

Recommendations for the Prophylactic Use of Analgesics and Antipyretics: Review of the Effect of Over the Counter Analgesics and Antipyretics on Adverse Events Following Immunization and Vaccine Efficacy

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Key Take Home Messages

- The advice provided by professional practice bodies and individual health care practitioners is inconsistent with respect to the prophylactic use of oral analgesics/antipyretics to prevent side effects associated with immunization.
- Research evidence has become available on the effectiveness of oral analgesics/antipyretics on the prevention of certain side effects associated with immunizations and their impacts on vaccine efficacy.
- The evidence does not support the prophylactic use of oral analgesics/antipyretics before or immediately after immunization to reduce pain at the time of vaccine injection or to prevent febrile seizures.
- There is no evidence to suggest that the prophylactic use of analgesics/antipyretics impacts the efficacy of vaccine.
- Analgesics/antipyretics can be used following immunization for treatment of pain or fever if it occurs.

Executive Summary

It is common practice for healthcare providers to recommend the prophylactic use of over the counter oral analgesics/antipyretics for children receiving immunizations. Over the past year Peel Public Health Nurses on the Immunization Services team in the Communicable Diseases Division became aware of an interdisciplinary discussion questioning the impact and effectiveness of this practice. A randomised control trial published in 2009 in the Lancet (6) suggested that the prophylactic use of paracetamol may interfere with antibody development following administration of some vaccines. The product monograph for SynflorixTM vaccine stated that “the use of prophylactic acetaminophen might reduce the immune response to SynflorixTM” (4). Additionally, in 2010 the Centre for Disease Control and Prevention (CDC) stated that all recommendations for prophylactic use of acetaminophen or other analgesics prior to or at the time of immunization were being removed from CDC publications and those of the American Academy of Paediatrics (AAP).

Peel Public Health Nurses (PHNs) had also been questioned internally about what Peel Public Health’s official position was on using analgesics/antipyretics prior to immunization. In light of the emerging evidence and the changes being made to recommendations from leading advisory bodies, a systematic review was conducted to answer the following questions:

- 1) What effect does the prophylactic use of over the counter (OTC) oral analgesics/antipyretics have on vaccine efficacy when given to people receiving immunizations?
- 2) What effect does the prophylactic use of OTC oral analgesics/antipyretics have on

adverse events following immunization (AEFI)?

Two clinical practice guidelines and one randomised controlled trial (RCT) were reviewed. The two clinical practice guidelines were found to be of strong and moderate quality and were recommended for use. The RCT was found to be of moderate quality and the authors indicated that the clinical relevance of their findings is unknown and requires further study.

The final recommendation of this systematic review is to continue advising clients against the routine use of oral analgesics/antipyretic prior to or immediately following immunization. Clients should be advised to use oral analgesics/antipyretics if symptoms occur. In addition, clients and healthcare providers should be provided with information on effective strategies for reducing pain at the time of immunization.

An applicability and transferability workshop was held with program staff to discuss the results of this review. The recommendations do not represent a substantial change to current practice and internal acceptability is high. Internal staff working in a number of program areas in Peel Public Health receive questions from their clients on this topic, therefore the results should be disseminated across the organization and tools provided to support effective knowledge translation. It is also recommended that Peel Public Health develop a communication strategy for local physicians and other health care providers so that they are aware of the results of the literature review and of Peel Public Health's recommendations.

Implementation of these recommendations will be undertaken by the Immunization Services

team. Previous literature reviews done at Peel Public Health have identified effective strategies to increase knowledge and change behaviour of health care providers. Those results will be used to inform the implementation of these recommendations.

1 Issue

Parents are often concerned about the pain of immunization and the potential for discomfort or other more serious side effects that may be experienced after immunization. Health care providers seek to address these concerns and offer advice on what to expect and how to prevent or respond to side effects. Over-the-counter analgesics and antipyretics such as acetaminophen and ibuprofen are often recommended by nurses, physicians and pharmacists for prevention of side effects associated with childhood immunizations (1). Currently the Canadian Immunization Guide – 7th ed. 2006 (2) recommends prophylactic acetaminophen in adults when immunized with the influenza vaccine to decrease the frequency of some side effects. The Canadian Paediatric Society’s “Myths and Facts” sheet on MMR also makes reference to using acetaminophen prophylactically to reduce pain caused by immunization (3).

Over the past year, Public Health Nurses (PHNs) on the Immunization Services team in the Communicable Diseases Division became aware of information suggesting that the use of oral analgesics/antipyretics prior to immunization may not be effective in preventing some of the adverse events for which they are used. In addition, early in 2010 there were discussions among health units regarding a statement in the SynflorixTM Product Monograph (4) that “the use of prophylactic acetaminophen might reduce the immune response to SynflorixTM”. The clinical relevance of this observation, as well as the impact of antipyretics other than acetaminophen, remains unknown.”(4). The statement did not point to clear evidence, and because it is not the practice of Peel Public Health Nurses to recommend prophylactic use of analgesics/antipyretics, no further investigation was undertaken. Then, during the Immunization Update 2010 Broadcast

that took place August 5, 2010 (5), the Center for Disease Control and Prevention (CDC) stated that all recommendations for prophylactic use of acetaminophen or other analgesics prior to or at the time of immunization were being removed from CDC publications and those of the American Academy of Paediatrics (AAP). Finally, the PHNs became aware of a study published in the Lancet (6) that suggested the use of analgesics/antipyretics may reduce the immune response to vaccine when given prophylactically immediately after to immunization

2 The Context

Public Health Nurses (PHNs) in the Vaccine Preventable Diseases programs are responsible for providing information about immunization to the general public, health care providers and clients they immunize. In the context of these roles PHNs encounter questions from the public regarding strategies to prevent pain and adverse events. In order to provide accurate advice Peel Public Health staff need to be aware of current evidence related to this topic.

A number of immunization advisory bodies provide recommendations to the public regarding the prophylactic use of analgesics/antipyretics to prevent immunization side effects in a variety published documents. Recently, some leading advisory bodies have updated their recommendation which has been a signal that previously accepted standard practice may be changing. Unfortunately, the recommendations provided are not consistent across advisory bodies and in some cases no recommendations are provided.

Table 1: Recommendations of Canadian and American advisory bodies on the prophylactic use of analgesics/antipyretics to prevent immunization side effects

Recommend prophylactic use of analgesics/ antipyretics	Recommend against prophylactic use of analgesics/ antipyretics	Alternative methods recommended	Recommend use of analgesics/ antipyretics but unclear about timing of administration
Canadian Coalition for Immunization Awareness and Promotion	<i>Centers for Disease Control</i> and Prevention (<i>CDC</i>)	Hospital for Sick Children: About Kids Health Website	Canadian Paediatric Society: Caring for Kids Website
Canadian Immunization Guide (7 th edition, 2006)	"The Pink Book"		Public Health Agency of Canada (PHAC)
Canadian Paediatric Society: Caring for Kids Website			<i>Centers for Disease Control</i> and Prevention (<i>CDC</i>)
Ministry of Health and Long Term Care (MOHLTC)			
Public Health Agency of Canada (PHAC)			

(see Appendix E for specific references)

3 An Anecdote

A PHN from the Immunization Services team provided an “Immunization Updates” presentation to an internal group of prenatal health educators. Members of the Immunization Services team had recently read a study by Prymula, R. et al. that had been published in the Lancet in 2009 (6), which suggested that giving paracetamol prophylactically at the time of immunization may impact the efficacy of vaccine. This study appeared to be of good quality and the PHNs creating the presentation decided to mention the study. When this information was shared during the “Immunization Updates” presentation, the prenatal educators had some good questions. What was Peel Public Health’s official position on using analgesic/antipyretics prophylactically and could they have the reference for the study? The PHN giving the presentation wasn’t prepared for these questions. She could have provided the reference for the study but it hadn’t been formally appraised by Peel Public Health staff. She didn’t believe that the findings in the Prymula, R. et al. study would result in a change of practice for Peel Public Health, but she also didn’t know if the current practice had been reviewed since the study was published.

