% each year after the fifth DTaP dose, consistent with waning immunity (18). The switch from whole-cell to acellular pertussis vaccine occurred in 1997 in Ontario. The oldest members of the cohorts who have received solely acellular vaccine are now approximately 15 years of age and may have received a further dose of acellular pertussis vaccine through the adolescent booster (due between 14-16 years of age). Given the evidence of waning immunity recently documented with the childhood series of acellular pertussis vaccines, it is very likely that waning immunity will also occur following the adolescent booster, supporting the case for immunization in adulthood.

5. Antibody persistence following Tdap vaccination

Protection against pertussis is associated with antibodies against pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN) and fimbriae types 2 and 3 (collectively referred to as FIM). However, no single immune correlate of protection for pertussis has been identified. The immune mechanisms following natural pertussis infection and following immunization are incompletely understood and it is likely that antibodies to a variety of pertussis antigens play a role in protection, probably in cooperation with cell-mediated immunity (19). Clinical trials aiming to quantify the duration of vaccine response to Tdap in adolescents and adults have used a variety of approaches, including estimating the proportion of individuals who are seropositive to anti-pertussis antibodies, estimating the proportion of individuals with detectable anti-pertussis antibodies above some pre-determined threshold, and calculating the geometric mean concentrations for anti-pertussis antibodies at different points in time. Unfortunately, the clinical significance of any one of these measures is not known. Quantifying the duration of protection associated with acellular
pertussis vaccines is challenging and must rely on epidemiological and other data to complement immunological findings. A further challenge in interpreting the literature in the area of duration of antibody persistence is that while an international reference serum to standardize the reporting of pertussis antibody assays has been developed (20), it has not been implemented on a wide scale basis. Thus, a variety of assays are used in the studies summarized below, each with differing thresholds for the detection of specific pertussis antibodies.

Three peer-reviewed publications have presented immunogenicity data 10 years following the administration of acellular pertussis vaccines in adolescents and adults (7,21,22). An additional study integrated immunogenicity data at 5 years following immunization into a mathematical model in order to make predictions about duration of antibody persistence (23). Given the timing of these studies and the ages of their participants, it is likely that all or part of the vaccine series these individuals received prior to the dose of Tdap vaccine, contained whole cell products. All studies excluded individuals with a history of pertussis illness or history of vaccination against pertussis since their original enrollment in the respective studies. In the study by Halperin et al. (7) which included a group naïve to Tdap vaccine, individuals with a history of pertussis illness or vaccination in the last 10 years were excluded.

Halperin et al. conducted an open-label, multi-center study comparing the safety and immunogenicity of first dose versus repeat dose of Tdap vaccine (Adacel®) in adults who had been immunized 10 years prior (7). A total of 769 subjects were enrolled with 407 in the Tdap vaccine naïve group and 362 in the repeat dose group. The GMCs for anti-PT, anti-FHA, anti-PRN, and anti-FIM were all low pre-vaccination in both groups, but were still significantly higher (1.3 to 3-fold) for individuals who had been immunized 10 years prior as compared to those observed in the Tdap naïve group. This study did not report on the proportion of individuals in each group with detectable anti-pertussis antibodies. Tdap vaccine was found to highly immunogenic whether it was a first or repeat dose.

Mertsola et al. examined the immunogenicity and safety of a second dose of Tdap vaccine to young adults 10 years (n=75) following vaccination with either Tdap or DT+aP at 10-14 years of age at a single centre in Finland using Boostrix® vaccine (21). The ten year follow-up study included 82 of the original 510 study subjects. Seropositivity against PT, FH and PRN was defined as an antibody concentration of 5 EU/ML or higher. Seropositivity for pertussis toxin was 61.3% (95% CI 49.4-72.4%) 10 years following immunization, which was equivalent to the proportion of individuals who were seropositive before the dose of Tdap vaccine 10 years earlier (62.2%, 95% CI 50.1-73.2%). There were also overlapping confidence intervals for the geometric mean concentrations (GMCs) of anti-pertussis toxin antibodies between the two groups. Seropositivity for FH and PRN remained at high levels (96-100%) 10 years following Tdap vaccine. The authors concluded that “10 years after vaccination..., antibodies against pertussis approach levels observed before vaccination, suggesting that 10 years represents an appropriate interval for a pertussis booster dose” (21).

