

Appendix 3: Measles, Mumps, Rubella (MMR), Diphtheria, Tetanus, Pertussis (DTaP/Tdap) & Polio Immunization: Evidence review for newly arriving immigrants and refugees

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ABSTRACT

Background: The majority of newly arrived immigrants originate from countries where they may have had access to sub-optimal vaccination programs. In most parts of the world national childhood vaccination programs (including measles, diphtheria, pertussis, tetanus, polio and BCG) began in the 1970s and were widely implemented in the 1980s but have variable effectiveness (coverage ranging from 50% to 90%). In addition rubella and mumps are not part of the routine vaccination programs of many countries. We conducted an evidence review to determine the susceptibility to childhood vaccine preventable diseases in the immigrant population, and to assess the effectiveness of screening and vaccination programs to prevent morbidity and mortality from these diseases.

Methods Systematic search for evidence of the burden of measles, mumps, rubella (MMR), diphtheria, pertussis, tetanus (DPT) and polio in the immigrant population, and the benefits and harms, applicability, clinical considerations, and implementation issues of screening and vaccination programs in the general and the immigrant populations. The quality of this evidence was assessed and ranked using the GRADE approach.

Results: Childhood vaccination program have dramatically decreased the incidence (92%-99%) and associated mortality (>99%) from measles, mumps, rubella, diphtheria, tetanus, pertussis and polio. Immigrants have been over represented in outbreaks of rubella and most reports of congenital rubella and neonatal tetanus in Canada and the US have occurred in children born to unvaccinated foreign-born mothers. Seroprevalence studies show that a large proportion of immigrants are susceptible to rubella (~80-85% immune), tetanus (~50%-60% immune) and diphtheria (~35-50% immune) and possibly mumps (~80% immune) and are at risk for disease associated morbidity and mortality.

Interpretation: Newly arrived immigrants are an important unrecognized group at risk for childhood vaccine preventable diseases and would benefit from having MMR, DPT and Polio vaccines updated after arrival in Canada.

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Box 1: Recommendations on vaccination from the Canadian Collaboration for Immigrant and Refugee Health

Measles Mumps and Rubella (MMR)

Vaccinate all adult immigrants without immunization records with 1 dose of MMR to reduce associated morbidity and mortality. Immigrant children with absent or uncertain vaccination records should be given age appropriate vaccination with MMR.

Basis of Recommendation

- **Balance of benefits and harms:** Net benefits: Childhood vaccination program have dramatically decreased the incidence and associated mortality from measles, mumps, rubella and congenital rubella (absolute difference of 95.9-99.9% in reduction of cases and 100% reduction in deaths). There are no significant data demonstrating serious adverse events, including autism (RR 0.92 95% CI 0.68-1.24). Mumps and rubella are not part of the routine vaccination programs of most source countries of origin for the majority of new immigrants. A large proportion of adult immigrants may be susceptible to rubella (20-30%) and at risk for having a child with congenital rubella syndrome.
- **Quality of evidence:** High
- **Values and preferences:** The committee attributed more value to preventing morbidity and mortality from measles, mumps or rubella and preventing disease transmission and less value to cost of vaccination.

Diphtheria, Tetanus, Pertussis (DTaP/Tdap) and Polio

Vaccinate all adult immigrants without immunization records with a primary series of Td and IPV (3 doses) the first one of which should include Tdap to also protect against pertussis. Immigrant children with absent or uncertain vaccination records should be given age appropriate vaccination with diphtheria, tetanus, pertussis and polio.

Basis of Recommendation

- **Balance of benefits and harms:** Net benefits: Childhood vaccination program have dramatically decreased the incidence and associated mortality from diphtheria, tetanus, pertussis and polio (absolute difference of 92.9-99.9% in reduction of cases and 99.2-100% in reduction of deaths) as compared to the pre-vaccination period without associated increased serious adverse events. A large proportion of adult immigrants are susceptible to tetanus 40-50% and diphtheria ~60% and the proportion susceptible increases for both with increasing age. To prevent individual morbidity and mortality and in order to prevent outbreaks susceptible individuals must be identified and vaccinated.

Box 1: Continued

- **Quality of evidence:** High
- **Values and preferences:** The Committee attributed more value to preventing morbidity and mortality from diphtheria, tetanus, pertussis and polio and preventing disease transmission and less value to the cost of vaccination.

The cases

Maria a 26 year old in Mexican woman who immigrated to Canada 3 years previously and just delivered a male infant with congenital rubella syndrome (IUGR, cataracts, deafness, hepatosplenomegaly). In the first trimester she worked in a meat packing plant in which there was an outbreak of a viral illness characterized by rash and fever. What preventive intervention could Maria have been offered upon arrival in Canada so that this outcome could have been avoided?

Hong is a 50 year old Chinese man living in Canada for 15 years who presents with a 12-hour history of difficult speech due to trismus and is also noted to have a large wound on his left calf. He is diagnosed with tetanus (cultures from his left calf subsequently grew *Clostridium tetani*) and appropriate treatment is started. One week earlier he lacerated his left calf on the metal prongs of a hay baler on the farm he works on. What preventive intervention could Hong been offered upon arrival to Canada or any time prior to this injury so that this outcome could have avoided?

