Abstract of dissertation entitled

**Evidence-based clinical guidelines for applying topical anaesthetics to reduce injection pain in healthy children**

Submitted by

**CHAN YUE SIN**

for the degree of Master of Nursing
at the University of Hong Kong
in July 2013

According to the World Health Organization, life-threatening infectious diseases, even in remote and vulnerable locations, can be minimised through immunisation. Vaccines interact with the immune system to produce an immune response similar to that produced by natural infection. However, about 10% of the population avoid vaccination and other needle procedures because of ‘needle fear’. Because of the prevalence of injection pain and more concern about the adequacy of pain management, and with the steadily increasing number of recommended childhood immunisation, we identified a need for evidence-based guidelines on pain management to be developed in our local setting through translational nursing practice.
After a critical appraisal of randomised controlled trials and systematic reviews, it is highly recommended that ‘topical anaesthetics are effective in reducing vaccination pain’ (Grade A recommendation, based on level I evidence by SIGN). In order to facilitate practice from evidence, the implementation potential, transferability, feasibility and cost-benefit ratio - has been examined, and an evidence-based guideline has been developed simultaneously for the new practice. With the identification of stakeholders and the development of a communication plan, potential users of the guideline and pilot testing are discussed. Innovation outcomes and their effectiveness are examined and explored. It is expected that, through this translational nursing practice, vaccination induced pain and distress among healthy children can be managed well, according to the best evidence and up-to-date recommendations.
Evidence-based clinical guidelines for applying topical anaesthetics to reduce injection pain in healthy children

by

CHAN YUE SIN

BSc.(Hons) Nursing Studies HKU
Master of Medical Science HKU

A dissertation submitted in partial fulfillment of the requirements for the degree of Master of Nursing at the University of Hong Kong.

July 2013
Declaration

I declare that this dissertation represents my own work, except where due acknowledgement is made, and that it has not been previously included in a thesis, dissertation or report submitted to this University or to any other institution for a degree, diploma or other qualification.

Signed ………………………………………………………………

CHAN YUE SIN
Acknowledgements

I would like to convey my heartfelt gratitude to my supervisor, Dr Marie Tarrant for her well-directed guidance, attention to detail and timely response in the process of my writing this dissertation.

I would also like to thank the Department of Health for providing the sponsorship allowing me to complete the Master of Nursing programme at the University of Hong Kong. Special thanks must be given to my seniors and colleagues working in the Family Health Service and Public Health Nursing Division, my classmates and friends, for their cooperation, positive feedback and encouragement throughout the programme.

My gratitude is due to my father for his famous motto ‘Face challenges with enthusiasm and a smile’, which has been a key to many successful endeavours throughout my life. Special thanks to my husband and daughter for their unconditional love, endurance and sharing throughout my work.

I also cherish the motto of the University of Hong Kong ‘Wisdom & Virtue’, as a beacon guiding me to reach the pinnacle both in academic work and virtue, in memory of studying on the campus these past few years. Finally, thanks for God’s mercy and strength, enabling me to overcome any obstacle.
## Contents

*Declaration* ........................................................................................................................................i  
*Acknowledgement* ............................................................................................................................ii  
*Table of contents* ..................................................................................................................................iii  

**Chapter 1: Statement of the problem.** .................................................................................................1  
  Introduction ........................................................................................................................................1  
  Background to the problem. ..................................................................................................................2  
  Rationale of the intervention. ................................................................................................................3  
  Significance of the problem. ..................................................................................................................3  
  Research objectives .............................................................................................................................4  
  Research questions ...............................................................................................................................5  
  PICO components .............................................................................................................................5  

**Chapter 2: Review of evidence** ..........................................................................................................7  
  Selecting studies for review ..................................................................................................................7  
  Search strategies ..................................................................................................................................8  
  Methods of the review ..........................................................................................................................10  
  Description of studies ..........................................................................................................................10  
  Characteristics of included intervention .............................................................................................11  
  Results of review ...............................................................................................................................22  
  Quality assessment .............................................................................................................................23  
  Summary and synthesis .......................................................................................................................29  

**Chapter 3: Implementation potential** .................................................................................................32  
  Target setting and population .............................................................................................................32  
  Transferability of the findings .............................................................................................................33  
  Feasibility ...........................................................................................................................................35  
  Cost-benefit analysis of the innovation ...............................................................................................38  

**Chapter 4: Evidence-based practical guidelines** ..............................................................................41  
  Overview of guidelines .......................................................................................................................41  
  Recommendations ..............................................................................................................................42  

**Chapter 5: Implementation plan** .......................................................................................................45  
  Plan for communication with potential users ....................................................................................45  
  Communication process .......................................................................................................................45  
  Communication methods ......................................................................................................................46  
  Sustaining the change process ..........................................................................................................47  
  Pilot testing .........................................................................................................................................48  

**Chapter 6: Evaluation plan** ...............................................................................................................50  
  Intervention outcomes and outcome measurements ...........................................................................50  
  Nature and number of clients involved ...............................................................................................51
Chapter 1

Statement of the problem

Introduction

Immunisation is an inevitable element of complete child services within the public health domain, and is one of the most creditable epidemiological/medical achievements of the 20th century (Jacobson et al., 2001; Taddio et al., 2009). The positive effect of immunisation on disease prevention and the minimisation of suffering and death are almost incalculable. Vaccines save lives, resist disease and are cost-effective for the economy as they reduce hospitalisations.

To reduce infecting media circulating within the community, a high level of immunised population is a consequence of vaccination in order to achieve ‘herd immunity’ (Arinaminpathy, Lavine & Grenfell, 2012). To provide such protection, the current Centre for Disease Control and Prevention’s schedule recommends immunisation against 14 diseases, involving 14 to 20 separate injections before the age of two, depending on the number of combination vaccines available (Jacobson et al., 2001; Schechter et al., 2007) (CDC Vaccine Schedule 2012, Appendix A). Immunisations are the most frequent painful procedures executed in paediatric practice.

