Effect of Topical Anesthetics on Vaccine:
A Focused Practice Question

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1 Issue

Topical anaesthetics offer an effective pain management option for individuals receiving injections. There can be hesitation to administer a vaccine in a site where a topical anaesthetic has been applied when the efficacy and effectiveness of the vaccine has not been studied with use of these products.

2 Context

This Research Review asks the question: Do topical anesthetics such as EMLA have an effect on vaccine efficacy and effectiveness in children ages 4 years to 18 years? Pain associated with immunization and/or being fearful of immunization needle pain is often cited as reason for not receiving immunization. Thousands of students are immunized by PPH nurses each year in the school-based immunization clinics. The nurses often observe students who are anxious about pain associated with the needle. Students who are eligible to receive the vaccine but are anxious about needle stick pain may refuse the vaccine. If used according to manufacturer recommendation, topical anesthetics are effective in decreasing pain as the needle penetrates the skin and reduces muscle spasm associated with this pain (PHAC, 2014). The use of topical anesthetics is often presented as an option to reduce pain associated with vaccine injection. In the past some nurses delayed immunization when the student had applied a topical anesthetic and the product monograph of the vaccine to be administered identified that efficacy of the vaccine had not been researched with topical anesthetic. The Canadian Immunization Guide (CIG) states, “There is no evidence that the application of a topical local anaesthetic poses a risk of decreased immune response to vaccines if the topical anaesthetic is used as directed in the product leaflet and only for the ages
recommended by the manufacturer.” However, the evidence on which this statement is made is not specified. In order to address any concerns about recommending the use of topical anesthetics and/or administering a vaccine when one had been used, we want to look at the best available evidence on the use of topical anesthetics and the impact on vaccine effectiveness.

3 Literature Review Question

The research question for this research review is:

*Do topical anesthetics such as EMLA have an effect on vaccine efficacy and effectiveness in children ages 4 to 18 years?*

**Table 1: PICO**

<table>
<thead>
<tr>
<th>Population (P)</th>
<th>School-aged children, ages 4-18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure (E)</td>
<td>Application of topical anesthetics such as EMLA cream or patch prior to receiving immunization</td>
</tr>
<tr>
<td>Outcome (O)</td>
<td>Effect on vaccine efficacy and effectiveness</td>
</tr>
</tbody>
</table>

4 Literature Search

In May/June 2015 databases and grey literature sources were searched including the Cochrane Database of Systematic Reviews, Global Health, Ovid Healthstar, Ovid MEDLINE(R), and Ovid MEDLINE(R) In-Process and Other Non-Indexed. A supplementary literature search was conducted after the library search was completed.
The main search terms were “EMLA or lidocaine or prilocaine”, “immunization or vaccination”, and “immune response”. See Appendix A for a complete search strategy.

Grey literature was also searched using similar keywords. The grey literature sources included National Institute for Health and Care Excellence (NICE), TRIP, Center for Disease Control and Prevention (CDC), and the Public Health Agency of Canada (PHAC).

The search was limited to publications in English language and a date filter was not applied.

5 Relevance Assessment

Three independent reviewers assessed the relevance of the search results based on titles and abstracts. Discrepancies were resolved and mutual agreement was reached through discussion. Articles and guidelines that met the following inclusion criteria were selected.

5.1 Inclusion Criteria:

- Focus on topical anesthetics, e.g EMLA patch or cream, used for immunization pain reduction

- Vaccine effectiveness and efficacy when topical anesthetics are used

- English language

5.2 Exclusion Criteria:

- Studies that include animals
• Topical Anesthetics used for purposes other than immunization pain reduction

• Response to medication other than vaccines

• Effectiveness and efficacy of anesthetics

6 Results of the Search

The initial search yielded 11 potentially relevant articles; four of these were duplicates and were eliminated using the de-duplication feature. An additional two duplicates were manually eliminated. Three guidelines and two single studies were identified as relevant. The single studies were included in the guidelines, and were eliminated. An additional guideline was identified through the supplementary literature search, and it was included in the search result. The guidelines that were assessed for their quality were published by the Public Health Agency of Canada (PHAC), the Centre for Disease Control (CDC), and Taddio et al and they were all relevant to the question. In total four guidelines were found.