Tomovici et al. examined antibody levels to PT, FHA, PRN and FIM among clinical trial recipients who had received Tdap vaccine (Adacel®) 10 years earlier as part of one of three studies (22). The first study involved a comparison of three lots of Tdap vaccine (participant age range 11-54 years). Fifteen out of the original 55 who received Tdap vaccine as adolescents provided data at 10 years and 127/394 adults contributed 10 year follow-up data. The second study examined concurrent versus sequential Tdap + hepatitis B vaccines among adolescents aged 11-13 years; a total of 150 of the original 269 subjects participated. The third study compared Tdap versusTd vaccines among those aged 19-60 years. Only 32 of the original 250 adults (12.8%) provided data at 10 years. Seropositivity in this study was evaluated by determining the proportion of individuals having antibody levels > the lower limit of quantitation (LLOQ) as well as in relation to four times the LLOQ; the clinical significance of LLOQ is not clear. The ELISA assays were performed at two Sanofi Pasteur laboratories, one in Canada and one in the United States using the following LLOQ cut-offs in Elisa units per
Among those who received Tdap vaccine as adolescents, antibodies against FHA, PRN and FIM remained high and at 10 years were higher than pre-immunization levels (74.5-96.3% > LLOQ pre-immunization; 94.7-100% > LLOQ ten years post immunization). Similar findings were observed in adults, although the proportion with antibody levels > LLOQ was considerably higher 10 years post-immunization as compared to pre-immunization (54.6-93.7% > LLOQ pre-immunization; 93.8-100% > LLOQ 10 years post-immunization). However, anti-PT antibody was undetectable (< LLOQ) in between 21 and 30% of adolescents and between 7 and 18% of adults. When antibody persistence was examined using the threshold of four times the LLOQ, a less conservative measure of antibody detection, 35-36% of adolescents and 30-57% of adults had undetectable anti-PT antibodies. Confidence intervals around the proportions were not provided. Geometric mean concentration (GMC) data were presented only in graphical format. The figure containing GMC data demonstrated that all pertussis antibodies declined rapidly between 1 month and 1 year post-vaccination, followed by a much slower, but persistent, decline from 1 year to 10 years post-immunization. The authors conclude that “antibodies to the antigens in Tdap vaccine persisted for 10 years after immunization of adolescents and adults” and that the data presented “indicated that 10 years is a reasonable interval for a booster dose of Tdap vaccine” (22).

Bailleux et al. applied five year follow-up data following the administration of Tdap vaccine (Adacel®) in adolescents, to a mathematical model developed to predict duration of antibody persistence (23). The original study examined concurrent versus sequential Tdap vaccine administration with hepatitis B vaccine to subjects between the ages of 11 and 14 years. A total of 269 subjects participated in the original study, 160 provided at least 2 blood samples within the 5 year follow-up study to be included within the model. A linear mixed model with antibody data at 1, 3, and 5 years post-immunization was used to predict the decay of GMCs for up to 20 years post-Tdap vaccine administration and the time required for a given titer to fall beneath the GMC pre-booster administration. For all antigens, the mean time required for the GMC to return to pre-booster levels ranged from 9.5 to 15.3 years: FM (9.5 years, 95% CI 3.6-24.7 years), PT 10.5 years (95% CI 4.2-24.6 years), FIM 11.0 years (5.7-18.9 years) and PRN 15.3 years (95% CI 7.0-28.0 years). The authors concluded that their findings indicate that antibody persistence to all pertussis antigens will be sufficient to provide sustained levels of antibody for 10 years following immunization and advocated for the replacement of Td with Tdap vaccine to improve population immunity against pertussis (23).

6. Summary

Clinical trial data is available up to 10 years post-immunization with Tdap vaccines in adolescents and adults which demonstrate that after an initial rapid decrease in antibody levels during the first year post-immunization there is a slow phase of antibody decay. At ten years following Tdap vaccine administration, antibody levels against pertussis toxin are undetectable in 7-61% of subjects, while other antibodies are more conserved. The challenge in interpreting this data is that there is no single, established immune correlate of protection for pertussis. However, given that studies in this area report on the proportion of individuals who are seropositive, e.g. having detectable antibodies against pertussis antigens, this is an extremely conservative estimate of the vaccine’s protective effect. Specifically, the proportion of individuals seropositive for pertussis antibodies is likely to be greater that the proportion of individuals seroprotected against pertussis infection. Given the lack of an immune correlate of protection, this immunogenicity data must be interpreted in light of pertussis epidemiology which suggests waning immunity following vaccination. Evidence of waning of vaccine-induced immunity was used to support the use of Tdap vaccine in adolescence. Therefore, it follows that immunity is also likely to wane following the receipt of the Tdap adolescent booster dose, supporting a further booster dose of Tdap vaccine at some point in adulthood.
B. Burden of pertussis and vaccine immunogenicity and safety among adults 65 years and older

Since August 2011, Ontario adults aged 19 to 64 years of age who did not receive Tdap vaccine in adolescence are eligible to receive one lifetime, publicly-funded dose of the vaccine. This lifetime dose replaces one of the Td booster doses given every 10 years.