Multiple injections during the same visit are recommended as a necessity for the current schedule. In 2009, Hong Kong commenced an immunisation catch-up programme of pneumococcal 7-valent conjugate vaccine in the Maternal and Child Health Centre, Department of Health. Since then, pneumococcal conjugate vaccine has been included in the local immunisation program, eventually evolving into the present-day 13-valent version (Department of Health, 2009b). An expanded immunisation schedule has increased the number of vaccines in the first 18 months of life, including 13 injections with the recent inclusion of the pneumococcal
conjugate vaccine. Such procedures are quite similar to those found in the US, Canada, Europe and other developed areas of the world.

**Background to the problem**

Pain associated with needle puncture is a particular problem for children experiencing vaccination, venepuncture, venous cannulation etc. Early in the 19th century, paediatricians often accepted the theory that infants and toddlers were incapable of feeling pain, but Dr MacKenzie recognised such pain and proposed a method of alleviating it by providing localized analgesia by freezing a 1:1000 solution of zephiran in ice cubes in order to achieve temporary pain relief. In health supervision and counselling, modern paediatric practice takes a further step in clinical practice as many children who are still preoccupied with the possibility of an injection will be frightened by the consulting room ambience. For children and their parents, a needle is a powerful negative symbol (Schechter et al., 2007; Sokolowski, Giovannitti & Boynes, 2010). Even nurses and doctors report that about 55-65% of practising physicians have concerns about three injections at a single visit, and 80% about four at a time (Woodin et al., 1995). In Hong Kong, infants routinely receive two injections (BCG and hepatitis B vaccine) at birth whether in government or private hospitals. Subsequently, infants of two and four months routinely receive DTaP-IPV (diphtheria, tetanus, and acellular pertussis & inactivated poliovirus vaccine) and PCV-13 (pneumococcal 13-valent conjugate vaccine) simultaneously. At six months, they receive the 3-dose of DTAP-IPV, 3-dose of PCV-13 and 3-dose of hepatitis B vaccine simultaneously. At 12 months, a booster PCV-13 and the 1-dose MMR (measles-mumps-rubella) vaccine would be given simultaneously. At 18 months, with the booster DTaP-IPVs, the primary series of immunisation in Hong Kong is completed. Children under 6 who have not completed
this age-specific immunisation series receive the missing vaccines by a ‘catch-up’ approach in order to reach full compliance.

**Rationale for intervention**

The pain experienced by infants and young children is often underestimated and undertreated (Dilli, Kucuk & Dallar, 2009; Hamilton, 1995). As a consequence, if the pain is not addressed, it can lead to pre-procedural anxiety with needle fear and healthcare avoidance behaviour, including non-adherence to vaccination schedules (Taddio et al., 2009; Taddio et al., 2010a). Therefore, it is vital to address non-adherence with paediatric vaccine schedules; every possible aspect like injection pain, local reaction, anaphylaxis etc must be considered in order to encourage parents taking children to healthcare providers for vaccination (Kennedy, Basket & Sheedy, 2011)

**Significance of the problem**

Pain is defined as ‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage’ (Gidudu et al., 2012). A needle stick invasion is the most frightening event for children in the clinical setting because it often results in pain and distress, which may lead in adulthood to the avoidance of concerned medical care (Halperin et al., 2000; Hamilton, 1995). Inadequate relief of pain and distress during childhood medical procedures may have long-term negative effects on future pain tolerance and responses. Taddio et al., (2007) and Hamilton (1995) report that about 25% of adults have a fear of needles developed during childhood, and 10% of the population avoid vaccination and other needle procedures because of needle fear or phobia.

Currently, 95% of locally born children receive a complete immunisation at the Maternal and Child Health Centre, Department of Health (Centre for Health Protection, Health Facts of
Hong Kong, 2012). Although the immunisation coverage rate is high, well-documented literature reveals that the management of paediatric pain, particularly in needle-related procedures, is under-recognised and under-treated, while the availability of pharmacological and non-pharmacological methods that reduce pain are under-utilised (Young, 2005; Taddio et al., 2012). Dilli et al. (2009) hold that topical anaesthetic use should be reserved for children who are phobic or particularly anxious about a pending injection.

The Nursing Procedure Guidelines on Immunization (2011) developed by the Quality Assurance Committee of the Public Health Nursing Division (PHND), Department of Health (DH) advocate the value of immunisation with safe, accurate and efficacious administration. It is a brochure for assessing immunisation procedures with measurable outcomes. Standardising the immunisation procedure in 31-MCHCs, as a spring-board for quality assurance as well as a directory for newly joined healthcare professionals, it consists of important and relevant issues and procedures concerning immunisation with evidence, and in line with the recommendations of the Red Book (2012). However, immunisation-induced pain and distress remain under-recognised in our local setting, and pain management is quite inconsistent, tradition-based and under-utilised in Maternal and Child Health Centres, which might well cause parental dissatisfaction and non-compliance.

Research objectives

Most vaccines are rendered by needle injection through the skin, a drug delivery system which children, parents and healthcare providers all find distressing. Several studies (Schechter et al., 2007; Taddio et al., 2010a; Taddio et al., 2009) highlight the fact that vaccine injections are the most common source of iatrogenic pain in childhood. With the steadily increasing
number of recommended vaccinations, concern has grown about the adequacy of pain management. The objectives of the present review are:

1. To assemble relevant empirical evidence relating to the effectiveness of topical anaesthetics for reducing pain during needle procedures.
2. To conduct a quality assessment of the selected evidence for synthesis of a topical anaesthetic protocol for children undergoing injection/immunisation procedures in paediatric/out-patient/primary care settings.
3. To determine the characteristics of topical anaesthetics and their associated clinical outcomes.