7 Critical Appraisal

Three reviewers independently critically appraised the Canadian Immunization Guide (CIG), published by PHAC. The AGREE II tool was used to assess the quality of the CIG guideline. Discrepancies were resolved through discussion until a consensus is reached. The CDC and the 2010 Taddio guideline had been critically appraised in the past, using the AGREE II tool. We applied the results from the previous appraisals to this review. There have been no updates to the CDC guideline since the previous appraisal. The guideline, published by Taddio et al. in August 2015 was an update to
the previous Taddio guideline. It is relevant to the question and was assessed for quality by one reviewer.

The guidelines were each rated strong.

8 Description of Included Studies


The objective of this guideline is to provide practice guidelines, comprehensive information and recommendations on the use of vaccine for healthcare providers and decision makers who are interested in immunization across Canada. 26 articles, including two guidelines that had been previously appraised, were included in the reference list. A description of the evidence that informed the guideline’s statement about the effect of anesthetics on vaccine immune response was not included.


The CDC guideline provides practice guidance, information and recommendations for health care providers about concerns that arise when health care providers immunize individuals of all ages. A description of the evidence that informed CDC’s statement about the effect of anesthetics on vaccine immune response was not included.

This clinical practice guideline focused on providing clinicians with information for managing procedure-related pain and distress among children receiving vaccine injections. The scope of the guideline is limited to acute pain at the time of vaccine injection in children 0 to 18 years of age, and did not consider injection pain management after the injection. The guideline answered the question: Among children receiving intramuscular and subcutaneous injection of vaccines, does application of topical anesthetics on skin before the injection reduce pain at the time of injection? The authors assessed 10 trials that evaluated the effects of topical anesthetics in 1156 infants and children up to 15 years of age in a clinical setting. Seven of the trials compared topical anesthetic cream with placebo.


This guideline provides an update and an expansion to the previous clinical practice guideline published by Taddio and colleagues in 2010. Similar to the previous guideline, it provides clinicians with information for managing vaccine injection related pain and distress among adults in addition to children, receiving vaccine injections. The guideline includes recommendations for pain mitigation based on five domains of pain management interventions including procedural, physical, pharmacological, physiological and process approaches. The use of topical anesthetics was listed under the pharmacological domain; the topical anesthetics assessed in this guideline were
lidocaine–prilocaine 5% cream or patch and amethocaine 4% gel. Management of delayed pain after injection was not considered.

The 13 studies included, specifically for topical anesthetic as a pain mitigation intervention, investigated immunization pain during intramuscular and subcutaneous injections in 1424 children. Three studies including children 0 to 12 years receiving vaccination in a clinical setting were included in a systematic review that assessed the effect of topical anesthetics on antibody responses to measles-mumps-rubella; diphtheria, tetanus and pertussis, polio virus, *Hib*; and Hep B vaccines. In addition, a controlled trial reported the effect of topical anesthetics on immune response to Bacillus Calmette-Guérin (BCG) vaccine.

9 Synthesis of Findings

The primary focus of all four guidelines regarding topical anesthetics and vaccines was on the effectiveness of the anesthetic itself. However, consistent information was found in all four guidelines regarding the effect of topical anesthetics on vaccine effectiveness or efficacy.

The CIG recommends the use of topical anesthetics as an immunization pain management strategy for children age two months up to school age. The CIG states that there is no evidence that the use of topical anesthetics poses a risk of decreased immune response, as long as the anesthetics is used for the age recommended and as directed by the manufacturer, indicating there is no risk of antibody response reduction with the use of anesthetics.
Similarly, the CDC guideline concludes that anesthetic cream does not interfere with immune response to MMR vaccine. It does not refer to the evidence about the effect of topical anesthetics on other childhood immunizations such as Tetanus, acellular pertussis, polio virus, Hib, and Hep B vaccines.

The Taddio clinical practice guideline recommends the use of topical anaesthetics during immunization of children, as the evidence demonstrated that topical anesthetics are effective in reducing pain and found no interference with vaccine immunogenicity for measles-mumps-rubella, or for diphtheria, tetanus and, pertussis, polio virus, Hib; and Hep B vaccines. The guideline states that there is no evidence of interference with vaccine immunogenicity with the use of the two topical anesthetics, lidocaine-prilocaine 5% cream or patch and amethocaine 4% gel, studied. This recommendation is based on findings from Randomised Controlled Trials (RCTs). The guideline acknowledged the need for additional studies to rule out interaction of topical anesthetics with all other childhood vaccines, such as the HPV and meningococcal-C-ACYW vaccines.