The questions from the educators about the Lancet article had not been anticipated. However, upon reflection the PHN realized that the educators’ reaction made perfect sense. The use of analgesics/antipyretics prior to immunization is a longstanding and familiar practice. While health care providers may differ in the advice they give about the use of analgesics/antipyretics they would understand the intervention as either helpful or benign, no one would consider that it may be potentially harmful. In addition, parents work very hard to do ‘the best’ for their children. The suggestion that the use of analgesics/antipyretics prior to immunization was not

‘the best’ could be very upsetting for many parents.

Given this experience and the conversations that had been unfolding among immunization professionals, as well as Peel Public Health’s commitment to evidence informed decision making, it was agreed that a review of the literature and formal appraisal of the article in question be conducted. This would allow the Immunization Services team to determine if Peel Public Health’s position was still consistent with the available research evidence. Additionally, if the research suggested that it was harmful to use analgesics/antipyretics prior to immunization there would be a need to inform physicians and other healthcare providers in the Region of Peel. They would certainly have a similar reaction to that of the prenatal educators and Peel Public Health would need to help them understand the available evidence.

4 Literature Review & Critical Appraisal

Two plain language questions were used for the literature search:

- 1) What effect does the prophylactic use of over the counter (OTC) oral analgesics/antipyretics have on vaccine efficacy when given to people receiving immunizations?
- 2) What effect does the prophylactic use of OTC oral analgesics/antipyretics have on adverse events following immunization (AEFI)?

Question # 1: What effect does the prophylactic use of over the counter (OTC) oral analgesics/antipyretics have on vaccine efficacy when given to people receiving immunizations?

PICO #1

P = People receiving immunization

I = OTC analgesics/antipyretics

C = No intervention

O = Effect on vaccine efficacy

Inclusion Criteria:

- Single studies (high quality RCTs)
- Meta-analysis
- Systematic Reviews
- Evidence based clinical practice guidelines
- Studies that included the prophylactic use of acetaminophen, paracetamol, ibuprofen, aspirin, acetylsalicylic acid and naproxen (these were identified as the most commonly used over the counter analgesics and antipyretics)

Exclusion Criteria:

- Articles published before to July 1997 (due to changes in vaccines)
- Commentaries or discussion papers
- Published literature reviews that were not critically appraised by the authors
- Articles published in a language other than English

The following databases were searched: Medline full database, Medline in process and nonindexed citations and CINAHL1 resulting in 40 articles (see Appendix A for search strategies). Initially, the searches were limited to systematic reviews or meta-analyses. The final searches used in this review for the Medline databases were broadened to include single studies and were ultimately not limited to systematic reviews or meta-analyses. The CINAHL searches remained the same and were limited to systematic reviews or meta-analyses. Keywords and Medical Subject Headings (MESH) related to vaccination or immunization, over the counter oral analgesics/antipyretics and terms related to immune response, antibodies, effectiveness or protective factors were utilized in these searches. Thirty nine (39) articles were assessed as not relevant based on inclusion/exclusion criteria, one (1) randomised control trial (RCT) met the inclusion criteria: *Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody response in children: two open-label, randomised controlled trials* (6).

The article was critically appraised by three independent reviewers using the Critical Appraisal Skills Program (CASP) tool (7). All three reviewers were in agreement that the study was of moderate quality based on the following limitations in study design:

- Open label study – researchers and participants were not blinded to the intervention, however, laboratory staff analysing blood samples were blinded to group allocation.
- No power calculation to determine if the population studied was adequate.
- One (1) participant in the no intervention group received paracetamol prophylactically.

¹ CINAHL search terms are available upon request

- Self reporting by parents for incidence of fever and other solicited and unsolicited adverse events.

Question # 2: What effect does the prophylactic use of OTC oral analgesics/antipyretics have on adverse events following immunization (AEFI)?

PICO #2

P = People receiving immunization

I = OTC analgesics/antipyretics

C = No intervention

O = Effect on AEFI

Inclusion Criteria:

- Single studies
- Meta-analysis
- Systematic Reviews
- Evidence based clinical practice guidelines
- Studies that included the prophylactic use of acetaminophen, paracetamol, ibuprofen, aspirin, acetylsalicylic acid and naproxen (these were identified as the most commonly used over the counter analgesics and antipyretics)

Exclusion Criteria:

- Articles published before to July 1997 (due to changes in vaccines)
- Commentaries or discussion papers
- Published literature reviews that were not critically appraised by the authors
- Articles published in a language other than English

The following databases were searched: Medline full database, Medline in process and nonindexed citations, CINAHL1, Cochrane Database, as well as the National Collaborating Centre for Methods and Tools, health-evidence.ca, Canadian Paediatric Society, Centers for Disease Control and Prevention (CDC) and National Advisory Committee on Immunization (NACI) resulting in 46 articles (see Appendix A for search terms). Keywords and Medical Subject Headings (MESH) related to vaccination or immunization, over the counter oral analgesics/antipyretics and various adverse reactions were utilized in the searches in the Medline and CINAHL databases. Again, the final Medline searches were not limited to systematic reviews or meta-analyses. One (1) article was a duplicate and 43 were assessed as not relevant based on inclusion/exclusion criteria (see Appendix B). The two (2) remaining clinical practice guidelines met the inclusion criteria and were critically appraised using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool (8).

The two guidelines were critically appraised by five independent reviewers. The 2011 *Centres for Disease Control and Prevention: General Recommendations on Immunization* guideline was rated as strong in the following domains: Editorial Independence (98%), Scope and Purpose (92%) and Clarity of Presentation (83%). It received a moderate score for Rigour of Development (66%) and Stakeholder Involvement (67%). Due to differences in health care systems between the USA and Canada, the guideline was rated as weak in the area of Applicability (46%). However, these differences have no impact on the recommendation of interest to this review. Overall the guideline received a moderate rating of 73% and all reviewers recommended the guideline for use.

The 2010 *Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline* was rated strong in all domains: Scope and Purpose (99%), Stakeholder Involvement (89%), Rigour of Development (93%), Clarity of Presentation (100%), Applicability (99%) and Editorial Independence (100%). Overall the guideline received a strong rating of 97% and all reviewers recommended the guideline for use. (Appendix D: Agree II Scores).

5 Synthesis of Findings

Question #1: What effect does the prophylactic use of over the counter (OTC) oral analgesics/antipyretics have on vaccine efficacy when given to people receiving immunizations?

There is no evidence that the prophylactic use of analgesics/antipyretics impacts the efficacy of vaccine.

No synthesized evidence was found on the effects of using analgesics/antipyretics prophylactically on vaccine efficacy. One RCT was assessed for quality:

- 1) *Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody response in children: two open-label, randomised controlled trials (6).*

This open-label, unblinded study was designed to determine the effect of prophylactic paracetamol on febrile reactions, minor side effects and antibody concentrations following immunization. Study participants were randomly assigned to intervention and control groups. Participants in the intervention group received one dose of paracetamol via suppository immediately after vaccine administration and two subsequent doses of paracetamol administered 6-8 hours apart. The control group did not receive a placebo. Only the results on the impact of prophylactic paracetamol following immunization on antibody concentrations are reported in this review.