Introduction

Immunization is one of the most beneficial and cost-effective disease prevention measures.^{1,2} The incidence and mortality from measles, rubella, diphtheria and polio has been reduced >99%, for mumps >95% and for pertussis and tetanus >92% compared with the annual morbidity and mortality prior to introduction of the corresponding vaccines.^{3,4} Despite these successes the recent outbreaks of pertussis in California, the outbreaks of mumps in the US and Canada in 2005-2006 and the ongoing transmission of polio in the past 5 years with recent spread to Tajikstan highlight the need to identify and vaccinate susceptible groups to prevent outbreaks.⁵⁻⁸ In the past 30 years >70% of immigrants have originated from countries where vaccination programs may be sub-optimal or where several of the routine childhood vaccinations in Canada are not part of their national schedule.^{9,10} We conducted an evidence review to guide primary care practitioners in the need to assess and

update childhood vaccines in the immigrant population. CCIRH recommendations on updating vaccines are outlined in Box 1.

Methods

We used the 14-step method developed by the Canadian Collaboration for Immigrant and Refugee Health.¹¹ To identify relevant systematic reviews and guidelines to address the effectiveness of screening for measles, mumps, rubella, diphtheria, pertussis, tetanus (MMR/DPT) and Polio and the efficacy of MMR/DPT/Polio vaccination in the immigrant population, 5 electronic databases MEDLINE (Ovid), MEDLINE InProcess, EMBASE, CINAHL, and Cochrane Database of Systematic Reviews were searched from 1950 to January 14, 2010. The terms immigrant or refugee AND MMR/DPT/Polio were used and restricted to guidelines and systematic reviews. A similar search for systematic reviews and guidelines for MMR/DPT/Polio with the same objectives in the general population was performed for the same 5 databases but the search dates were restricted to Jan 1, 1996- January 14, 2010 and the immigrant/refugee term was removed. Any eligible systematic reviews were assessed for their application of a consistent and comprehensive approach, transparency (clarity about the process involved), quality of methods (appropriate methods and analysis) and relevance. We also searched the websites of official organizations that produce guidelines on immunizations up until September 6, 2010: the Canadian Task Force on Preventative Health Care (CTFPHC), the Public Health Agency of Canada (PHAC), the Canadian National Committee on Immunization (NACI), the U.S. Preventative Task Force (USPTF), Centre for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practice (ACIP), Infectious Disease Society of America (IDSA), National Institute of Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), and the World Health Organization (WHO).

We conducted a separate search for MMR/DPT/Polio and the immigrant/refugee population to address population specific concerns classified as; 1) baseline risk or prevalence in comparison to the Canadian born population; 2) risk of clinically important outcomes; 3) genetic and cultural factors (e.g. preferences values, knowledge); and 4) compliance variation (including at the primary care to search for population specific burden. We searched the terms MMR/DPT/Polio AND immigrants or refugees in 5 electronic databases MEDLINE, MEDLINE InProcess, CINAHL, Embase

and Cochrane Database of Systematic Reviews from 1950 to January 14, 2010. To increase retrieval of articles documenting important outcomes resulting from implementation of vaccination programs, we also performed a separate search with the terms MMR/DPT/Polio AND hospitalization or mortality in the same five electronic databases mentioned above but restricted the search from Jan 1, 1996 to December 2009 (Appendix 1).

Synthesis of evidence and values

We synthesized evidence from systematic reviews and pertinent cohort studies and clinical trials using the GRADE summary of findings tables which assesses both relative and absolute effects of interventions (relative risk and absolute event rate). We also appraised quality of each outcome using the GRADE quality assessment tool which assesses study limitations, directness, precision, consistency, and publication bias across all studies (Box 2). In the search and synthesis of data on clinical considerations we identified both clinically relevant considerations and implementation issues relevant to our population. Finally, we identified gaps in the research and evidence base.

Results

In the search for systematic reviews and guidelines for immigrants and MMR, DPT and polio, 242 records were identified and screened and none met eligibility criteria. There were three narrative reviews that addressed the need to review vaccines and update childhood vaccination in immigrants and adopted children but none used a systematic review method.¹²⁻¹⁴ In the search for systematic reviews and guidelines involving the general population AND MMR/DPT/polio, 6,293 articles were identified, 204 met eligibility criteria (were guidelines or reviews) but only 24 were included due to relevance, recency or quality. There were 9 guidelines^{4,15-22} and 15 systematic reviews that addressed epidemiology and control^{2,23}, vaccine efficacy²⁴⁻²⁶, vaccination adverse events²⁷⁻³², vaccine knowledge and compliance.³³⁻³⁶ A flow chart of these combined searches is outlined in Figure 1. In addition, a search for immigrant and MMR/DPT/Polio identified 1177 articles (duplicates removed) of which 54 were relevant and addressed the following areas; epidemiology, pre-vaccination screening, knowledge and compliance, treatment and vaccination in the immigrant population. A search for hospitalization or mortality AND MMR/DPT/polio was performed in which 3,888 articles were identified, 59 of which were relevant and 1 which was critical for this review.³

What is the burden of MMR/DPT/Polio in the immigrant population?