The updated Taddio guideline investigated immunization pain during intramuscular and subcutaneous injections. It found that topical anesthetics are substantially beneficial in reducing acute distress in children ages 0-12 years receiving immunization injection. There was no evidence of a negative effect of topical anesthetics on immune response to for diphtheria, tetanus and, pertussis, polio virus, Hib; and Hep B. vaccines. The guideline also reported no effect of topical anesthetics on immune response to BCG vaccine in children 0-12 years of age. The authors did not make a statement about the effect of topical anesthetics on immune response to vaccines for children greater than
12 years old and adults. The guideline does recommend the use of topical anesthetics on pain in children greater than 12 years of age and adults.

In summary, there is evidence that the application of topical anesthetics does not have an effect on, or interfere with the immune response of MMR, tetanus, acellular pertussis, polio virus, Hib, and Hep B vaccines. It is recognised that additional research is needed to address the interaction of topical anesthetics on other childhood immunizations that have not been studied. None of the guidelines made a specific statement about the effect of topical anesthetics on vaccine efficacy or effectiveness in children older than 12 years. There is no indication in the guidelines of a negative effect of topical anesthetics on immune response to vaccine in this group of children.
Table 2: Evidence statements

<table>
<thead>
<tr>
<th>Authors</th>
<th>Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHAC (NACI), 2014</td>
<td>“There is no evidence that the application of a topical local anesthetic poses a risk of decreased immune response to vaccines if topical anesthetic is used as directed in the product leaflet and only for the ages recommended by the manufacturer”.</td>
</tr>
<tr>
<td>CDC (ACIP), 2011</td>
<td>“Evidence indicates that this cream does not interfere with the immune response to MMR. Topical Lidocaine-prilocaine should not be used on infants aged &lt; 12 months who are receiving treatment with methemoglobin-inducing agents because of possible development of methemoglobinemia”.</td>
</tr>
<tr>
<td>Taddio et. al, 2010</td>
<td>“We found no evidence of interference with vaccine immunogenicity for measles-mumps-rubella vaccine or the vaccine for diphtheria, tetanus, acellular pertussis, poliovirus, Hemophilus influenza type B and hepatitis B”.</td>
</tr>
<tr>
<td>Taddio et. al, 2015</td>
<td>“There was no evidence of a negative effect of topical anesthetics on immune response to vaccine…no demonstrated effect on antibody responses to measles-mumps-rubella vaccine or the vaccine for diphtheria, tetanus, acellular pertussis, poliovirus, Hemophilus influenzae type B (DTaP-IPV-Hib)and hepatitis B”.</td>
</tr>
</tbody>
</table>
10 Recommendations

- PPH may continue to present the option of using topical anesthetics prior to immunization to numb the injection site thereby reducing needle stick pain at the time of immunization.
References


Appendix A: Search Strategy

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to April 2015>, Global Health <1973 to 2015 Week 21>, Ovid Healthstar <1966 to April 2015>, Ovid MEDLINE(R) <1946 to May Week 4 2015>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 02, 2015>

Search Strategy:

--------------------------------------------------------------------------------
1  "EMLA".ti,ab. (1517)
2  exp Lidocaine/ (33552)
3  "lidocaine".ti,ab. (26847)
4  exp Prilocaine/ (3327)
5  "prilocaine".ti,ab. (2269)
6  "immun* response".ti,ab. (284968)
7  exp Antibody Formation/ (76608)
8  "antibod*".ti. (288230)
9  exp Immunization/ (275689)
10 "immuni*".ti,ab. (384612)
11 exp Vaccination/ (150561)
12 "vaccin*".ti,ab. (435963)
13 1 or 2 or 3 or 4 or 5 (43970)
14 6 or 7 or 8 (601744)
15 9 or 10 or 11 or 12 (760670)
16 13 and 14 and 15 (21)
17 limit 16 to english language [Limit not valid in CDSR; records were retained] (16)
18 ("mouse" or "mice*" or "canine*").ti,ab. (1318326)
19 17 not 18 (8)
Appendix B: Literature Search Flowchart

Do topical anesthetics such as EMLA have an effect on vaccine efficacy and effectiveness in children ages 4 years to 18 years?