1. Pertussis Vaccine Recommendations from National Advisory Bodies

As previously stated, since 2003, NACI has recommended that: “For adults who have not previously received a dose of acellular vaccine, it is recommended that a single diphtheria-tetanus (Td) booster dose be replaced by the combined diphtheria-tetanus-acellular pertussis (dTap) vaccine” (1). Of note, there is no upper age limit specified in the recommendation. In February 2012, ACIP expanded their recommendation for Tdap in adults to “all adults aged 19 years and older” (3). This followed an October 2010 ACIP recommendation that unvaccinated adults aged 65 years and older be vaccinated if in close contact with an infant, despite the lack of an FDA-approved Tdap vaccine product in the United States at the time (24). Prior to 2010, ACIP had recommended the use of Tdap for adults only up to age 64 years (2). The 2012 ACIP recommendation for use in adults aged 65 years and older was based on epidemiologic data on the burden of pertussis in this age group, namely that its true burden was estimated to be 70-100 fold higher than reportable disease notifications in this age group (further details provided below), and the results of two unpublished cost-effectiveness models developed by GlaxoSmithKline and CDC (3). ACIP’s interpretation of the conclusions of both models is that the cost per case averted and cost per quality-adjusted life-year saved were “modest”. Safety and immunogenicity data of Tdap vaccine use among adults 65 years of age and older were also reviewed by ACIP and provided support for the recommendation.

2. Regulatory status of Tdap vaccines in Canada for use in adults 65 years of age and older

Both Adacel® and Boostrix® vaccines have an age indication of use in individuals 4 years of age and older with no upper age limit specified (9,10). The removal of an upper age limit of age 64 occurred in August, 2011 for Adacel® (25). Boostrix® vaccine has never had an upper limit to its age indication since it was first authorized for use in Canada in 2007.

3. Burden of pertussis among older adults in Ontario

The burden of pertussis among adults aged 65 years and older in Ontario and elsewhere is currently unknown. Drawing upon the Ontario pertussis epidemiologic summary that was presented to PIDAC-I in September 2011, between 2000 and 2010 the incidence of confirmed pertussis in Ontario among adults aged 60 years and over ranged from a high of 1.6/100,000 in 2001 to a low of zero cases/100,000 in 2010 (26). As a proportion of total cases of pertussis, the smallest proportion of cases for all years was observed among adults aged 65 years and older. The proportion of pertussis cases occurring in adults 65 years and older ranged from 4.6% of the 463 cases observed in 2001 to zero of the 102 cases observed in 2010 (26). However, it is well-recognized that pertussis reportable disease data under-estimates the true burden of pertussis among adults. This is because of under-recognition of pertussis as the responsible diagnosis in prolonged cough illnesses; an increased likelihood of atypical presentations of pertussis among adults; and a low index of suspicion for pertussis among adult patients by clinicians.

The discrepancy between incidence rates estimated using pertussis notifications and incidence approximated in prospective studies which have collected biological specimens among adults with prolonged cough is striking. Nenning et al, conducted IgG antibody levels to pertussis toxin among 153 members of a Health
Maintenance Organization in San Francisco, aged 18 years and older who had a chief complaint of cough with a duration of 2 or more weeks (27). The study was conducted in 1994. The mean age was 47.5 years (range 23-82 years). The prevalence of pertussis was 12.4% (n=19, mean age 42 years, age range 24-78 years). From this, the incidence of adult pertussis was estimated to be 176/100,000 person years with a 95% CI of 97-255/100,000. In 1994, the incidence rate for pertussis (all ages) in San Francisco was 1.6 cases/100,000 population. Using national data, the 1994 incidence rate for pertussis was 1.8 cases/100,000 among all ages and 0.2 cases/100,000 for adults aged 20 years or older. A similar prospective study in Paris, conducted in 2008-2009, used polymerase chain reaction (PCR) or measurement of anti-pertussis toxin IgG levels by ELISA to confirm the infection (28). A total of 204 patients were enrolled in this study which used general practices involved in a sentinel surveillance system for other health outcomes. All patients 13 years of age or older with a cough persisting for more than 7 days and who had least one specific sign of pertussis (whooping, paroxysmal cough, vomiting, increased coughing at night) were enrolled. The mean age of patients enrolled in the study was 44 years (range: 14-89 years). Pertussis cases were classified as confirmed (laboratory confirmed) (n=22), clinical cases (clinically diagnosed with pertussis but without laboratory confirmation) (n=23), and epidemiological cases (no lab confirmation but close contact with a confirmed case in the previous 3 weeks) (n=1). The mean age and range among these classifications were not presented. The incidence of pertussis was estimated to be as high as 145 per 100,000 population (95% CI: 121-168/100,000) using all pertussis cases and 66/100,000 population (95% CI: 46-76/100,000) using only lab-confirmed cases. Pertussis is not a notifiable disease in France so a quantitative comparison between these estimates and reportable disease information cannot be conducted.