A large proportion of immigrants and refugees, particularly adults, are likely to be susceptible to vaccine preventable disease (VPD) due to under immunization, waning immunity, or both. This is because the WHO Extended Program on Vaccination (EPI) only began in the 1970s (includes measles, diphtheria, pertussis, tetanus, polio and BCG) and although programs were widely implemented in the 1980s, the effectiveness is highly variable (coverage ranging from 50% to 90%).¹⁰ In addition, many countries did not have rubella (56% of countries; only 4% of African and 18% South East Asian countries) or mumps (56% of countries; 4% of African and 9% of South East Asian countries) as part of their national schedules as reported by WHO in 2003.¹⁰ Immigrant children and adolescents are more likely to have received WHO EPI vaccines as compared to their parents however, many may not have received other vaccinations that are part of the routine childhood vaccination program in Canada (ie. rubella, mumps, varicella, *H. influenzae*, *S. pneumoniae*). Many immigrants, especially adults, do not have vaccination records, and when they are do, <50% of individuals were current according to the host country vaccination schedule in one study.^{37, 38}

Seroprevalence studies have consistently shown that a large proportion of adult immigrants are susceptible to rubella (~80-85% immune but as low as 75%) and tetanus (~50-60% immune in those 20-30 years of age and decreased with increasing age).^{37, 39-43} A higher than expected portion of immigrants are involved in rubella outbreaks and most reported cases of congenital rubella syndrome and neonatal tetanus over the past 20 years have occurred in children born to unimmunized foreign-born mothers.⁴⁴⁻⁴⁷ Seroprevalence studies of measles (most adults >95% immune) and mumps (80-92% immune but as low as 70%) in adult immigrants have generally shown adequate antibody levels, with some exceptions.^{37, 48} In addition, immigrants have not been over represented in recent measles and mumps outbreaks.^{5, 6, 49, 50} Diphtheria seroprevalence in immigrants is low (range 35-50%) and decreases or plateaus with age.^{41, 43} To maintain herd immunity in the population certain threshold levels of antibodies need to be maintained; 91-94% for measles, 90-92% for mumps, 83-85% for rubella, 80-85% for diphtheria, 80-85% for polio and 90-94% for pertussis.^{51, 52} Immigrants likely fall below this threshold for rubella and diphtheria and a large proportion are also susceptible to tetanus and at risk for the associated morbidity and mortality from this

disease.^{37, 39-41} Any population where a large proportion of individuals are susceptible to VPD will be at risk for disease transmission and outbreaks.

Does vaccination with MMR, DTaP/Tdap and Polio decrease associated morbidity and mortality?

Relative benefits and harms of vaccination

In the pre-vaccination era diseases such as measles, mumps, rubella, diphtheria, tetanus, pertussis, smallpox and polio were very frequent and were a major cause of morbidity and mortality. These diseases also had enormous societal and economic costs including, time off school and work, physician visits and hospitalizations. Childhood vaccination programs have decreased the morbidity from these disease by >92-99% and mortality by >99%.³ (See Summary of Findings Tables – Appendix 2) Childhood vaccination programs have repetitively been found to be one of the most cost-effective medical interventions.²

Measles, Mumps and Rubella (MMR)

Almost 100% of individuals are protected against measles after 2 doses and >95% protected after a single dose of rubella with antibodies persisting for at least 15 years.^{1, 53} Effectiveness of mumps vaccine is lower and depends on the vaccine strain used, time since vaccination and possibly the mismatch of the genotype of wild-type and vaccine virus.⁵⁴ In the recent US outbreaks the effectiveness of mumps vaccine was estimated to be as low as 64% after one dose and 79% after two doses (Jeryl Lynn strain).⁵⁴ MMR has been associated with fever (~5%), febrile convulsions (0.3%), benign thrombocytopenia purpura (<0.01%), parotitis (rarely), arthritis (up to 25% in post-pubertal women) usually within two weeks of vaccination.^{24, 29, 53} The frequency of adverse reactions in seronegative women however, is higher in those who have never been vaccinated than in revaccinated seronegative women.⁵³ In 1998 Wakefield et al. published a case-series of 12 children with development disorders and chronic gastrointestinal inflammation that sparked widespread concern that MMR was associated with autism. Subsequently, several studies have shown no association between MMR and autism, including a population based study of all Danish children born from 1991-1998 (>500,000) where no association between MMR and autism RR 0.92 (95% CI 0.68-1.24) was found.^{27, 28, 55}