Medline, Medline in-Process & non-indexed, Cochrane, Healthstar Global Health (8) → TRIP (1) → PHAC (1) → CDC (1) → Supplementary Search (1)

Total identified articles (12)

Removal of Duplicates (4)

Primary Relevance Assessment (8)

Non-relevant (based on title & abstract screening) (2)

Relevance assessment of full document versions (6)

Non-relevant articles (0)

Total Relevant Articles (6)

Summaries (4) Syntheses (0) Single studies (2)

Quality assessment of relevant articles (4)

Weak articles (0)

Strong articles (4) Moderate articles (0)
Appendix C: Data Extraction Tables

<table>
<thead>
<tr>
<th>Items Reviewed</th>
<th>Guideline # 1: PHAC- NACI, CIG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Information and Quality Rating for Review</strong></td>
<td></td>
</tr>
<tr>
<td>1. Author(s) &amp; Date</td>
<td>Public Health Agency of Canada (PHAC) - National Advisory Committee on Immunization (NACI), Canadian Immunization Guide (CIG) 2014. This guideline is produced by NACI, published in Canada.</td>
</tr>
<tr>
<td>2. Country</td>
<td>Canada</td>
</tr>
<tr>
<td>3. Quality Rating</td>
<td>Assessed by 3 Peel Public Health reviewers, using the AGREE II tool: Scope and Purpose=91 Stakeholder Involvement = 81 Clarity and Presentation = 86 Applicability = 72 Editorial independence = 75 Overall guideline Assessment =72 Recommendation for Use: Yes</td>
</tr>
<tr>
<td>4. Objectives of Review</td>
<td>The objective of this guideline is to provide practice guidelines, comprehensive information and recommendations on the use of vaccine for healthcare providers and decision makers who are interested in immunization across Canada.</td>
</tr>
<tr>
<td><strong>Details of Review</strong></td>
<td></td>
</tr>
<tr>
<td>5. Number and quality of Studies included</td>
<td>This guideline referenced 26 articles in the chapter that addresses vaccine administration practices. The number of studies that addressed the research question on the effect of topical anethetics on vaccine efficacy and effectiveness was not specified, however, studies that inform recommendations are assessed using the NACI GRADE system.</td>
</tr>
<tr>
<td>6. Types of Studies</td>
<td>Guidelines, research reviews, randomized controlled trials and single studies were included in the reference list.</td>
</tr>
<tr>
<td>7. Search Period</td>
<td>Not specified. The guide is updated as needed.</td>
</tr>
</tbody>
</table>
8. Number of databases searched | Not specified: Details of the methods of the search (search terms, databases searched, restrictions on language of publication, method for extracting titles, number of reviewers, etc) are provided in the methods section of the literature search.

9. Inclusion and exclusion criteria | Not specified: Details of the methods of the search inclusion and exclusion criteria are provided in the methods section of the literature search.

10. Target groups | The guide provides recommendations for the vaccination of specific populations including adults, persons with inadequate immunization records, women who are pregnant or breastfeeding, infants born prematurely, persons in health care institutions, immunocompromised persons, and those who are new to Canada.

11. Primary outcome | The intervention of interest for this review is vaccine administration practice using topical anesthetics to reduce pain during immunization.

### Results of Review

12. Main results of review | **NACI Statement Regarding Effect of topical Anesthetics on Vaccine Immune response**

The evidence indicates that there is no evidence that the application of topical anesthetics poses a risk of decreased immune response, as long as the anesthetics is used for the age recommended and as directed by the manufacturer.