Research question(s)

In view of the need to improve current pain management during and after vaccine injections, clinical experience-sharing among colleagues regarding the current clinical setting and the availability of interventions, several questions and thoughts arise, as follows.

♦ Is current nursing practice in childhood immunisation based on the best evidence?
♦ How effective is the application of topical anaesthetic intervention in comparison with no-treatment groups in the reduction of immunisation-induced pain and distress for children above one year old?
♦ Does the application of topical anaesthetic intervention reduce children’s distress levels perceived by nurses/parents?

PICO components

Research studies have found that the lidocaine-prilocaine anaesthetic (EMLA) patch effectively controls pain from injection or venepuncture (Cassidy et al., 2001; Halperin et al., 2000; Nilsson, Boman, Wallin & Rotstein, 1994) in family clinics and inpatient or outpatient
settings without affecting the antibody response. To respond to uncertainty or a clinical inquiry, focused foregrounded questions are essential in judiciously finding the right evidence to acknowledge them (Melnyk & Fineout-Overholt, 2011), which usually have four components, termed *PICO*, the acronym deriving from:

<table>
<thead>
<tr>
<th>Patient /Population of interest</th>
<th>-healthy children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention of interest</td>
<td>-topical anaesthetics</td>
</tr>
<tr>
<td>Comparison /control of interest</td>
<td>-usual care of immunisation/vaccination/injection procedures</td>
</tr>
<tr>
<td>Outcome of interest</td>
<td>-reducing needle pain</td>
</tr>
</tbody>
</table>

The *PICO* formulation of the present enquiry is:

‘Can evidence-based clinical guidelines for applying topical anaesthetics reduce injection pain in healthy children?’
Chapter 2

Review of evidence

With the PICO question identified, a systematic search of recent available literature is required. An elaborated literature review was performed in order to identify the details and quality of the research studies. An analysis of the interventions and their effectiveness was performed with a summary of evidence and the implications for nursing practice.

Selecting studies for review

Inclusion criteria

Type of studies. Studies were included on the basis of original research, with a full report published in English. Randomised controlled/comparative trials that included topical anaesthetics as intervention to reduce needle-induced pain were compared with those lacking such intervention and simply involving standard care.

Type of participants. Healthy infants (aged above three months) or children without any history of allergy, sensitivity or other form of reaction to lidocaine (lignocaine)/prilocaine/ester types of local anaesthetics.

Type of intervention. The intervention should only include topical anaesthetics as intervention to minimise needle pain induced by vaccine injection or venepuncture, and not by other procedures such as acupuncture.

Type of outcome measures. Outcomes were pain, distress, antibody response or other local reactions etc.

Exclusion criteria

1. Studies not aimed at reducing immunisation/vaccination/needle pain, but only at reducing post-operative or chronic pain etc.
2. Pilot study.


**Search strategies**

**Databases and keywords**

Four bibliographical databases were searched (from March 2012 till third week of September 2012): PubMed <1950 to 2012>, CINAHL Plus (EBSCOhost) <from 1980 to 2012>, Cochrance Library <1980 until 2012>, Google Scholar and reference lists. Relevant studies were challenged using four keywords, (1) topical anaesthetics, (2) EMLA /lidocaine-prilocaine, (3) injection/vaccination/immunisation pain and (4) infant/child in the title and abstract fields in PubMed, CINAHL, Cochrane Library as well as Google Scholar. No published local studies in relation to the use of topical local anaesthetics in reducing injection pain have been encountered. Studies were further limited to randomised studies of infants/children. The numbers of studies yielded by keywords are listed in Table 1. The titles and abstracts were screened for potential studies, and full papers were located and read to identify eligible studies. A flowchart is used to demonstrate the process of the search and its results (Figure 1). The reference lists of all identified studies and reviews were also examined for additional relevant works.
**Table 1.** Search database and results

<table>
<thead>
<tr>
<th></th>
<th>PubMed</th>
<th>CINAHL</th>
<th>Cochrane</th>
<th>Reference lists</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of relevant studies by individual keywords</td>
<td>10485</td>
<td>759</td>
<td>4172</td>
<td></td>
</tr>
<tr>
<td>No. of studies after combination of keywords</td>
<td>4023</td>
<td>51</td>
<td>478</td>
<td></td>
</tr>
<tr>
<td>No. of studies remaining after limitation</td>
<td>447</td>
<td>12</td>
<td>75</td>
<td>82</td>
</tr>
<tr>
<td>No. of studies remaining before screening full text</td>
<td>58</td>
<td>2</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>No. of studies appropriate for literature review</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>No. of studies appropriate for literature review</td>
<td></td>
<td>6 (RCT) &amp; 1 (SR)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1.** Flow chart of studies included and excluded

- 75 potential studies remained before full text screening
- 57 non-RCTs studies were excluded
- 2 non-English studies were excluded
- 7 not fulfilling the criteria were excluded
- 1 duplicated study was excluded
- 6 RCTs and 1 systematic review were selected for literature review
Methods of the review

Data extraction

The data extracted from the selected studies were organised in tables of evidence with reference to the checklists established by the Scottish Intercollegiate Guidelines Network (SIGN, 2008). The checklists were developed as critical appraisal tools for different study designs, and are to be applied inclusive of the methodology checklists for randomised controlled trials (see Appendix B) and systematic reviews (see Appendix C).

Quality assessment

Quality assessment was conducted according to the recommendations in SIGN (see Appendix D).

Data analysis

Analysis was executed on data pertaining to demographics, interventions and outcomes.