MMR is a live attenuated vaccine that should be avoided in immunosuppressed individuals but can be given to HIV infected individuals with a mild to

moderate symptoms and a CD4 count >200 x 106/L or >15%.^{53,56}

Tetanus, Diphtheria, acellular Pertussis (DTaP, Tdap) and Polio

Diphtheria and tetanus vaccines are highly effective with >95% of individuals developing protective antibody levels after a primary series. Antibodies to diphtheria wane more rapidly than those for tetanus and persist for up to 10 years as compared to up to 25 years for tetanus.^{1,53} There is no immunologic correlate of protection for pertussis but DTaP has an approximate clinical protective efficacy of 85%.⁵³ Over 99% of vaccinees develop protective antibodies to all 3 serotypes of polio vaccine after 3 doses and a one-time booster in adulthood is required to maintain immunity. For those who have received a primary series of tetanus and diphtheria vaccine, booster doses for Td are recommended every 10 years to maintain immunity.⁵³ For individuals > 7 years of age who have not received a primary series should be given 3 doses of Td, the first one being Tdap to protect against pertussis. For wounds other than those that are clean or minor, a primary series of vaccine and also tetanus immune globulin should be given.⁵³ Given the facts that infants are the highest risk group at risk for developing severe pertussis, that adults are the main reservoir for pertussis and that antibodies wane overtime (5-10 years after a primary series), all adults should be given a one-time booster of Tdap.⁵³

Local pain, swelling, and erythema are common after DTaP administration and are reported in up to 40% of vaccinees, in 75% after Tdap vaccine and 60-70% after Td vaccine. Fever occurs in <5% during a primary series however DTaP and Tdap have not been associated with an increase risk of serious adverse events.^{1,30,32,53,30,32} In individuals with no or inadequate vaccination records there is concern that over-immunization with Td will lead to a higher incidence of local adverse reactions or

rare systemic reactions. Local reactions increase with the number of doses administered. Recent studies have shown that boosters of Tdap given to adolescents and adults <2 years since the last dose did not lead to an increase in moderate or severe injection site side effects.^{57,58} Persons who develop a serious adverse local reaction after administration of vaccines containing tetanus, diphtheria and pertussis should be individually assessed before they receive additional doses of these vaccines.⁵³

Serologic tests for immunity

Serologic tests for measles, mumps and rubella are generally available in many labs but they have differing abilities to predict protective antibody levels. Plaque reduction neutralization antibody test (PRNT) is the gold standard for detecting neutralizing antibody levels for measles, but this is time-consuming and requires trained personnel to perform. Certain enzyme immunoassays (EIAs) which are much easier to perform in routine labs correlate well with the neutralizing antibody.⁵⁹ Commercial EIAs are available to detect antibodies for rubella and results are reported in a standardized manner in international units (IU). It is generally agreed upon that a minimum of 10IU is required for protection however 15IU always provides protection.¹ There are several EIAs available to detect antibodies to mumps but there is no agreed upon correlate of immunity to mumps.⁶⁰ Serologic tests, including EIAs, for diphtheria and tetanus are not widely available. A cutoff of 0.1 IU/ml is to be protection against diphtheria but EIAs often overestimate immunity at this level (as compared to the gold standard Vero Cell Assay). EIAs are generally reliable to accurately determine tetanus antibodies at a cut-off 0.15 IU/mL.¹ There are no accepted correlates for protection for pertussis and there is no commercially available test. Polio serology is not

Table 1. Different available formulations for Diphtheria, Tetanus and Pertussis Vaccines

	Td (Adsorbed)	Tdap	DTPolio (Adsorbed)	DTaP	DTap-Hib-IPV
Trade Name	Decavac (Sanofi Pasteur)	Adacel (Sanofi Pasteur) Boostrix (GlaxoSmithKline)	Diphtheria and Tetanus Toxoids (for Pediatric use) (Sanofi Pasteur)	Daptacel (Sanofi Pasteur) Infanrix (GlaxoSmithKline)	Pentacel (Sanofi Pasteur) Infanrix-Hib-IPV (GlaxoSmithKline)
Diphtheria toxoid	2 Lf units	2-2.5 Lf units	6.7 Lf units	15-25 Lf units	15-25 Lf units
Tetanus toxoid	5 Lf units	5 Lf units	5 Lf units	5-10 Lf units	5-10 Lf units
Pertussis Toxoid	None	2.5-8 µg	None	10-25 µg	20-25 µg
FHA*		5-8 µg		5-25 µg	20-25 µg
Pertactin (PRN)		2.5-3 µg		3-8 µg	3-8 µg
Fimbriae		0-5 µg		0-5 µg	0-5 µg
Hemophilus	None	None	None	None	Yes
Influenza					
Polio	None	None	Yes	None	Yes
Age range	≥ 7 years	7-64 years	6 weeks to 6 years	6 weeks to 6 years	6 weeks to 6 years

* Filamentous hemagglutinin

routinely available.