It is recommended that children be observed during and after application of topical anesthetics as there have been reports of adverse event with application of excessive topical anesthetics.
<table>
<thead>
<tr>
<th>Items Reviewed</th>
<th>Guideline # 2: CDC- ACIP, General Recommendation on Immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Information and Quality Rating for Review</strong></td>
<td></td>
</tr>
</tbody>
</table>
| 1. Author(s) & Date | Centres for Disease Control - General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). Kroger, A, et al.  
Note: An erratum has been published for this issue on July 29, 2011 |
| 2. Country | USA |
| 3. Quality Rating | Assessed by 5 Peel Public Health reviewers, using th AGREE II tool:  
Scope and Purpose = 92  
Stakeholder Involvement = 67  
Rigor of Development =  
Clarity and Presentation = 83  
Applicability = 46  
Editorial independence = 98  
Overall guideline Assessment =73  
Recommendation for Use: Yes |
<p>| 4. Objectives of Review | The guideline provides recommendation for 17 vaccine preventable diseases, and is intended for use by clinicians and other health care immunization providers. |
| <strong>Details of Review</strong> | |
| 5. Number of Studies included | A total of 239 research articles were referenced. The number of studies that addressed the research question on the effect of topical anethetics on vaccine efficacy and effectiveness was not specified. CDC uses the US Preventive Taskforce Methodology to grade its recommendations. |
| 6. Types of Studies | Not specified. |
| 7. Search Period | Data presented in the guide is current as of 2014 based on information found on CDC website. |</p>
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Number of databases searched</td>
<td>Not specified. The U.S. Preventative Services Task Force searches at least the MEDLINE English-language database and the Cochrane Collaboration Library.</td>
</tr>
<tr>
<td>9. Inclusion and exclusion criteria</td>
<td>Not specified.</td>
</tr>
<tr>
<td>10. Target groups</td>
<td>Persons of various ages receiving immunization.</td>
</tr>
<tr>
<td>11. Primary outcome</td>
<td>The intervention of interest for this review is vaccine administration practice using topical anesthetics.</td>
</tr>
<tr>
<td>Results of Review</td>
<td></td>
</tr>
<tr>
<td>12. Main results of review</td>
<td>“The Evidence indicates that 5% topical lidocaine – prilocaine cream does not interfere with immune response to MMR vaccine”.</td>
</tr>
<tr>
<td></td>
<td>5% topical lidocaine – prilocaine emulsion cream should not be used on infants less than 12 months receiving treatment for a blood disorder called methemoglobinemia.</td>
</tr>
<tr>
<td>Items Reviewed</td>
<td>Guideline # 3: Taddio et. al, Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>General Information and Quality Rating for Review</td>
<td></td>
</tr>
<tr>
<td>1. Author(s) &amp; Date</td>
<td>Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline. Taddio, A, et al.</td>
</tr>
<tr>
<td></td>
<td>This guideline was published in Canada in 2010.</td>
</tr>
<tr>
<td>2. Country</td>
<td>Canada</td>
</tr>
<tr>
<td>3. Quality Rating</td>
<td>Assessed by 5 Peel Public Health Reviewers in, using the AGREE II tool:</td>
</tr>
<tr>
<td></td>
<td>Scope and Purpose = 99</td>
</tr>
<tr>
<td></td>
<td>Stakeholder Involvement = 89</td>
</tr>
<tr>
<td></td>
<td>Rigor of Development = 93</td>
</tr>
<tr>
<td></td>
<td>Clarity and Presentation = 100</td>
</tr>
<tr>
<td></td>
<td>Applicability = 99</td>
</tr>
<tr>
<td></td>
<td>Editorial independence = 100</td>
</tr>
<tr>
<td></td>
<td>Overall guideline Assessment = 97</td>
</tr>
<tr>
<td></td>
<td>Recommendation for Use: Yes</td>
</tr>
<tr>
<td>4. Objectives of Review</td>
<td>This guideline provides recommendations on 18 vaccination pain management interventions.</td>
</tr>
<tr>
<td>Details of Review</td>
<td></td>
</tr>
<tr>
<td>5. Number of Studies included</td>
<td>10 trials that evaluated the effect of topical anesthetics in a total of 1156 infants and children articles were included.</td>
</tr>
<tr>
<td>6. Types of Studies</td>
<td>Evidence was limited to randomized controlled trials (RCTs) and studies with quasi-experimental design.</td>
</tr>
<tr>
<td>7. Search Period</td>
<td>Not specified.</td>
</tr>
<tr>
<td>8. Number of databases searched</td>
<td>Not specified, search methods are based on the US preventative services Task Force which searches at least the MEDLINE English language databases and the Cochrane Collaboration Library.</td>
</tr>
<tr>
<td>9. Inclusion and exclusion</td>
<td>Inclusion and exclusion criteria not explicitly provided however search methods is based.</td>
</tr>
<tr>
<td>criteria</td>
<td>on the US preventative services Task Force.</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>10. Target groups</td>
<td>Children 0-15 years of age.</td>
</tr>
<tr>
<td>11. Primary outcome</td>
<td>The intervention of interest for this review is vaccine administration practice using topical anesthetics to reduce vaccination injection pain.</td>
</tr>
</tbody>
</table>