In phase one of the study, a primary series of vaccine was administered at ages 3, 4 and 5 months of age. In phase two, a booster dose was administered between 12 and 15 months of age.

Table 2: Immunization schedule used in the Prymul, R. et al. study, 2009

Age	Vaccine Name	
	Intramuscular Injection (IM)	Oral
3 & 4 months	PHiD-CV* DTPa-HBV-IPV/Hib**	HRV [±]
5 months	PHiD-CV DTPa-HBV-IPV/Hib	
12-15 months	PHiD-CV DTPa-HBV-IPV/Hib	

* Ten valent pneumococcal non-typable *Haemophilus influenza* protein D-conjugate vaccine

**Hexavalent diphtheria-tetanus-3-component acellular pertussis - hepatitis B inactivated poliovirus types 1, 2 and 3 - *H influenza* type b vaccine

± Human rotavirus

Blood samples were collected before the primary and booster doses were administered and one month after completion of the primary series and one month following the booster dose. The researchers observed that there were statistically significant differences in the antibody response/antibody concentrations for some vaccine serotypes between the intervention and control groups. Despite reduced antibody response/concentrations in the group receiving paracetamol prophylactically, following the primary vaccine series, almost all (96%) of children had seroprotective antibody concentrations against *H influenzae* type b, diphtheria, tetanus, hepatitis B and three acellular Pertussis antigens. All children were seropositive for poliovirus types 1, 2 and 3. Rotavirus seroconversion rates were in the same range for both groups.

Based on the immunogenicity results from the primary vaccine series, the study protocol was changed and prophylactic paracetamol was discontinued for children who were in the

intervention group who had not yet received their booster dose. This created a third study group: children who received prophylactic paracetamol with their primary series of vaccine but did not receive prophylactic paracetamol with their booster dose.

Blood tests collected before the booster dose showed that antibody concentrations for all vaccine serotypes were lower in children who had received paracetamol prophylactically and fewer children had protective antibody concentration levels than the group that did not receive prophylactic paracetamol. However, the authors stated “one (1) month after booster, antibody concentrations were similar for all antigens, apart from tetanus, in groups receiving or not receiving prophylactic paracetamol.”(6) There was a statistically significant difference in the Geometric Mean Concentration/Titre (GMC/T) for antitetanus, however seroprotective levels for antitetanus were achieved in all children in all groups.

Given the importance of vaccine efficacy there was interest in determining if the RCT by Prymula, R. et al. had informed the two guidelines that were reviewed. In the guideline published in the Canadian Medical Association Journal in December 2010, *Reducing the pain of Childhood Vaccination: An Evidence-Based Clinical Practice Guideline* (9) the authors do include Prymula, R. et al. but do not make a recommendation based on this study. They do use the findings to make a statement that “...recent data have indicated that this type of drug [acetaminophen] may interfere with the immunogenicity of common childhood vaccines. As a result of these data, this practice is being questioned.”(9)

Turning to the Centre for Disease Control and Prevention (CDC) Guideline, an enquiry was

made of the (CDC) to determine if they had considered the study by Prymula R. et al. when developing their recommendations. In email communication with Dr. Kroger at the CDC, the primary author of their guideline, he indicated that the CDC had become aware of the Prymula, R. et al. article and had consulted the Advisory Committee on Immunization Practices (ACIP) for their opinion. ACIP determined that “...the study did not provide enough evidence to warrant restricting antipyretic use...” but left the decision on how to proceed with the CDC. Dr. Kroger indicated that many members felt that antipyretics are overused when given prior to vaccination. This concern in combination with research that indicates that prophylactic use of antipyretics is not effective to prevent febrile seizures (see next section) prompted the change of language in the CDC guideline.

In conclusion, there is no evidence to say that the prophylactic use of antipyretics/analgesics reduces the efficacy of vaccine. However, the possibility of harm has been a catalyst for reconsideration of prophylactic use of analgesics/antipyretics. In the guidelines there is a move toward endorsement of a more cautious principle to only use medications to treat symptoms that are present.

Question #2: What effect does the prophylactic use of OTC oral analgesics/antipyretics have on adverse events following immunization (AEFI)?

The evidence does not support the prophylactic use of analgesics/antipyretics before or at the time of immunization to reduce pain at the time of vaccine injection or for prevention of febrile seizure. Delayed, minor adverse events may be reduced by prophylactic use of acetaminophen.

Two clinical practice guidelines met the inclusion criteria were assessed for quality:

- 1) *Centres for Disease Control and Prevention: General Recommendations on Immunization, 2011* (10)
- 2) *Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline, 2010* (9)

The evidence related to the impact of prophylactic use of analgesics/antipyretics on potential adverse effects of immunization addresses two effects: acute pain at time of vaccine injection and febrile seizures. Both guidelines are in agreement that the evidence does not support the prophylactic use of oral analgesics/antipyretics to prevent acute pain at the time of vaccine injection. Additionally, the CDC guideline indicates that evidence does not support the prophylactic use of analgesics/antipyretics to prevent febrile seizures. Both guidelines provide similar recommendations for effective alternative methods for alleviating acute pain at the time of vaccine administration which may be useful in a clinical setting.

The Taddio, et al. guideline, *Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline* includes a section titled “Clinical Considerations” in which they suggest that the prophylactic use of acetaminophen may reduce delayed minor adverse events following immunization (AEFIs) (9). This statement referenced the Prymula, R. et al. article which studied the effect of prophylactic paracetamol on the rate of febrile reactions. The authors of this study found that the incidence of low grade fever (<39°C) were significantly reduced in the group receiving paracetamol prophylactically when compared to the no prophylactic paracetamol group. High grade fevers (>39°C) were uncommon in both groups.

6 Applicability & Transferability

The findings in the literature are transferable to Peel Public Health's population. While internal and external stakeholders will require different types of communication, overall acceptability of the recommendations is expected to be high. The outcome of this review is consistent with Peel Public Health's current position to not recommend analgesics/antipyretics prophylactically to prevent adverse events following immunization. Externally, some professional advisory bodies and individual practitioners continue to recommend prophylactic use of oral analgesics/antipyretics. Communicating the results of this review will provide opportunities for Region of Peel health care providers to access the evidence on this topic and for dialogue on evidence based practice options.

6.1 Political Acceptability

Given that some health care organizations recommend the use of antipyretics/analgesics prophylactically, some debate and or resistance among health care providers may ensue. It is anticipated that communication with these organizations and health care providers in reference to emerging evidence may mitigate any resistance that occurs.

Internally there is no change to practice regarding the prophylactic use of analgesics/antipyretics, however there is some inconsistency among Peel Public Health staff regarding the advice given to clients if symptoms occur. Some nurses advise clients to use medication that they normally use to treat fever and pain when they occur, others recommend consulting with a physician or a pharmacist. The advice given by nurses is most influenced by the interpretation of the scope of practice guidance provided by the College of Nurses. It will be beneficial to liaise with the

College of Nurses of Ontario (CNO) to clarify their position on nurses' scope of practice when advising clients on the management of fever/pain that results from immunization.