Clinical considerations

Individuals without written vaccination records and pre-vaccination serotesting

All adults and children without written immunization records should restart a primary immunization schedule appropriate for their age.⁵³ An alternative, although, somewhat less practical approach is to test for antibodies to the major vaccine antigens and administer those vaccines to susceptible individuals. A limitation to this approach is that diphtheria, tetanus, and polio serology are not widely available and the patient needs to return for the results prior to starting a vaccination series. In one study it was less costly and more effective to vaccinate all if >80% had not completed the full DT vaccine series or if antibody seroprevalence to both diphtheria and tetanus was <51%.⁶¹

Presence of overseas vaccination records and adopted children

Children are more likely to have written immunization records than adults however, the optimal approach to those with vaccination records is challenging. Interpreting written records can be difficult due to language barriers and the fact that immunization schedules and products may differ from those used in Canada. In several studies of internationally adopted children with seemingly appropriate records many did not have serologic evidence of protective immunity (up to 30%) to the specific antigen. This discordance has been ascribed to falsification of records, breaches in cold chain in their countries of origin or due to poor host response due to malnutrition.⁶²⁻⁶⁵ Given this uncertainty the most conservative approach would be to give a full vaccination series.⁵³

What are the potential implementation issues?

Barriers to uptake of vaccination in children, adolescents and adults have been recently reviewed and summarized.^{4,33,66-70} Low socioeconomic status, low parental education, younger maternal age, lack of knowledge about the disease and vaccination, negative beliefs or attitudes towards immunization, fear of side-effects or risks or contraindications, lack of transport, inconvenient clinic hours and cost are important patient and parental barriers for childhood vaccination.^{33,66,67} Provider barriers to vaccination include lack of knowledge about indications and contraindications for vaccination (especially with the recent addition of new vaccines and complex schedules), logistical barriers (eg,

vaccine storage or capacity or lack of access to prior immunization records), missed visits and missed opportunities for immunization.⁶⁶ Additional vaccination barriers for adolescents and adults include lack of awareness of the need for vaccination by parents, patients and providers, the lack of routine well adolescent or well adult visits and the lack of coordinated immunization programs for these populations.^{4,68-71} For catch-up vaccinations that are not covered in provincial plans, cost is an important potential barrier to vaccine uptake.⁷²⁻⁷⁵

The data on vaccination coverage of immigrant children after arrival in a host country is mixed. In the United States, children and adults of racial or ethnic minorities consistently have lower immunization rates.⁷⁶⁻⁸¹ The generalizability of this data to other countries however, is unclear as, often when adjusted for socio-economic status and parental education (importance predictors of poor vaccine uptake) the effect of race is no longer significant.⁸¹⁻⁸³ In Canada and the UK (where many of the migrants are South Asian) immigrant children were more likely to be vaccinated as compared to the host population.⁸⁴⁻⁸⁸ This may be due to cultural factors particular to this community that favour immunization uptake. In contrast, in Spain, Germany, Austria and Holland immigrant children were less likely to have been vaccinated as compared to their host populations.⁸⁹⁻⁹² An interesting and consistent finding across many studies and several countries is that immunization rates appear to be higher in recently arrived immigrants, those with limited English proficiency and those who are less acculturated.^{80,85,88,93} This may be due to the fact that these communities may be shielded from anti-vaccine messaging that may be prominent in local media sources, increased trust of physicians or other unmeasured cultural factors.^{85, 88, 94}

We did not identify any studies that examined interventions to increase uptake of vaccines in immigrant populations however interventions to improve uptake of vaccinations in the general population has been recently systematically reviewed.^{34,35,95,96} The most effective interventions were instituting reminder or recall systems (median of 17% increased vaccine uptake), education of target populations and vaccine providers (increase by a median of 16% when combined with other interventions) and reducing out of pocket costs (increased by a median of 10%)^{34,35} Improving vaccination coverage in adults is a particular challenge and having standing orders where non-physicians prescribe or deliver vaccines to client populations by protocol without direct physician involvement increased

vaccine coverage by a median of 28% in adults and 51% overall.³⁴ Expanding access to vaccines in non-traditional settings (schools, work place, social gathering places such as church, sports clubs etc) may enhance uptake of vaccines for adolescents and adults although a recent systematic review did not find this to be statistically significant.^{4,34,68,69} Newly arrived immigrants and refugees, both children and adults, are less likely to be up to date with their immunizations and have barriers to uptake of vaccination including missed opportunities for vaccination.^{97,98}

Other recommendations

The National Advisory Committee on Vaccination (NACI) recommends that all persons without written vaccination records should receive an age appropriate primary series of vaccination. Adults with no records or an unclear history of prior immunization should receive a primary series of Td (3 doses one of which should be Tdap to protect against pertussis) as well as a primary series of polio as IPV (3 doses- 0, 4-8 wks and 6-12 mo). NACI also recommends that a single dose of MMR be given to adults born after 1970 and who do not have a history of measles or if they are seronegative for mumps or rubella.⁵³ Although polio vaccine is not included in the routine vaccination of adults, any adult who has not had a primary series and may potentially be in contact with polio (during travel etc) should be given a primary series of polio vaccine. Our recommendations highlight the importance of making primary care providers aware of the gaps in vaccination in newly arrived immigrants and refugees of all ages and the need to update MMR, DPT vaccines in this population.