Description of studies

Characteristics of included studies

Of the six selected randomised controlled studies (Cassidy et al., 2001; Chang et al., 1994; Halperin et al., 2000; Nilsson et al., 1994; O’Brien et al., 2004; Taddio et al., 1994) all were written in English and published in the period from 1994 to 2004. The six studies cover a total of 779 children, with the sample size ranging from 60 to 178. Four were double-blind (O’Brien et al., Cassidy et al., Halperin et al., Taddio et al.) and the other two were open trials with a parallel/comparative group design (Chang et al., Nilsson et al.). Five were funded. Cassidy et al. was supported by a Distinguished Scientist Award from the Canadian Institute of Health Research and funded by a Swedish pharmaceutical company. O’Brien et al. and Taddio et al. were funded by a Canadian pharmaceutical company, while Halperin et al. was funded by a
Swedish pharmaceutical company. Two out of the six were multicentre studies (Cassidy et al., Chang et al.), while the other four were single-centre.

The participants in the six studies were healthy infants/children with a mean age ranging from five months (Taddio et al.) to eight years (Nilsson et al.), while Taddio et al. mainly focused on children aged ≥ 12 months. Most studies reported no gender difference or other demographic characteristic between the intervention and controlled/parallel groups (p > 0.05), which were intended to compare the difference between usual care and the application of topical anaesthetics (i.e. EMLA/amethocaine) to reduce immunisation pain. Five studies had pain as a primary outcome, while the primary outcome of Halperin et al. was the effect of topical anaesthetics on the antibody response, with pain as a secondary outcome. In Taddio et al., (1994) and Halperin et al., (2000), the pain was measured on the Modified Behavioural Pain Scale (MBPS), while (Cassidy et al., Chang et al., Nilsson et al.) applied the Visual Analogue Scale (VAS) as the pain measurement tool. Details of the study characteristics are displayed in Tables 2, 3, 4, 5, 6 and 7).

The systematic review by Shah, Taddio, & Rieder, (2009) set out to evaluate the effectiveness and safety profiles of numerous pharmacological and combined interventions for pain management during routine childhood immunisation, and to guide parents and healthcare professionals in the best clinical practice. The study consists of 32 randomised controlled trials (RCTs) and quasi-RCTs involving 3,856 infants and children from two weeks to 15 years of age. Details of the study characteristics are presented in Table 8.

**Characteristics of included interventions**

The intervention applied in the selected studies for reducing intramuscular/subcutaneous injection pain was similar, i.e. the use of pharmacotherapy. Among the six studies, five used
EMLA either in patch form (5%-1g, circle-shaped matrix with 1g of 5% eutectic emulsion with lidocaine, 25mg/g and prilocaine, 25mg/g) or cream-formed (2.5g EMLA) (Taddio et al.) as study intervention, which should be applied 60 minutes before the injection procedure. Only (O'Brien et al.) used a relatively new topical anaesthetic, 4% amethocaine gel as intervention to reduce the pain of subcutaneous MMR injections, that produces anaesthesia within 30 minutes. The intervention follow-up period of the six studies consisted mainly of three phases and video recording. The three phases were:

I. before injection/venepuncture (10 seconds to few minutes) → 
II. during injection/venepuncture (within 5seconds) → 
III. after injection (within 30 seconds) 

O'Brien et al. and Halperin et al. have longer follow-up periods of one month after the injection procedure, since both studies intended to measure post-injection antibody response through a blood collection procedure.