Among political decision makers it is anticipated that there will be moderate or strong support of Peel Public Health's position as the Regional Council is likely to be in support of any program decisions made through an evidence based decision making process. Currently the use of analgesics/antipyretics is not a controversial topic in government and there is no expectation that there will be opposition by the Regional government.

Implementation of this intervention is not a direct priority within Peel Public Health's 10-Year Strategic Plan; however the process of reaching this decision is consistent with Peel Public Health's strategic plan to become a leader in Evidence Informed Decision Making to improve Peel Public Health program practices.

6.2 Social Acceptability

Socially, Peel Public Health's position will be moderately or strongly supported. Peel Public Health may be seen as progressive, reliable, and transparent in its method of responding to emerging health issues.

Staff will likely accept the decision as it will have a modest impact on programs and job roles. Parents may receive different advice from their health care provider than from Peel Public Health. Communication gaps between external health care providers and Peel Public Health could lead to confusion or conflict of information for clients and will need to be addressed.

The potential impact of the recommendations in a culturally diverse population may be related to the client's level of eagerness to medicate or to take the advice of a health care provider, as well as cultural acceptability of non-medical interventions across populations and socio economic status; however clarifying information for clients may be viewed as helpful.

6.3 Resources

The implementation of this intervention is achievable within the Communicable Diseases Division resources. The impact of this decision on the workload of staff is expected to be moderate. Promoting new immunization messaging falls within the role of the Immunization Services team. A strategy will be developed for the dissemination of this information to health care practitioners in Peel, internally and externally. Both of the guidelines reviewed provide alternative pain management techniques that may be worth integrating into health care providers' practices.

6.4 Magnitude of Change

The degree to which health care providers' recommend the use of the prophylactic analgesics/antipyretics prior to or at the time of immunization is unclear. It is anticipated that application of advice grounded in good quality evidence will guide health care providers in their practices.

7 Recommendations

Based on the evidence it is recommended that Peel Public Health:

- 1) Continue to advise clients against the routine use of oral analgesics/antipyretics prior to immunization. If clients are concerned about the prevention of minor adverse effects they should be advised to monitor themselves or their children following immunization for side effects. Analgesics/antipyretics can be given if pain or fever occurs.
- 2) Utilize knowledge transfer opportunities to inform clients and internal and external health care providers of the current research and of alternate methods to manage pain at the time of vaccine injection.

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Appendices

Appendix A: Search Terms

Appendix B: Literature Search Flow Charts

Appendix C: Search Strategy

Appendix D: Data Extraction Tables

Appendix A: Search Terms

PICO Question #1: What effect does the prophylactic use of over the counter (OTC) oral analgesics/antipyretics have on vaccine efficacy when given to people receiving immunizations?

Medline Search Terms:

Database: Ovid MEDLINE(R) <1948 to July Week 3 2011>

Search Strategy:

-
- 1 Acetaminophen/ (12230)
 - 2 acetaminophen.tw. (8097)
 - 3 paracetamol.tw. (6353)
 - 4 Ibuprofen/ (5810)
 - 5 ibuprofen.tw. (7485)
 - 6 Aspirin/ (34455)
 - 7 aspirin.tw. (30643)
 - 8 Naproxen/ (3039)
 - 9 naproxen.tw. (3900)
 - 10 exp Vaccination/ (48873)
 - 11 exp Immunization/ (120725)
 - 12 prophylaxis.tw. (58179)
 - 13 10 or 11 (120725)
 - 14 (acetylsalicylic adj acid).tw. (6411)
 - 15 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 14 (71660)
 - 16 immune response.tw. (83665)
 - 17 antibody.tw. (364125)
 - 18 Antibody Formation/ (56782)
 - 19 16 or 17 or 18 (461681)
 - 20 13 and 15 and 19 (13)
 - 21 vaccinat\$.tw. (81014)
 - 22 immuniz\$.tw. (92315)
 - 23 immunis\$.tw. (8016)
 - 24 10 or 11 or 21 or 22 or 23 (216559)
 - 25 prophlactic\$.tw. (3)
 - 26 premedicat\$.tw. (7134)
 - 27 pre-medicat\$.tw. (337)
 - 28 pre medicat\$.tw. (337)
 - 29 meta-analysis.mp,pt. (46978)
 - 30 (search or systematic review or medline).tw. (147990)
 - 31 cochrane database of systematic reviews.jn. (7668)
 - 32 guideline\$.ti. (37726)
 - 33 29 or 30 or 31 or 32 (213075)
 - 34 vaccine response\$.tw. (476)

- 35 immunit\$.tw. (97398)
- 36 protect\$.tw. (407684)
- 37 effectiveness.tw. (199104)
- 38 16 or 17 or 18 or 34 or 35 or 36 or 37 (1078375)
- 39 12 or 25 or 26 or 27 or 28 (65481)
- 40 15 and 24 and 33 and 38 (3)
- 41 15 and 24 and 38 (84)
- 42 limit 41 to yr="2009 -Current" (8)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 28, 2011>
Search Strategy:

-
- 1 acetaminophen.tw. (359)
 - 2 paracetamol.tw. (339)
 - 3 ibuprofen.tw. (291)
 - 4 aspirin.tw. (1212)
 - 5 naproxen.tw. (170)
 - 6 prophylaxis.tw. (2100)
 - 7 adverse.tw. (10876)
 - 8 fever.tw. (5440)
 - 9 pain.tw. (16376)
 - 10 soreness.tw. (118)
 - 11 erythema.tw. (737)
 - 12 swelling.tw. (2897)
 - 13 redness.tw. (163)
 - 14 inflammation.tw. (9095)
 - 15 (acetylsalicylic adj acid).tw. (186)
 - 16 meta-analysis.mp.pt. (2328)
 - 17 (search or systematic review or medline).tw. (11911)
 - 18 cochrane database of systematic reviews.jn. (119)
 - 19 guideline\$.ti. (1862)
 - 20 16 or 17 or 18 or 19 (14864)
 - 21 febrile.tw. (785)
 - 22 seizure\$.tw. (2477)
 - 23 anaphyla\$.tw. (635)
 - 24 vaccinat\$.tw. (3705)
 - 25 immunis\$.tw. (295)
 - 26 immuniz\$.tw. (2794)
 - 27 premedicat\$.tw. (187)
 - 28 pre-medicat\$.tw. (19)
 - 29 pre medicat\$.tw. (19)
 - 30 27 or 28 or 29 (203)
 - 31 prophylactic\$.tw. (1833)
 - 32 6 or 27 or 28 or 29 or 31 (3829)

- 33 1 or 2 or 3 or 4 or 5 or 15 (2274)
- 34 6 or 31 (3637)
- 35 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 21 or 22 or 23 (45454)
- 36 24 or 25 or 26 (6000)
- 37 27 or 28 or 29 or 34 (3829)
- 38 1 or 2 or 3 or 4 or 5 (2158)
- 39 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 21 or 22 or 23 (45454)
- 40 20 and 36 and 38 and 39 (0)
- 41 37 and 38 and 39 (25)
- 42 36 and 41 (5)
- 43 antibod\$.tw. (14898)
- 44 (immune adj response).tw. (2943)
- 45 response\$.tw. (66581)
- 46 protect\$.tw. (19515)
- 47 effectiveness.tw. (11464)
- 48 43 or 44 or 45 or 46 or 47 (104031)
- 49 33 and 34 and 36 and 48 (3)
- 50 33 and 36 and 48 (8)

PICO Question #2: What effect does the prophylactic use of OTC oral analgesics/antipyretics have on adverse events following immunization (AEFI)?