The cases revisited

Maria originates from a country that only recently added rubella vaccine to its childhood vaccination program. She would have benefited from MMR vaccine soon after arrival in Canada or at any other time she may have come in contact with the health care system prior to her pregnancy.

Hong likely did not receive a primary series of DPT as a child as this would have been before the routine WHO EPI schedule would have been implemented in his country of origin. On arrival in Canada he should have received a primary series of Td. He has been living in Canada for 15 years and almost certainly had come in contact with the health care system at some time prior to the injury. Health care workers need to be made of these potential gaps in vaccination in the immigrant population

so they can take the opportunity to update vaccines when adults encounter the health care system for any reason.

Conclusions and research needs

A large proportion of newly arrived immigrants are susceptible to several childhood vaccine preventable diseases. Population based seroprevalence studies of childhood vaccine preventable disease in the immigrant populations are required to determine the groups of immigrants and refugees at greatest risk for these diseases. The optimal and most cost-effective approach to ensuring immunity in immigrants who have what appear to be adequate vaccination records still needs to be determined. Barriers to uptake of vaccination by the immigrant population need to be better defined so that effective programs to update vaccines can be designed. Primary care practitioners need to be made aware that immigrants are a group at increased risk for childhood vaccine preventable diseases and in order to improve the health of this population and they need to take all opportunities to update these vaccines (see Appendix 3).

Key points

- A large proportion of immigrants are susceptible to several childhood vaccine preventable diseases (esp. rubella, diphtheria and tetanus) and are at risk for associated morbidity and mortality
- Individuals susceptible to vaccine preventable diseases must be identified and vaccinated to maintain herd immunity and prevent outbreaks.
- Health care providers need to aware of these gaps and ensure that they take all opportunities to update vaccinations in newly arrived immigrants and refugee children and adults.

Box 2: Grading of Recommendations Assessment, Development and Evaluation Working Group grades of evidence (www.gradeworkinggroup.org)

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

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Clinical preventive guidelines for newly arrived immigrants and refugees

This document provides the review details for the CMAJ CCIHR MMR/DTP/Polio paper. The series was developed by the Canadian Collaboration for Immigrant and Refugee Health and published at www.cmaj.ca.