Among the six studies, four used a sham cream patch/dressing (1g of an inert oil, circle-shaped matrix) as a control (Cassidy et al., Halperin et al., O'Brien et al., Taddio et al.) to ascertain the effects of topical anaesthetics, while the other two (Chang et al., Nilsson et al.) applied an open, parallel group (EMLA cream 5%-1g under tagederm dressing) as a control to identify both the anaesthetic and ease of application of the patch. Details of the intervention characteristics are presented in Table 9.
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants/setting</th>
<th>N</th>
<th>Interventions</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
</table>
| Cassidy et al. (2001)    | - Normal, healthy children, aged 4-6 (54% boys) undergoing standard pre-school DPTP immunisation  
- 5 urban and 5 rural private clinic settings  
- Mean age 4.7 & S.D. =0.46 identical in both groups  
- Almost >97% (both groups) of children from two-parent families | 161 | **IG:**  
- EMLA patch applied to mid deltoid muscle  
- 60-120min before time of immunisation  
- Remove no more than 10 mins before immunisation | **Primary:**  
- (1) Children self-reported pain by Faces Pain Scale (FPS) (range: 0-6)  
- (2) Behavioural pain measures by the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) modified version (range: 3-9)  
- (3) the Child Facial Coding System (CFCS) (range: 0-13)  
- (4) Parent & technician-rated children's pain measured by The Visual Analogue Scale (VAS-pain) (range: 0-10)  
- (5) Parent-rated children's anxiety measured by The Visual Analogue Scale (VAS-anxiety) (range: 0-10)  
- (6) No. of adverse events associated with the application of patch.  
- (7) No. of children reported clinically significant pain.  
- (8) Effect of other factors like child's anxiety & patch adhesion | **Secondary:**  
- (6) No. of adverse events associated with the application of patch.  
- (7) No. of children reported clinically significant pain.  
- (8) Effect of other factors like child's anxiety & patch adhesion | Used All Patients Treated (APT) approach.  
**Primary:**  
- Pre-needle phase  
- (2) I: C = 0, p=0.33(ns)  
- (3) I: C = -1.2, p=0.20(ns)  
**Needle-phase**  
- (1) I: C = -1, p=0.02  
- (2) I: C = -0.3, p=0.02  
- (3) I: C = -2.2, p=0.03  
- (4) I: C = -15.1, p=0.001(parent)  
- I: C = -13.8, p=0.001 (technician)  
**Post-needle phase**  
- (2) I: C = -0.3, p=0.01  
- (3) I: C = -1.7, p=0.07(ns)  
**Correlation analyses**  
- (5) Parent's self-reported anxiety and their report of the child's anxiety correlated positively with parent's rating of the child's pain on VAS (r=0.22, p<0.01)  
- (6) Paller: I:C = 2.4% :1.3% (ns)  
- No oedema & no itchiness: I:C = 74.4% : 92.3% (ns)  
- (7) Pain reduction: I:C 43% : 17% (p <0.001)  
- (8) VAS-anxiety correlated positively with VAS-pain (r = 0.30, p<0.001)  
Patch adhesion correlated negatively with CFCSpain (r = -0.23; p<0.01) during needle phase |
Table 3: Characteristics of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants/setting</th>
<th>N</th>
<th>Interventions</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halperin et al.(2000)</td>
<td>Healthy infants at least 12 months old who were brought to their family physician for routine first dose of MMR.</td>
<td>160</td>
<td>IG:</td>
<td>• One patch of EMLA/placebo was applied to mid-thigh muscle (immunisation site)</td>
<td>Primary:</td>
</tr>
<tr>
<td></td>
<td>• Both groups were similar in age: 12.4 (mean), sex and previous needle experiences</td>
<td>I: 80</td>
<td>• The second EMLA/placebo patch was applied to a suitable venipuncture site.</td>
<td>• (1) Measles antibodies (proportion %) with titer ≥120 RD reciprocal dilution.</td>
<td>• (1) I: C = -1.4(%) (ns)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: 80</td>
<td>• The patches left in place for 60-180 minutes &amp; removed no longer than 10 minutes before the procedure</td>
<td>• (2) Mumps antibodies (proportion %) with titer ≥231EU/mL.</td>
<td>89.7%(I) &amp; 91.1%(C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• (3) Rubella antibodies (proportion %) with titer ≥8 IU/mL</td>
<td>(2) I: C = -6.6(%) (ns)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Secondary:</td>
<td></td>
<td>88.3%(I) &amp; 94.4%(C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• (4) Pain score (Modified Behavioural Pain Scale) (range:0-10)</td>
<td></td>
<td>(3) I: C = -1.4(%) (ns)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Cry</td>
<td></td>
<td>92.3%(I) &amp; 93.7%(placebo)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Facial expression</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Movement</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5) Adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• (4) Difference between baseline &amp; post-injection of I &amp; C by Student t-test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Cry: 0.7 p=0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Facial expression: 0.5 p=0.034</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Movement: 1.0 p=(ns)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Total: 3.1 p=0.043</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5) Rates were compared by using 95% CI &amp; Fisher exact test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pallor: 31% p=0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>I: C = 39% : 8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Irritability at first 15 minutes post-injection: -15% p=0.040</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>I:C = 16% : 31%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Participants/setting</td>
<td>N</td>
<td>Interventions</td>
<td>Outcome measures</td>
<td>Results</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------</td>
<td>----</td>
<td>---------------------------------------------------</td>
<td>-----------------------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
</tbody>
</table>
| Nilsson et al. (1994) | • Aged 5-15 boys and girls who required venous cannulation.  
  • Boy : girl = 33 : 26  
  Age (year): I : C = 9 : 7.5  
  Weight (kg): I : C = 29.5 : 29.5 | I: 30  
  C: 30 | IG:  
  • EMLA patch applied 60-180 minutes before venepuncture. The application time was recorded. | (1) 100-mm VAS score (pain score rating by child). “no pain” (0mm) to “worst possible pain” (100mm)  
(2) 3-point verbal rating scale (pain assessed by the investigator)  
(3) Application time | 2mm (median); (ns)  
I : C = 11mm : 9mm  
(2) No difference (p=0.72)  
(3) I: C= 120min (range 40-180) :109min (range 62-175)  
Application time had significant effect on pain experienced, with a negative correlation in both groups.  
(4) Mild paleness:  
I:C = 9:7 (ns)  
Moderate redness:  
I:C = 1:1 (ns)  
(5) Slight discomfort  
I:C = 4:2  
p=0.40  
(6) No significant difference between I & C in adhesiveness of EMLA patch : tegaderm cream |
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants/setting</th>
<th>N</th>
<th>Interventions</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
</table>
| Chang et al. (1994)   | • 196, children aged 3-10 scheduled for surgical/oncological procedures necessary for venepuncture  
  • Mean age: I:C= 6.1:6.2  
  Boy: girl: I:C = 100 :96 | I: 96 C:100 | IG:  
  • EMLA patch applied 60-180 mins before venepuncture  
  CG:  
  • EMLA cream (5%, 1g) under deader dressing applied 60-180 mins before venepuncture | (1) Pain (three-point rating scale): none/ slight/ severe, assessed by subject & observer  
 (2) Discomfort from removal of patch/ tegaderm (three-point rating scale): none/ slight/ severe, assessed by subject & observer  
 (3) Adhesiveness of EMLA patch/tegaderm (five-point scale): -from 100% (totally affixed), 75-99%, 50-74%, 1-49% to 0% (not affixed at all)  
 (4) Local sensation (four-point rating scale): none/ mild/ moderate/severe | (1) no /slight pain  
 I:C = 95% : 94% (ns) (assessed by subjects)  
 I:C = 95% : 97% (ns) (assessed by observer)  
 (2) Subject rating:  
 I:C = 0 (ns)  
 (3) I:C = less adhesive EMLA patch (p<0.001)  
 (4) A mild pallor was observed I:C = 5:1, no difference (p=ns) |
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants/setting</th>
<th>N</th>
<th>Interventions</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>O’Brien et al. (2004)</td>
<td>Healthy 1-year-old infants receiving their routine 1-year MMR vaccination</td>
<td>120</td>
<td>IG:</td>
<td>Primary:</td>
<td>All Patients Treated (APT) approach. The significance level set at 0.05</td>
</tr>
<tr>
<td></td>
<td>• Age, d, mean:</td>
<td></td>
<td>• 1.0g of 4% amethocaine gel applied on upper, outer part of the infant’s arm &amp; covered with a dressing</td>
<td>• (1) Pain: using the Modified Behavioral Pain Scale (MBPS) (range: 0-10)</td>
<td>(1) Pain (mean MBPS score, SD) baseline:</td>
</tr>
<tr>
<td></td>
<td>• Weight, kg, mean:</td>
<td></td>
<td>• CG:</td>
<td>Secondary</td>
<td>I:C = 3.3(2.1) : 3.0(2.0)  p=0.399</td>
</tr>
<tr>
<td></td>
<td>• No gender difference between I &amp; C p=0.201</td>
<td></td>
<td>• Placebo visually and cosmetically identical to 1.0g of 4% amethocaine gel applied on upper, outer part of the infant’s arm &amp; covered with a dressing</td>
<td>(2) Post-vaccination antibody response -combined immunity (%) -geometric mean, SD</td>
<td>Post-injection:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I:C = 4.8(2.6) : 5.3(2.5)  p=0.309</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Difference:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I:C = 1.5(1.6) : 2.3(2.2)  p=0.029</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2) Antibody response:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-combined immunity (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I:C = 87% : 88%  p=0.823</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-geometric mean, SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Measles (AU):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I:C = 53.2(43.9):55.0(35.8)  p= 0.863</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mumps (AU):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I:C = 119.3(74.9) : 163.3(55.0)  p= 0.012</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rubella (IU/mL):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I:C = 107.8(84.0) : 140.4(65.0)  p= 0.098</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(3) Local reaction:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>redness: I:C = 52:26  p &lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>pallor: I:C = 29:16  p= 0.018</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>oedema: I:C = 27:4  p &lt;0.001</td>
</tr>
<tr>
<td>Study</td>
<td>Participants/Setting</td>
<td>N</td>
<td>Interventions</td>
<td>Outcome Measures</td>
<td>Results</td>
</tr>
<tr>
<td>-----------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-------</td>
<td>-------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Taddio et al. (1994)</td>
<td>Healthy infants receiving their 4-month / 6-month regular DTP vaccination in shared paediatric outpatient clinic</td>
<td>100</td>
<td>IG: 2.5g of EMLA cream to the upper part of infant’s thigh</td>
<td>(1) Pain score (MBPA) (Modified Behavioural Pain Scale) (range: 0 - 10) -cry (0-4) -Facial expression (0-3) -Movement (0-3) -Total (0-10) (2) Pain score (VAS) Unmarked Visual Analogue Scale (range: 0 - 100mm) (3) Local reaction to the removal of tegaderm: (3-categories: no reaction/ mild reaction, severe reaction) (4) Local reaction after the removal of cream: (4-point rating scale: none/ mild/ moderate/ severe)</td>
<td>(1) Pain (MBPS) Before vaccination I: C = 0, p=0.975 After vaccination: I: C = -1, p=0.001 (2) Pain (VAS): I: C = -22, p=0.002 I: 26 (0-94), C: 48 (0-97) (3) Local reaction: 92(93%) did not react to removal of tegaderm 30 (30%) had mild skin redness after the removal of tegaderm only 3 (3%) infants cried when removing the dressing (4) Local reaction after removal of cream: I:C = 90% : 12% p&lt;0.0001 Most common adverse reaction with EMLA was minor skin blanching (60%), and redness (30%)</td>
</tr>
</tbody>
</table>
### Table 8. Characteristics of systematic review