ACIP used these two studies, as well as other prospective studies using biological specimens which did not include adults 65 years or older but which would also be applicable to this population, to conclude that the actual burden of pertussis in adults aged 65 years and older is “likely is at least 100 times greater than that reported” (3). This was based upon pertussis incidence rates estimated from prospective studies which ranged from 66-500 cases/100,000 population and reported pertussis incidence data from the United States for similar ages which ranges from 1-5 cases/100,000 population (3).

In summary, determining the precise burden of pertussis among Ontario adults aged 65 years and older is challenged by under-diagnosis and under-reporting of pertussis, which applies to all age groups, but is likely more pronounced in adults. On the basis of the literature, it is reasonable to conclude that the true burden of pertussis in this age group is substantially greater than the estimates provided through iPHIS.

4. Older adults as a source of pertussis infection among infants

Several epidemiologic studies have sought to determine the source of infection for infant cases of pertussis. The focus of most studies has been on parents and siblings, rather than grandparents. However, two studies did include grandparents as a discrete source category and found that 6-8% of infant pertussis infections were attributable to grandparents as the source (29,30).

5. Immunogenicity and safety of Tdap vaccines in adults 65 years of age and older

Two clinical trials have included adults aged 65 years and older in safety and immunogenicity assessments of the Tdap vaccine Boostrix® (31). A total of 1,104 subjects aged 65 and older received Tdap vaccine in these two trials. The first study was a Phase III, open-label, multi-center randomized clinical trial (RCT) to assess the immunogenicity and safety of sequential versus co-administration of Tdap with influenza vaccine (Fluarix®, GlaxoSmithKline). Adults aged 19-64 years were enrolled, and an additional cohort of adults aged 65 years and older was included for descriptive analyses (n=217). This study found that booster responses were achieved by 69-70% of subjects for PT, 89-92% of subjects for FHA, and among 73-77% of subjects for PRN. GMCs for anti-pertussis antibodies increased from 6 to 15 fold (31).
The second study was a Phase III, observer-blind, multi-center RCT to evaluate the immunogenicity and safety of Tdap versus Td vaccine (Decavac®, Sanofi Pasteur) in adults 65 years and older. There were 887 subjects who received Tdap vaccine in this study. Booster responses were achieved by 69% of subjects for PT, 93% of subjects for FHA and 74% for PRN; GMCs increased from 7 to 14 fold. The study objective for pertussis was to demonstrate non-inferiority of Tdap vaccine versus the 3rd dose of Infanrix® vaccine (DTaP) (i.e., delivered in infancy) with respect to GMCs for PT, FHA and PRN. Because there are no established serological correlates of protection, efficacy studies conducted in infants have provided immunological data for non-inferiority comparisons in adolescents and adults and have served as the basis for the approval of Tdap vaccines in the US. A priori, non-inferiority of the pertussis response would be demonstrated if the lower limit of the 95% CI for the GMC ratio for each antigen, one month after a single dose of Tdap in adults, compared to one month after the 3rd dose of DTaP in infants was $\geq 0.67$ for each antigen. The non-inferiority objective was met in this study (31).

With regards to safety, the incidence of solicited local and general symptoms was similar between the co-administrated versus sequential administration of Tdap and influenza vaccines, with injection site pain and muscle aches reported most frequently. A similar proportion of subjects reported symptoms within 31 days following Td or Tdap vaccine (0.7% in the Tdap group and 0.9% in the Td group). There were five deaths in the second study, in which 887 subjects received Tdap vaccine. Four deaths occurred in the Tdap vaccine group (myocardial infarction (n=2), acute cerebrovascular accident (n=2) and one in the Td vaccine group (metastatic non-small cell lung cancer). None of these deaths were considered by the investigator to be related to vaccination (31).