Appendix 1: Figure 1

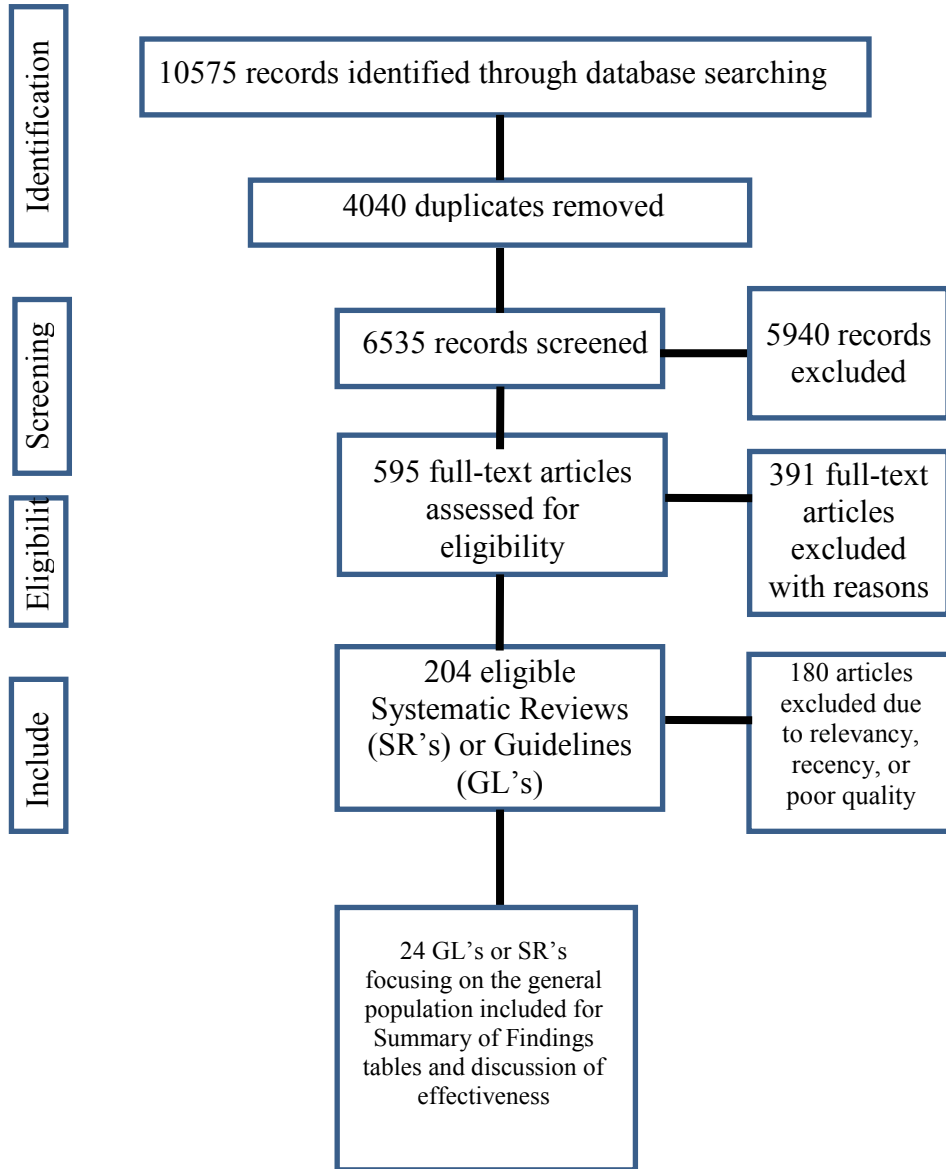


Figure 1: MMR/dpT/Polio Search for Systematic Reviews and Guidelines in the Immigrant/Refugee Population or General Population Selection Flow Sheet

Appendix 2: Summary of Findings Tables

MMR vaccine for preventing measles

Patient or population: patients with preventing measles

Settings: United States (general population)

Intervention: MMR vaccine

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Madsen et al. A population-based study of measles, mumps, and rubella vaccination and autism. N Engl J Med 2002;347:1477-82.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	MMR vaccine				
Cases of measles	¹ 530,217	² 55	N/A Absolute difference 530,162 (99.9% reduction)	0 (1 study)	high ^{3,4}	
Death from measles	¹ 440	⁵ 0	N/A Absolute difference 440 (100% reduction)	0 (1 study)	high ^{3,4}	
Autistic disorder	11 per 100,000 person-years	16 per 100,000 person-years	RR 0.92 (0.68 to 1.24) ⁶	0 (1 study)	moderate ^{3,7}	
Other autistic-spectrum disorders	16 per 100,000 person-years	21 per 100,000 person-years	RR 0.83 (0.65 to 1.07) ⁸	0 (1 study)	moderate ^{3,7}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ 1953-1962

² 2006

³ Only one paper

⁴ >90% reduction in absolute numbers

⁵ 2004

⁶ NNT (95% CI) = N/S [113,764 (-37,921, 28, 441)]

⁷ 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

⁸ NNT (95% CI) = N/S [36,850 (-89,492, 17,898)]

Vaccination for preventing rubella

Patient or population: patients with preventing rubella

Settings: United States (general population)

Intervention: vaccination

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Madsen et al. A population-based study of measles, mumps, and rubella vaccination and autism. N Engl J Med 2002;347:1477-82.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	vaccination				
Cases of rubella	¹ 47,745	² 11	N/A Absolute difference 47 734 (99.9% reduction)	0 (1 study)	high ^{3,4}	
Cases of congenital rubella syndrome	⁵ 152	² 1	N/A Absolute difference 151 (99.3% reduction)	0 (1 study)	high ^{3,4}	
Death from rubella	¹ 17	0	N/A Absolute difference 17 (100% reduction)	0 (1 study)	high ^{3,4}	
Autistic disorder	11 per 100,000 person-years	16 per 100,000 person-years	RR 0.92 (0.68 to 1.24) ⁶	2,129,864 (1 study)	moderate ^{3,7}	
Other autistic-spectrum disorders	16 per 100,000 person-years	21 per 100,000 person-years	RR 0.83 (0.65 to 1.07) ⁸	2,129,864 (1 study)	moderate ^{3,7}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ 1966-1968

² 2006

³ Only one paper

⁴ >90% reduction in absolute numbers

⁵ 1966-1969

⁶ NNT (95% CI) = N/S [113,764 (-37,921, 28, 441)]

⁷ 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

⁸ NNT (95% CI) = N/S [36,850 (-89,492, 17,898)]

Vaccination for preventing mumps

Patient or population: patients with preventing mumps

Settings: United States (general population)

Intervention: vaccination

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Madsen et al. A population-based study of measles, mumps, and rubella vaccination and autism. N Engl J Med 2002;347:1477-82.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	vaccination				
Cases of mumps	1 162 344	2 6584	N/A Absolute difference 155 760 (95.9% reduction)	0 (1 study)	high ^{3,4}	
Death from mumps	1 39	5 0	N/A Absolute difference 39 (100% reduction)	0 (1 study)	high ^{3,4}	
Autistic disorder	11 per 100,000 person-years	16 per 100,000 person-years	RR 0.92 (0.68 to 1.24) ⁶	2,129,864 (1 study)	moderate ^{3,7}	
Other autistic-spectrum disorders	16 per 100,000 person-years	21 per 100,000 person-years	RR 0.83 (0.65 to 1.07) ⁸	2,129,864 (1 study)	moderate ^{3,7}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ 1963-1968

² 2006

³ Only one paper

⁴ >90% reduction in absolute numbers

⁵ 2004

⁶ NNT (95% CI) = N/S [113,764 (-37,921, 28, 441)]

⁷ 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

⁸ NNT (95% CI) = N/S [36,850 (-89,492, 17,898)]