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of studies</th>
<th>Type of studies</th>
<th>Database searched</th>
<th>Main conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah et al. (2009)</td>
<td>• 32 studies, involving 3,856 infants and children from 2 weeks to 15 years of age</td>
<td>• 23 meta-analyses, 9 evaluated topical lidocaine-prilocaine</td>
<td>• Medline</td>
<td>• Topical local anaesthetics were associated with reduction in immunisation pain in children and should be recommended for routine use in clinical practice.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 10 trials, including 1156 infants and children, evaluated topical local anesthetics</td>
<td>• EMBASE</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• CINAHL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Cochrane Central Register of Controlled Trials</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Intervention components</td>
<td>Conducted by</td>
<td>Follow-up</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------</td>
</tr>
</tbody>
</table>
| Cassidy et al.| Multicentre, double-blind RCT with parallel groups | I: EMLA patch (5%-1g) (circle-shaped matrix with 1g of 5% eutectic emulsion with lidocaine, 25mg/g & prilocaine, 25mg/g)  
C: Placebo patch (1g of an inert oil) (circle-shaped matrix) | Medical doctors, nurses, scientists from Department of Medicine, Psychology, Paediatrics, Anaesthesia and Pain Service. | Pre-needle: 10s  
Needle phase: 10s  
Post-needle: 10-15s  
Frequency: not stated | A 26% ↓ in no. of children reported clinically sig. pain  
A small to medium effect size: d = 0.42 for all subjects |
| Halperin et al.| Single-centre, double-blind RCT | I: EMLA patch (5%-1g) (circle-shaped matrix with 1g of 5% eutectic emulsion with lidocaine, 25mg/g & prilocaine, 25mg/g)  
C: Placebo patch (1g of an inert oil) (circle-shaped matrix than could not be visually differentiated from EMLA)  
Blood sampling before and 28-35 days after immunisation for all children (I & C) | Medical doctors, scientists from departments of Paediatrics & Microbiology & Immunology, Psychology, Mathematics & Statistics.  
Study drug, placebo and funding from Astra Pharma Inc. Canada & Astra Pain Control, Sweden. | Baseline recording: 10s before vaccine injection  
Recording continued for 2 minutes after injection  
Venipuncture immediately after injection & videotaping process completed  
Local adverse events recorded at: 15min; 48hours after injection & 1 month post-immunisation visit | No deleterious effect on antibody response  
Pain score effect size : 0.5 |
<p>| Nilsson et al. | Open, randomised trial with parallel groups | I: Either EMLA patch (5%-1g) or EMLA cream (5%-1g) under tagederm dressing applied 60-180 minutes before venepuncture | Doctors, nurses in Department of Anaesthesiology &amp; Intensive Care University Hospital, Uppsala &amp; Astra Pain Control, Sweden | Before venepuncture to→venepuncture→ after venepuncture | NA. Both treatment groups VAS pain score was ≤15mm &amp; both obtained equal dermal analgesia effects provided that the application times ≥60 minutes |
| Chang et al.  | Open, randomised, comparative multicentre (three departments of anaesthesia &amp; two of oncology) | I: Either EMLA patch (5%-1g) or EMLA cream (5%-1g) under tagederm dressing applied 60-180 minutes before venepuncture | Doctors from department of anaesthesia &amp; paediatrics of Alberta Children’s Hospital, Canada | Before venepuncture to→venepuncture→ after venepuncture | NA. Both treatment groups Pain score by subjects and observers by using 3-point VAS. Both obtained equal dermal analgesia effects provided that the application times ≥60 minutes |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Intervention components</th>
<th>Conducted by</th>
<th>Follow-up</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Brien et al.</td>
<td>Single centre, double-blind RCT with parallel groups</td>
<td>I: 1.0g of 4% amethocaine gel &lt;br&gt; C: Placebo which was visually and cosmetically identical to 1.0g of 4% amethocaine gel</td>
<td>Paediatricians, nurses, pharmacists, technicians from Division of Clinical Pharmacology &amp; Toxicology, Departments of Pharmacy &amp; Paediatrics, Hospital for Sick Children, Faculty of Pharmacy and Institute of Medical Science, University of Toronto, Canada. &lt;br&gt; Sponsored by Smith and Nephew Ltd., Montreal, Canada.</td>
<td>From application time of study gel until removal &lt;br&gt; Before injection &gt; injection &gt; 30s after injection &lt;br&gt; One month after vaccination</td>
<td>Pain score (MPBS) effect size : 0.5</td>
</tr>
<tr>
<td>Taddio et al.</td>
<td>Single centre, double-blind randomised (in two blocks) clinical trial</td>
<td>IG: 2.5g of EMLA cream to the upper part of infant’s thigh with a dressing &lt;br&gt; CG: 2.5g placebo cream (coconut oil) which was visually and cosmetically identical to EMLA with a dressing</td>
<td>Paediatricians, nurses and pharmacists from the Division of Clinical Pharmacology and Toxicology, Hospital for Sick Children, Toronto, Canada. &lt;br&gt; Supported by Astra Pharma Inc, Canada.</td>
<td>From application time of study cream until removal &lt;br&gt; Before injection (within few minutes after removal of cream and infant was settled) &gt; injection (within 5s) &gt; after injection (within 15s) until infant settled down</td>
<td>Not reported directly Pain score (MBPS) difference IC was: 1 (effect size)</td>
</tr>
</tbody>
</table>
Results of Review