Medline Search Terms:

Database: Ovid MEDLINE(R) <1948 to July Week 3 2011>

Search Strategy:

-
- 1 Acetaminophen/ (12230)
 - 2 acetaminophen.tw. (8097)
 - 3 paracetamol.tw. (6353)
 - 4 Ibuprofen/ (5810)
 - 5 ibuprofen.tw. (7485)
 - 6 Aspirin/ (34455)
 - 7 aspirin.tw. (30643)
 - 8 Naproxen/ (3039)
 - 9 naproxen.tw. (3900)
 - 10 exp Vaccination/ (48873)
 - 11 exp Immunization/ (120725)
 - 12 exp Fever/ (30743)
 - 13 exp Pain/ (267539)
 - 14 prophylaxis.tw. (58179)
 - 15 adverse.tw. (206227)
 - 16 fever.tw. (97629)
 - 17 pain.tw. (309049)
 - 18 soreness.tw. (1426)

- 19 Erythema/ (8506)
- 20 erythema.tw. (18214)
- 21 swelling.tw. (46229)
- 22 redness.tw. (2882)
- 23 inflammation.tw. (180441)
- 24 10 or 11 (120725)
- 25 (acetylsalicylic adj acid).tw. (6411)
- 26 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 25 (71660)
- 27 meta-analysis.mp.pt. (46978)
- 28 (search or systematic review or medline).tw. (147990)
- 29 cochrane database of systematic reviews.jn. (7668)
- 30 guideline\$.ti. (37726)
- 31 27 or 28 or 29 or 30 (213075)
- 32 febrile.tw. (20143)
- 33 seizure\$.tw. (69604)
- 34 seizures/ or seizures, febrile/ (38394)
- 35 anaphyla\$.tw. (17658)
- 36 Anaphylaxis/ (14879)
- 37 vaccinat\$.tw. (81014)
- 38 immunis\$.tw. (8016)
- 39 immuniz\$.tw. (92315)
- 40 12 or 13 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 32 or 33 or 34 or 35 or 36 (1044282)
- 41 10 or 11 or 37 or 38 or 39 (216559)
- 42 premedicat\$.tw. (7134)
- 43 pre-medicat\$.tw. (337)
- 44 pre medicat\$.tw. (337)
- 45 42 or 43 or 44 (7442)
- 46 prophylactic\$.tw. (50181)
- 47 14 or 42 or 43 or 44 or 46 (107266)
- 48 26 and 31 and 40 and 41 and 47 (1)
- 49 26 and 31 and 40 and 41 (6)
- 50 26 and 40 and 41 and 47 (10)
- 51 26 and 40 and 41 (103)
- 52 limit 51 to yr="2009 -Current" (12)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 28, 2011>

Search Strategy:

-
- 1 acetaminophen.tw. (359)
 - 2 paracetamol.tw. (339)
 - 3 ibuprofen.tw. (291)
 - 4 aspirin.tw. (1212)
 - 5 naproxen.tw. (170)
 - 6 prophylaxis.tw. (2100)
 - 7 adverse.tw. (10876)

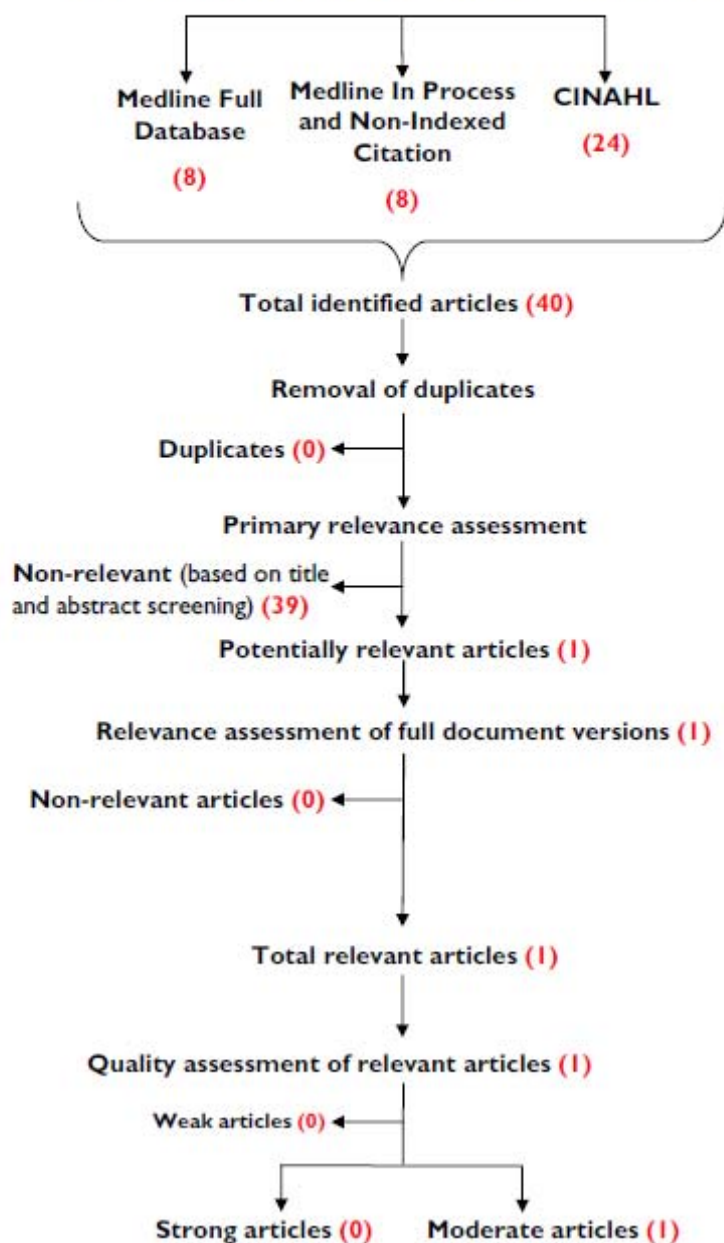
-
- 8 fever.tw. (5440)
 - 9 pain.tw. (16376)
 - 10 soreness.tw. (118)
 - 11 erythema.tw. (737)
 - 12 swelling.tw. (2897)
 - 13 redness.tw. (163)
 - 14 Inflammation.tw. (9095)
 - 15 (acetylsalicylic adj acid).tw. (186)
 - 16 meta-analysis.mp,pt. (2328)
 - 17 (search or systematic review or medline).tw. (11911)
 - 18 cochrane database of systematic reviews.jn. (119)
 - 19 guideline\$.ti. (1862)
 - 20 16 or 17 or 18 or 19 (14864)
 - 21 febrile.tw. (785)
 - 22 seizure\$.tw. (2477)
 - 23 anaphyla\$.tw. (635)
 - 24 vaccinat\$.tw. (3705)
 - 25 immunis\$.tw. (295)
 - 26 immuniz\$.tw. (2794)
 - 27 premedicat\$.tw. (187)
 - 28 pre-medicat\$.tw. (19)
 - 29 pre medicat\$.tw. (19)
 - 30 27 or 28 or 29 (203)
 - 31 prophylactic\$.tw. (1833)
 - 32 6 or 27 or 28 or 29 or 31 (3829)
 - 33 1 or 2 or 3 or 4 or 5 or 15 (2274)
 - 34 6 or 31 (3637)
 - 35 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 21 or 22 or 23 (45454)
 - 36 24 or 25 or 26 (6000)
 - 37 27 or 28 or 29 or 34 (3829)
 - 38 1 or 2 or 3 or 4 or 5 (2158)
 - 39 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 21 or 22 or 23 (45454)
 - 40 20 and 36 and 38 and 39 (0)
 - 41 37 and 38 and 39 (25)
 - 42 36 and 41 (5)