Vaccination for preventing tetanus

Patient or population: patients with preventing tetanus

Settings: United States (general population)

Intervention: vaccination

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk vaccination				
Cases of tetanus	¹ 580	² 41	N/A Absolute difference 539 (92.9% reduction)	(1 study)	high ^{3,4}	
Death from tetanus	¹ 472	⁵ 4	N/A Absolute difference 468 (99.2% reduction)	(1 study)	high ^{3,4}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ 1947-1949

² 2006

³ Only one paper

⁴ >90% reduction in absolute numbers

⁵ 2004

Vaccination for preventing diphtheria

Patient or population: patients with preventing diphtheria

Settings: United States (general population)

Intervention: vaccination

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk vaccination				
Cases of diphtheria	21 053	0	N/A Absolute difference 21 053 (100% reduction)	0 (1 study)	high	
Death from diphtheria	1822	0	N/A Absolute difference 1822 (100% reduction)	0 (1 study)	high	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Vaccination for preventing polio

Patient or population: patients with preventing polio

Settings: United States (general population)

Intervention: vaccination

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk vaccination				
Cases of acute polio	¹ 19,794	² 0	N/A Absolute difference 19 794 (100% reduction)	0 (1 study)	high ^{3,4}	
Death from acute polio	¹ 1,393	⁵ 0	N/A Absolute difference 1 393 (100% reduction)	0 (1 study)	high ^{3,4}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ 1941-1950

² 2006

³ Only one paper

⁴ >90% reduction in absolute numbers

⁵ 2004

Vaccination for preventing pertussis

Patient or population: patients with preventing pertussis

Settings: United States (general population)

Intervention: vaccination

Roush SW et al. Historical Comparisons of Morbidity and Mortality for Vaccine-Preventable Diseases in the United States. JAMA. 2007;298(18):2155-2163.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk vaccination				
Cases of pertussis	¹ 200,752	² 15,632	N/A Absolute difference 185 120 (92.2% reduction)	0 (1 study)	high ^{3,4}	
Death from pertussis	¹ 4,034	⁵ 27	N/A Absolute difference 4007 (99.3% reduction)	0 (1 study)	high ^{3,4}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ 1934-1943

² 2006

³ Only one paper

⁴ >90% reduction in absolute numbers

⁵ 2004

Appendix 3: MMR/DTP/Polio Evidence Based Clinician Summary Table

Measles Mumps and Rubella (MMR)

Vaccinate all adult immigrants without immunization records with 1 dose of MMR to reduce associated morbidity and mortality. Immigrant children with absent or uncertain vaccination records should be given age appropriate vaccination with MMR.

Diphtheria, Tetanus, Pertussis (DTaP/Tdap) and Polio

Vaccinate all adult immigrants without immunization records with a primary series of Td and IPV (3 doses) the first one of which should include Tdap to also protect against pertussis. Immigrant children with absent or uncertain vaccination records should be given age appropriate vaccination with diphtheria, tetanus, pertussis and polio.

Prevalence: Up to 36% of adult immigrants may be susceptible to one of measles, mumps for rubella. A large proportion of adult immigrants are susceptible to tetanus (~50-60% immune in those 20-30 years of age and decreased with increasing age) and 50%-65% are susceptible to diphtheria.

Burden: A higher than expected portion of immigrants are involved in rubella outbreaks and most reported cases of congenital rubella syndrome and neonatal tetanus have occurred in children born to unimmunized foreign-born mothers. Immigrants however, have not been more likely to be involved in measles or mumps outbreaks. Many immigrants likely fall below the threshold of population prevalence for herd immunity for rubella and diphtheria and are at risk for disease. A large proportion are also susceptible to tetanus and at risk for the associated morbidity and mortality from this disease.

Access to Care: Childhood vaccines are not routinely inquired about or updated in either children or adult immigrants before or after arrival in Canada. Primary care practitioners need to be made aware that newly arrived immigrants are a group at risk for childhood vaccine preventable diseases and need to remain vigilant in assessing and updating these vaccinations.

Key Risk Factors for MMR/DPT/Polio: Immigrants from countries with sub-optimal vaccine coverage may be at risk for childhood vaccine preventable diseases. Adults are at greater risk than children as they were born after the implementation of WHO EPI schedules.

Screening Tests: Serologic tests for measles, mumps and rubella are generally available in many labs but they have differing abilities to predict protective antibody levels. Serologic tests for diphtheria, tetanus is available only in a few labs in Canada, polio serology is only available in certain research settings and there is no serologic test for pertussis.

Vaccination: Childhood vaccination program have decreased the incidence of measles, mumps, rubella, diphtheria and tetanus by 99% as compared to the pre-vaccination period. Childhood vaccination programs are highly cost-effective and are cost-saving. Susceptible individuals must be identified and vaccinated to maintain herd immunity.

Special Considerations: MMR is a live attenuated vaccine and should be avoided in immunosuppressed individuals but can be given those with mild to moderate HIV and a CD4 count >200 mm/L.