A multi-center, double-blind RCT to evaluate the safety and immunogenicity of Tdap (Adacel®) versus Td vaccine among adults aged 65 years and older is found in the Adacel® product monograph (9), but was not found in the published peer-reviewed literature. A total of 1,563 subjects were enrolled, including 519 who were over the age of 75 years. A total of 1,094 subjects received Tdap vaccine and 371 received Td vaccine. The rise in GMCs from pre- to post-vaccination ranged from 4 fold (PT) to 15 fold (FIM). Booster responses were elicited by more than 70% of subjects for all pertussis antibodies with the exception of PT, for which 53% of participants achieved a booster response. The product monograph states that “when compared to pertussis antibody levels observed in infants after 3- or 4-dose primary vaccination series with Tripacel® (DTaP), adults aged $\geq 65$ years achieved lower GMCs for some antigens”. However, the product monograph does not state which antigens. Despite not meeting non-inferiority for all antigens, as noted previously, Adacel® does have regulatory approval for use in Canada for adults aged 65 years and older. Solicited injection site and systemic reactions were monitored for 14 days post-vaccination using a diary card and were monitored for 6 months for unsolicited adverse events. The observed rates for both injection site and systemic reactions were comparable between Tdap and Td vaccines. Among subjects, 42-43% reported any pain and 27-28% reported any myalgia (9).

Moro et al., reviewed adverse events following immunization (AEFIs) reported to the Vaccine Adverse Event Reporting System (VAERS) in the US among adults aged 65 years and older who received Tdap vaccine before Food and Drug Administration approval for the use of the vaccine in this age group (32). Data reported to VAERS over a five year period was reviewed (September 2005-August 2010). There were a total of 243 reports to VAERS meeting these criteria. The most common AEFIs were local reactions (n=100, 41%). There were a total of 11 serious reports, including 2 deaths. One death occurred in a 77 year-old male who received Tdap and yellow fever vaccines on the same date. He died 19 days after vaccination from multi-organ failure due to septic shock. The second death occurred in a 66 year-old female who received only Tdap vaccine. The patient died 2 months after vaccination with a cause of death listed as pulmonary hypertension due to acute interstitial lung disease. No unusual or unexpected clusters of AEFIs was found. The authors conclude that their report identified “no safety concerns” (32).
6. Cost-effectiveness analyses of Tdap vaccination among adults 65 years of age and older

Although several cost-effectiveness analyses have examined the cocooning strategy, there are no studies in the peer-reviewed literature that look at universal pertussis vaccination of older adults. Two unpublished health economic analyses of Tdap vaccination of older adults (≥ 65 years of age) are referenced in the 2012 ACIP statement, one having been developed by the Centers for Disease Control and the other independently developed by GlaxoSmithKline (3). The ACIP statement indicates that both models found that vaccination of adults 65 years and older resulted in moderate decrease in the number of pertussis cases and outcomes (including outpatient visits, hospitalizations and deaths) and that the cost per case averted and cost per Quality-Adjusted Life Year (QALY) were both modest (3). However, the ACIP statement did not indicate the dollar amounts for these two cost estimates.

7. Summary

Tdap vaccines are authorized for use in Canada among adults 65 years and older. They are immunogenic and have an acceptable reactogenicity profile. Although the true burden of pertussis in this age group is not currently known, it is well accepted that estimates from passive surveillance systems such as notifiable disease reports, will greatly under-estimate the true burden of disease in this age group. Source of infection studies have found that grandparents are a source of pertussis for approximately 6-8% of infants (29,30), the age group most vulnerable to severe complications and deaths due to pertussis. Though Canadian data are currently unavailable, evidence from ACIP suggests that universal vaccination of adults aged 65 years and over is associated with modest costs per case averted and per QALY. Furthermore, the wording of the NACI recommendation regarding pertussis vaccination among adults is permissive of vaccination of older adults as its recommendation does not state an upper age limit. High pertussis vaccination coverage at the population level is essential for pertussis control. The restriction of Ontario’s current pertussis vaccine policy to adults under the age of 65 years is an example of a barrier to high population coverage.
Recommendations

PIDAC-I reaffirms its early recommendation “that every adult should be eligible for a dose of adult pertussis vaccine and that it should not be contingent on the lack of receipt of the adolescent vaccine”.

- To operationalize this recommendation, PIDAC-I recommends the adult pertussis vaccine policy be revised to remove the upper age limit restriction, to extend eligibility for Tdap vaccine to all adults aged 19 years and over.

- Furthermore, it recommends that adults be eligible for Tdap vaccination, irrespective of receiving a prior dose of Tdap in adolescence.

- Given the emerging data on waning immunity among persons vaccinated solely with acellular pertussis vaccines, PIDAC-I recommends that Public Health Ontario continue to monitor the literature and evaluate Ontario pertussis epidemiology. A full evaluation of the pertussis vaccination program, including an assessment of waning immunity, is suggested once there is a critical mass of literature available.
Follow-up report on PIDAC-I recommendations for Ontario’s adult pertussis vaccine program

References


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