Appendix B: Literature Search Flow Charts



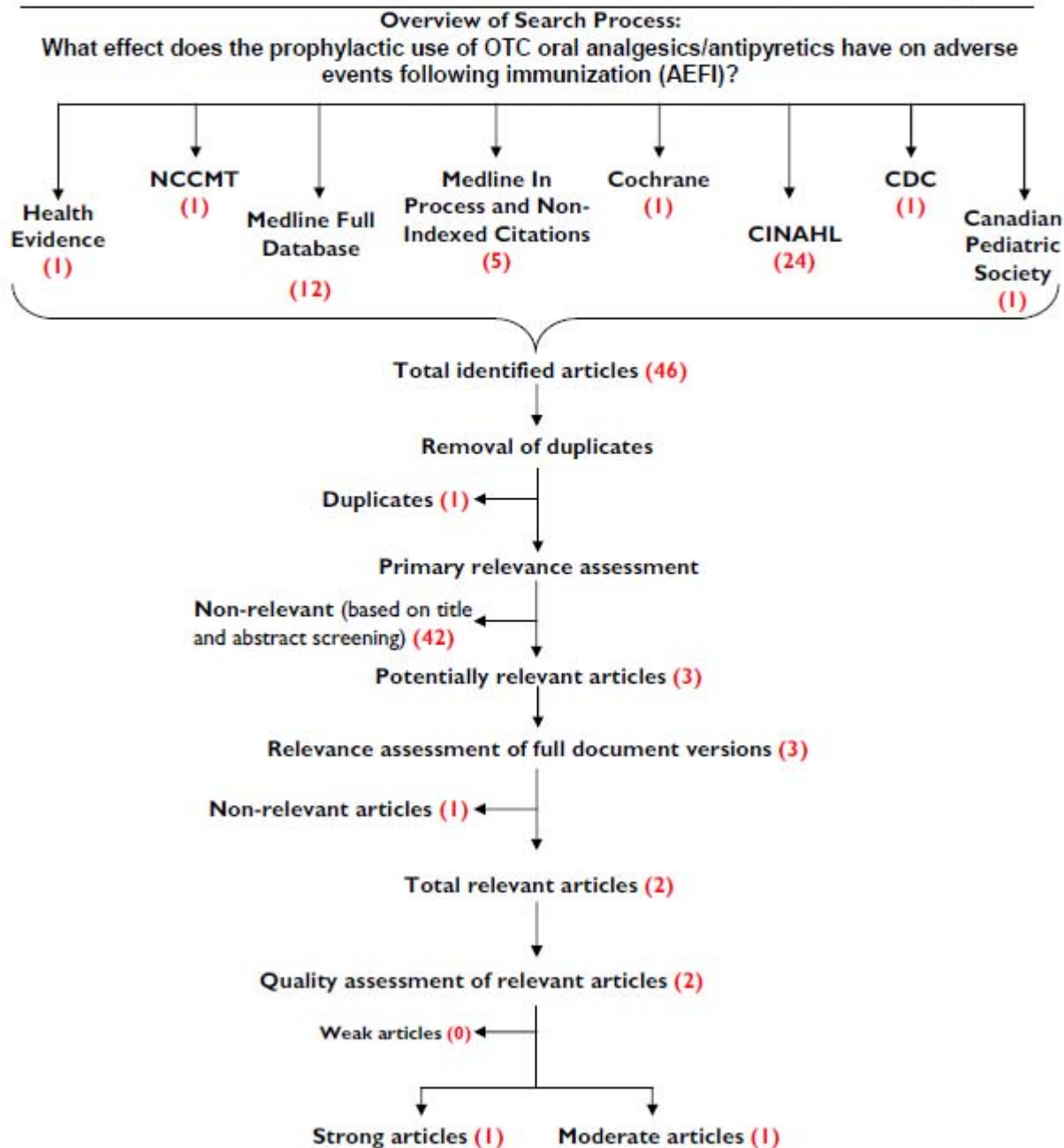
Health units are welcome to adapt this tool.
 Requirements for adapting this tool include: Health Evidence is acknowledged for tool development; adapted tool cannot be used for profit (not to be sold).

Overview of Search Process:
What effect does the prophylactic use of OTC oral analgesics/antipyretics have on vaccine efficacy when given to people receiving immunizations?





Health units are welcome to adapt this tool.
 Requirements for adapting this tool include: Health Evidence is acknowledged for tool development; adapted tool cannot be used for profit (not to be sold).



Appendix C: Data Extraction Table

General Info/ Quality Rating	Key Strengths & Weaknesses	Intervention of Interest for this Review	Outcome Measurements	Results of Review
<p>Centres for Disease Control - General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). Kroger, A, et al.</p> <p>Published in: USA, updated on January 28, 2011.</p> <p>The guideline reviewed 239 articles and is produced by ACIP.</p> <p>Population: Persons of various ages receiving vaccinations.</p> <p>Intended Audience: Clinicians and other health care vaccination providers.</p> <p>Rated by 5 Peel Public Health reviewers using the <u>Agree II Instrument</u>: Scope & Purpose = 92% Stakeholder Involvement = 67% Rigour of Development = 66% Clarity & Presentation = 83% Applicability = 46% Editorial Independence = 98% Overall Guideline Assessment = 73% Guideline Recommended for</p>	<p>The appropriate stakeholders were involved in developing the guideline.</p> <p>The recommendations are clear and well presented in text and tables.</p> <p>The recommendations are clearly linked to the evidence.</p> <p>“When data permit, specific rules of evidence – such as those followed by the U.S. Preventative Services Task Force – are used to judge the quality of data and to make decision regarding the nature and strength of recommendations.” (10) However, the quality rating for each recommendation is not provided.</p> <p>No search criteria are provided but the U.S. Preventative Services Task Force searches at least the MEDLINE English-language database and the Cochrane Collaboration Library.</p> <p>No inclusion/exclusion criteria are provided for the selection of the evidence.</p>	<p>The guideline provides recommendations for vaccination against 17 vaccine preventable diseases.</p> <p>The intervention of interest to this review: Vaccine Administration: Methods for Alleviating Discomfort and Pain Associated with Vaccination.</p>	<p>Benefit: Reduced Adverse Effects Following Immunization (e.g. pain, febrile seizures, etc.)</p>	<p>“Evidence does not support the use of antipyretics before or at the time of vaccination; however they can be used for the treatment of fever and local discomfort that might occur following vaccination.” (pg. 16) (10)</p>