Effect of interventions vs. usual care

Among the six selected RCT studies, four (Cassidy et al., Halperin et al., O’Brien et al., Taddio et al.) applied the Modified Behavioural Pain Scale (MBPS, modified from the Children’s Hospital of Eastern Ontario Pain Scale) to score pain in infants. The MBPS was used to score baseline pain and post-vaccination pain in vaccination procedures, examining facial expression (range: 0-3), crying (range: 0-4) and body movement (range: 0-3) by assigning each form of behaviour a score. Individual behaviour scores are summed, resulting in a total score per phase (before and after). The three phases’ total scores ranged from 0 (minimum) to 10 (maximum). In addition, the Visual Analogue Scale - pain (VAS) was another pain measurement tool applied by Cassidy et al., Taddio et al., and Nilsson et al. while Cassidy et al. applied both Visual Analogue Scale (VAS)-pain for parents and technicians to rate children’s pain, and VAS-anxiety for parents to rate their own and their child’s vaccination-related anxiety. A 10-cm/100-mm (VAS), on which the endpoints were ‘no pain’ (0 cm) and ‘worse possible pain’ (10 cm). The VAS has been found to be a highly sensitive measure of pain in adults with a homogenous distribution and good correlation in descriptive scales (Huskisson, 1974).

Cassidy et al. found a small to medium effect size (i.e. 0.42) for EMLA on children’s self-reported pain in comparison with the control group (CG). The EMLA patch caused a 26% reduction in the number of children who reported significant pain. Halperin et al. and O’Brien et al. reported a similar effect size of 0.5, while Taddio et al. reported a bigger effect between CG and IG (i.e. 1). Halperin et al. found a significant difference between IG and CG in terms of the geometric mean for the mumps titers only (p = 0.012). However the levels were still protective.
Taddio et al. found no pre-vaccination (MBPS) score difference between the two groups 
\((p = 0.975)\), but both post-vaccination (MBPS) scores and the difference between the pre & post-
vaccination (MBPS) scores were lower for the EMLA group (IG) \((p = 0.001)\). Similarly, lower 
Visual Analogue Scale (VAS) scores were found in (IG) \((p = 0.002)\). Hence, Taddio et al., 
(1994) reported significant Pain (VAS) difference between (IG) and (CG) \((-22, p = 0.002)\).

Both Chang et al. and Nilsson et al. demonstrated that there was no difference between 
EMLA cream and EMLA patch in either analgaesthetic effectiveness or local reaction, and as a 
single-dose, easily applied product the EMLA patch may have a role as a convenient form of topical anaesthetic prior to injection, venepuncture, cannulation etc.

All six of the selected studies assessed the local reaction to either EMLA /amethocaine after the removal of patch/tegaderm, and post-vaccination/venepuncture procedures, and found minor local reactions only, such as redness of skin or itchiness.