**Results of Review**

<table>
<thead>
<tr>
<th>12. Main results of review</th>
<th>“No evidence of interference with vaccine immunogenicity for Measles Mumps and Rubella (MMR), Tetanus, acellular pertussis, polio virus, hemophilius influenza type B (Hib), and hepatitis B (Hep B) vaccines.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Topical Anesthetics are considered safe for children of all ages.</td>
</tr>
<tr>
<td></td>
<td>Administration of excessive doses and or prolonged application times may lead to serious side effects.</td>
</tr>
<tr>
<td></td>
<td>Additional studies recommended ruling out interaction between topical anesthetics and all of the other common childhood vaccines.</td>
</tr>
<tr>
<td></td>
<td><strong>Clinical Considerations:</strong></td>
</tr>
<tr>
<td></td>
<td>➢ Educate parents on site of administration and time of administration.</td>
</tr>
<tr>
<td></td>
<td>➢ Provide information about monitoring the skin for allergic reaction.</td>
</tr>
</tbody>
</table>
### Items Reviewed

<table>
<thead>
<tr>
<th>Guideline # 4: Taddio et. al, Reducing pain during vaccine injections: clinical practice guideline</th>
</tr>
</thead>
</table>

### General Information and Quality Rating for Review

1. **Author(s) & Date**
   - This guideline was published in Canada in 2015.

2. **Country**
   - Canada

3. **Quality Rating**
   - Assessed by 5 Peel Public Health Reviewers in, using th AGREE II tool:
     - Scope and Purpose = 94
     - Stakeholder Involvement = 100
     - Rigor of Development = 100
     - Clarity and Presentation = 100
     - Applicability = 100
     - Editorial independence = 100
     - Overall guideline Assessment = 99
     - Recommendation for Use: Yes

4. **Objectives of Review**
   - This guideline expands and provides an update to the recommendations on vaccination pain management interventions in the 2010 guideline.

### Details of Review

5. **Number of Studies included**
   - 13 studies were included in a meta-analysis; including 1424 children 0-12 years old, undergoing immunization.

6. **Types of Studies**
   - Evidence was limited to RCTs.

7. **Search Period**
   - Search was conducted from the date of inception of studies until February 2015.

8. **Number of databases searched**
   - Relevant articles identified by searching MEDLINE, Embase, PsycINFO, CINAHL and ProQuest Dissertations & Theses Global.

9. **Inclusion and exclusion criteria**
   - Inclusion and exclusion criteria not explicitly provided however search methods is based on the US preventative services Task Force.

10. **Target groups**
    - Children 0-12 years of age, and Children > 12 years and adults.

11. **Primary outcome**
    - The primary outcome: Acute distress in infants and young children (0-12 years) and self
reported pain in children 12 years or older and adults.

The intervention of interest for this review is vaccine administration practice using topical anesthetics.

### Results of Review

#### 12. Main results of review

The guideline strongly recommends the use of topical anesthetics for children 0-12 years to reduce pain during immunization as there is demonstrated benefit of topical anesthetics on acute distress and pain during immunization.

**Critical outcome - vaccine injection acute distress in children 0-12 years old receiving immunization:** Standardize mean difference (SMD) = -0.91 (95% CI -1.36, -0.47).

Children 0-12 years who were exposed to topical anesthetics (lidocaine-prilocaine 5% or amethocaine 4%) before receiving vaccines experienced less acute distress during immunization. There was a substantial benefit of topical anesthetics on acute distress during immunization.

**Critical outcome - vaccine injection pain in children > 12 years old and adults receiving immunization:** SMD- 0.85(95% CI -1.38. -0.32).

Children >12 years of age and adults who were exposed to topical anesthetics (lidocaine-prilocaine 5%) before receiving vaccines experienced less pain during immunization. There was benefit of topical anesthetics on pain during immunization.

There is no evidence of a negative effect of topical anesthetics on immune response to vaccines studied.