General Info/ Quality Rating	Key Strengths & Weaknesses	Intervention of Interest for this Review	Outcome Measurements	Results of Review
Use: Yes	The U.S. Preventative Services Task Force published methods were used to rate questions related to methods for this guideline. (11-13)			
<p><i>Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline.</i> Taddio, A, et al.</p> <p>Published in: Canada, December 14, 2010.</p> <p>71 studies were evaluated which included 8050 children.</p> <p>Population: Children 0 – 18 years of age.</p> <p>Intended Audience: Vaccination providing clinicians.</p> <p>Rated by 5 Peel Public Health reviewers using the <u>Agree II Instrument</u>: Scope & Purpose = 99% Stakeholder Involvement = 89% Rigour of Development = 93% Clarity & Presentation = 100% Applicability = 99% Editorial Independence = 100% Overall Guideline Assessment = 97% Guideline Recommended for Use: Yes</p>	<p>The appropriate stakeholders were involved in developing the guideline.</p> <p>The guideline was externally reviewed by relevant experts using the Agree Instrument and their feedback was incorporated into the document.</p> <p>The recommendations were clear and well presented and implementation tools are provided.</p> <p>The recommendations are clearly linked to the evidence and each recommendation is rated according to the quality of the available evidence (see Table 1, pg.E844). (9)</p> <p>No search criteria are provided but the methods are based on the U.S. Preventative Services Task Force which searches at least the MEDLINE English-language database and the Cochrane Collaboration</p>	<p>The guideline provides recommendations on 18 vaccination pain management interventions.</p> <p>The intervention of interest to this review: #18. Oral Analgesics</p>	<p>Benefit: Reduced pain at the time vaccination.</p> <p>Harm: reduction of vaccine immunogenicity.</p>	<p>Benefit: Grade I recommendation based on Level III evidence: “The evidence does not support the use of antipyretics before or at the time of vaccination to reduce the pain associated with vaccination.”(pg. E852) (9)</p> <p><u>Grade I Recommendation:</u> There is insufficient evidence (in quantity or quality or both) to make a recommendation; however, other factors may influence decision-making.</p> <p><u>Level III Evidence:</u> Opinions of respected authorities, based on clinical experience; descriptive studies of expert committees.</p> <p>Harm: “...recent data have indicated that this type of drug [acetaminophen] may interfere with the immunogenicity of common childhood vaccines. As a result</p>

General Info/ Quality Rating	Key Strengths & Weaknesses	Intervention of Interest for this Review	Outcome Measurements	Results of Review
	<p>Library.</p> <p>Evidence was limited to randomised control trails (RCT's) and studies with quasi-experimental design.</p> <p>Evidence was appraised based on the published methods used by the U.S. Preventative Services Task Force.</p> <p>The U.S. Preventative Services Task Force published methods were used to rate questions related to methods for this guideline. (11-13)</p>			of these data, this practice is being questioned.” (pg. E852) (9)

General Info/ Quality Rating	Methods	Randomisation	Intervention	Results
<p><i>Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody response in children: two open-label, randomised controlled trial</i> Prymula, R., et al.</p> <p>Czech Republic</p> <p>Published October 17, 2009</p> <p>The study “assessed the effect of the prophylactic administration of paracetamol at the time of vaccination and within the next 24 h on the rate of febrile reactions and vaccine response in</p>	<p>Open label, randomised control trial conducted in two consecutive phases.</p> <p>Children were recruited from ten centres in Czech Republic from Sept 18, 2006 to April 10, 2007 and July 2, 2007 and April 2008.</p> <p>Phase one participants were healthy infants aged 9-16 weeks at time of enrolment and primary vaccination.</p> <p>Phase two participants were</p>	<p>Children were randomly assigned to intervention and control groups (1:1) using a computer program with a blocking scheme to ensure balance between groups. The investigator was not aware of the randomisation block size.</p> <p>Children retained their original group assignment for both phase one and two of the study.</p> <p>The control group did not receive a placebo therefore</p>	<p>Primary series of a ten valent pneumococcal non-typable <i>Haemophilus influenza</i> protein D-conjugate vaccine (PHiD-CV) and a hexavalent diphtheria-tetanus-3-component acellular pertussis - hepatitis B inactivated poliovirus types 1, 2 and 3 - <i>H influenza</i> type b vaccine (DTPa-HBV-IPV/Hib), administered via intramuscular injection (IM) at ages 3, 4 and 5 months of age. HRV (human rotavirus)</p>	<p>Fever greater than 39.5°C was uncommon and within the same range for both groups.</p> <p>“Antibody geometric mean concentrations (GMCs) were significantly lower in the prophylactic paracetamol than the no prophylactic paracetamol group after primary vaccination for all ten pneumococcal vaccine serotypes, protein D, antipolyribosyl-ribitol phosphate, antidipteria, antitetanus and anti</p>

<p>infants after primary vaccination...followed by a booster dose..." (6)</p> <p>The study was rated as moderate quality</p> <p>Randomisation to intervention and control groups was unbiased.</p> <p>The intervention was not blinded as the control group did not receive a placebo drug.</p> <p>Some measurement limitations were identified:</p> <ul style="list-style-type: none"> • Self reporting of paracetamol use by parents may make this measure less reliable • Self reporting of fever and the tool used to measure fever may not be reliable and parent records of recorded fever may not be accurate • Per-protocol analysis of immunogenicity findings was conducted 	<p>aged 12-15 months at time booster dose vaccination.</p> <p>459 children were enrolled in phase one.</p> <p>414 children were enrolled for phase two.</p> <p>Children were excluded if paracetamol was contraindicated or therapy with paracetamol unrelated to the study was required or the child was previously vaccinated with the vaccines being studied.</p>	<p>participants and physicians were not blind to the intervention.</p> <p>Laboratory staff was masked to group assignment.</p>	<p>was administered orally at 3 and 4 months of age.</p> <p>Booster dose of PHiD-CV and DTPa-HBV-IPV/Hib was administered IM between 12-15 months of age.</p> <p>Prophylactic paracetamol was administered in three doses via suppository within the first 24 hours following immunization. The first dose was administered by study staff immediately following immunization. Subsequent doses were administered at home every 6-8 hours.</p> <p>A protocol amendment was introduced; prophylactic paracetamol was discontinued at the time of booster dose vaccination, following the results of the immunogenicity study for primary doses.</p>	<p>pertactin. After [booster doses], lower antibody GMCs persisted in the prophylactic paracetamol group for antitetanus, protein D, and all pneumococcal serotypes apart from 19F" (6)</p> <p>1 month after booster doses, antibody concentrations were similar for all antigens in both groups with the exception of tetanus.</p>
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Appendix D: Agree II Scores

Centres for Disease Control and Prevention: General Recommendations on Immunization			Appraiser #1	Appraiser #2	Appraiser #3	Appraiser #4	Appraiser #5	Overall Score	Scaled Domain Score
Domain Name	Min	Max	Score	Score	Score	Score	Score		
Scope and Purpose									
Item 1			7	7	6	7	7	34	
Item 2			7	5	6	7	7	32	
Item 3			6	6	6	7	7	32	
Total	15	105	20	18	18	21	21	98	92%
Stakeholder Involvement									
Item 4			6	6	4	6	6	28	
Item 5			2	4	2	4	4	16	
Item 6			7	6	6	7	5	31	
Total	15	105	15	16	12	17	15	75	67%
Rigour of Development									
Item 7			5	5	4	5	5	24	
Item 8			5	5	5	6	6	27	
Item 9			1	2	1	2	2	8	
Item 10			6	6	6	6	7	31	
Item 11			7	6	6	6	7	32	
Item 12			2	3	2	4	2	13	
Item 13			7	7	6	7	7	34	
Item 14			6	5	6	7	6	30	
Total	40	280	39	39	36	43	42	199	66%
Clarity and Presentation									
Item 15			7	6	6	7	6	32	
Item 16			7	5	5	6	6	29	
Item 17			7	3	5	7	7	29	
Total	15	105	21	14	16	20	19	90	83%
Applicability									
Item 18			3	2	1	3	2	11	
Item 19			7	6	5	6	6	30	
Item 20			5	6	5	5	5	26	
Item 21			1	4	1	1	1	8	
Total	20	140	16	18	12	15	14	75	46%
Editorial Independence									
Item 22			7	7	7	7	7	35	
Item 23			7	6	7	7	7	34	
Total	10	70	14	13	14	14	14	69	98%
Overall Quality of Guideline Total	5	35	5	5	6	6	5	27	73%
Recommendation	(Yes, Yes with modifications, No)		Yes	Yes with modifications	Yes	Yes	yes	Yes	Yes

Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline			Appraiser #1	Appraiser #2	Appraiser #3	Appraiser #4	Appraiser #5	Overall Score	Scaled Domain Score
Domain Name	Min	Max	Score	Score	Score	Score	Score		
Scope and Purpose									
Item 1			7	7	7	7	7	35	
Item 2			7	7	7	7	7	35	
Item 3			7	7	7	6	7	34	
Total	15	105	21	21	21	20	21	104	99%
Stakeholder Involvement									
Item 4			7	6	6	4	7	30	
Item 5			7	7	6	6	7	33	
Item 6			7	7	6	5	7	32	
Total	15	105	21	20	18	15	21	95	89%
Rigour of Development									
Item 7			6	6	6	6	6	30	
Item 8			7	6	7	7	7	34	
Item 9			7	7	7	6	7	34	
Item 10			7	7	7	6	7	34	
Item 11			7	7	7	7	7	35	
Item 12			7	7	7	7	7	35	
Item 13			7	6	6	6	7	32	
Item 14			6	6	6	6	6	30	
Total	40	280	54	52	53	51	54	264	93%
Clarity and Presentation									
Item 15			7	7	7	7	7	35	
Item 16			7	7	7	7	7	35	
Item 17			7	7	7	7	7	35	
Total	15	105	21	21	21	21	21	105	100%
Applicability									
Item 18			7	6	7	7	7	34	
Item 19			7	7	7	7	7	35	
Item 20			7	7	7	7	7	35	
Item 21			7	7	7	7	7	35	
Total	20	140	28	27	28	28	28	139	99%
Editorial Independence									
Item 22			7	7	7	7	7	35	
Item 23			7	7	7	7	7	35	
Total	10	70	14	14	14	14	14	70	100%
Overall Quality of Guideline Total	5	35	7	7	7	6	7	34	97%
Recommendation	(Yes, Yes with modifications, No)		Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix E: Recommendations of Canadian and American Advisory Bodies

1) Clearly do not recommend prophylactic use of analgesics

- **Centers for Disease Control and Prevention (CDC): General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP)**

“Evidence does not support use of antipyretics before or at the time of vaccination; however, they can be used for the treatment of fever and local discomfort that might occur following vaccination. Studies of children with previous febrile seizures have not demonstrated antipyretics to be effective in the prevention of febrile seizures.”

<http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf>

- **The Pink Book**

Appendix D: Vaccine Administration

“Antipyretics - An age-appropriate dose of a non-aspirin-containing pain reliever may be considered to decrease discomfort and fever if it should occur after vaccination. ACIP does not recommend the prophylactic use of analgesics before or at the time of vaccination.”

http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/D/vacc_admin.pdf

2) Alternate methods suggested (No mention of prophylactic use of analgesics)

- **Hospital for Sick Children: About Kids Health Website:**

Tips for parents and children on making vaccinations as easy and pain-free as possible

<http://www.aboutkidshealth.ca/En/HealthAZ/TestsAndTreatments/GivingMedication/Pages/Pain-Free-Injections.aspx>

Pain Management for Common Childhood Pain and Injuries

<http://www.aboutkidshealth.ca/En/ResourceCentres/Pain/AtHome/Pages/Pain-Management-for-Common-Childhood-Pain-and-Injuries.aspx>

3) **Explicitly recommend prophylactic use of analgesics**

- **Canadian Coalition for Immunization Awareness and Promotion**

2008 Influenza Pocket Guide: Who Should Receive the Vaccine?

“Prophylactic acetaminophen may minimize pain at injection site.”

<http://www.immunize.ca/en/publications-resources/posters/fluposters.aspx#pocket>
http://www.immunize.ca/uploads/posters/flu/pocket_e.pdf

- **Canadian Immunization Guide (7th edition, 2006)**

“Prophylactic acetaminophen may decrease the frequency of some side effects in adults.”
(p. 218)

“Acetaminophen prophylaxis may reduce discomfort with subsequent doses [of pertussis].”
(p.265)

http://www.phac-aspc.gc.ca/publicat/cig-gci/pdf/cig-gci-2006_e.pdf

- **Canadian Paediatric Society: Caring for Kids Website:**

MMR vaccine: Myths and facts

“Serious side effects to vaccines are very rare. Some children feel pain where the needle went in to the arm or leg and may develop a fever or rash several days after getting the vaccine. Taking acetaminophen before or after a vaccination can help.”

<http://www.caringforkids.cps.ca/immunization/MMRMythsFacts.htm>

- **Ministry of Health and Long Term Care (MOHLTC)**

Patient Fact Sheets:

- Immunization - Diphtheria, Tetanus, acellular Pertussis, Polio and Infant Haemophilus type B (DTaP-IPV-Hib) Vaccine: *“Your doctor may suggest that you give your child a medicine called acetaminophen to prevent pain and fever.”*
- Immunization: Diphtheria, Tetanus, Pertussis and Polio (DTaP-IPV) Vaccine: *“Your doctor may suggest that you give your child a medicine called acetaminophen to prevent pain and fever.”*

- Immunization: Your Best Protection: *“Physicians may recommend acetaminophen to prevent fever and pain.”*

http://www.health.gov.on.ca/english/providers/pub/pub_menus/pub_immun.html

- **Public Health Agency of Canada**

FAQ: Will my child have a reaction?

“With any vaccine, there may be some redness, swelling or pain at the place where the needle was given. To help deal with any pain or soreness, adults can take Tylenol™ and children can take Tylenol™ or Tempra™ (acetaminophen) before or after they get vaccinated.”

<http://www.phac-aspc.gc.ca/im/vs-sv/vs-faq18-eng.php>

4) **Recommend prophylactic use but unclear about timing of administration**

- **Centers for Disease Control and Prevention (CDC)**

2010 Parent’s Guide to Immunizations

“You can give your child a non-aspirin pain reliever to reduce any pain or fever that might follow vaccinations.”

<http://www.cdc.gov/vaccines/pubs/parents-guide/downloads/parents-guide-508.pdf>

- **Canadian Paediatric Society: Caring for Kids Website:**

Vaccination and your child:

“Some children may have a fever after a vaccine. Ask your doctor what to give for the fever or pain.”

“If your child is crying or fussy after getting the shot, you can give her acetaminophen.”

<http://www.caringforkids.cps.ca/immunization/VaccinationChild.htm>

Influenza Vaccine:

“If needed, taking acetaminophen can help ease the pain.”

<http://www.caringforkids.cps.ca/immunization/influenza.htm>

Meningococcal vaccine:

“Ask your doctor what you can do to control pain or swelling.”

<http://www.caringforkids.cps.ca/immunization/Meningococcal.htm>

- **Public Health Agency of Canada**

A Parent's Guide to Immunization:

“You can give your baby medicine to help with the pain and lower her fever.”

<http://www.phac-aspc.gc.ca/im/iyc-vve/pgi-gpv/section6-eng.php>