The systematic review by Shah et al (2009) included 32 studies, involving 3,856 infants and children aged from 2 weeks to 15 years. 23 of these trials were included in meta-analyses. Ten trials, including 1,156 infants and children aimed to evaluate topical anaesthetics, showing that they could decrease injection pain than placebo in six trials based on the difference between MBPS. Observer-rated pain by VAS score was significantly lower in intervention groups.

Quality assessment

Overview of methodological quality

An appraisal of the methodology of each study was undertaken with reference to the checklists established by SIGN. Quality assessment of the six randomised controlled trials is presented in Table 10. According to SIGN, there are ten parameters in this aspect that need to be considered: (1) clearly focused question; (2) randomisation; (3) adequate concealment; (4)

23
double blind treatment/allocation; (5) comparability of the intervention and control groups; (6) only difference is treatment; (7) valid measurement of outcomes; (8) drop-out rates; (9) intention to treat analysis and (10) comparable results from all sites.

All the six RCT studies described a focused research question or a purpose statement with clearly stated proposed interventions, and all obtained approval from the Ethics Committee of the university/ hospital/ review board in accordance with the principles of the Helsinki Declaration. Moreover, informed consents (in verbal or written form) were collected from parents before the randomisation procedure. Nilsson el al. and Chang et al. could not achieve masking/blinding treatment allocation because of the different appearance of the two treatments, while the other four studies were able to achieve a double blinding design, which could keep people unaware of the participants’ treatment allocation, in order to minimise difference sources of potential bias.

High quality studies

Three of the RCTs (Cassidy et al., Halperin et al., O’Brien et al.) were high quality studies in which a grade of 1++ was achieved (Table 11). They not only reported clear randomisation procedures and group allocations, but blinding was also considered, bias thus being minimised. Moreover, the sample size calculation was explained in detail in these three studies so that the numbers of participants ensured proper power analysis, allowing the results to be considered robust. O’Brien et al’s study even accounts for possible dropouts and technical failure in videotaping and blood collection, recruiting a sample of 120 participants (60 per group), instead of 48 per group (calculated by using previous data from Taddio et al.). The drop-out rate of the three studies were very low, with a range of zero (O’Brien et al.) to 5% (Cassidy
et al.). Nevertheless, intention to treat (ITT) was applied during the data analysis procedure for these three studies (see Table 10).

The systematic review by Shah et al. was graded 1++ high quality, addressing the question with clarity and a rigorous search (i.e. four search engines were covered Medline, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials), with quality assurance. Shal et al. reported that the use of topical anaesthetics was associated with less pain between (IG) and (CG) in four trials (527 infant/children) based on the difference from the Modified Behavioural Pain Score (MBPS) (range, 0-10). The weighted mean difference (WMD) was -0.79 (95% CI, -1.10 to -0.48, p < 0.001), and the SMD was -0.43 (95% CI, -0.60 to -0.26, p = 0.001). Shah et al. concluded that topical local anaesthetic and combined analgesic interventions were associated with reduced pain during immunisation and should be recommended for use in clinical practice (Tables 12 and 13).

**Medium quality studies**

The other three selected RCTs (Nilsson et al. Chang et al. Taddio et al.) were graded 1+, which defined as medium quality. The RCTs carried out by Nilsson et al. and Chang et al. had moderate methodological quality only as both failed to include blinding (because their study objectives were to compare the analgesic effect of EMLA patch and EMLA cream in combination with tegaderm). Chang et al. did not report their sample size calculation before randomisation. Moreover, their study participants were from diverse departments (three anaesthesia and two oncology) which were scheduled for surgical or oncological procedures, which might affect the generalisation and internal validity of the study. Nilsson et al. also failed to report the sample size calculation or any pilot study before the actual study. Furthermore, the demographic characteristics of participants were not being defined and reported with clarity. For
example, it was mentioned that ‘sixty children, boys and girls, aged between 5 and 15 years who
required venous cannulation were studied’. All this uncertainty might affect the internal validity
of studies.

Taddio et al.’s drop-out rate was the highest among the six selected RCTs at 11% (still
within an acceptable range), but did not practise intention to treat (ITT) during the data analysis
procedure, and so only 96 subjects were available for study. But this sample size was exactly
equal to the calculated sample size of 96 (48 each group), which had been produced before
randomisation and could still show a 50% difference in pain scores with an SD that was twice
this difference. Taddio et al. applied coconut oil as a sham ingredient visually and cosmetically
identical to EMLA patch as a control. Since coconut oil has a natural odour, the sham might
interfere with the double-blinding design. To sum up, these three studies did not clearly mention
whether the treatment and control groups were similar at the start of the trial, and it was therefore
uncertain whether the participants accounted for the conclusions reached. Details of the overall
quality assessment of selected studies are given in Table 11.
Table 10: Internal validity assessment of selected studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Clearly Focused Question</th>
<th>Random Allocation</th>
<th>Adequate Concealment</th>
<th>Double Blind Treatment Allocation</th>
<th>Groups Comparable</th>
<th>Only Difference is Treatment</th>
<th>Valid Measurement of Outcomes</th>
<th>Drop-out Rate</th>
<th>Intention to Treat analysis</th>
<th>Comparable Results From all Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassidy et al.</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>~5%</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Halperin et al.</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>~3%</td>
<td>++</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Nilsson et al.</td>
<td>+++</td>
<td>++</td>
<td>NA</td>
<td>NA</td>
<td>++</td>
<td>++</td>
<td>~5%</td>
<td>+++</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Chang et al.</td>
<td>+++</td>
<td>++</td>
<td>NA</td>
<td>NA</td>
<td>++</td>
<td>++</td>
<td>~9%</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>O’Brien et al.</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>0</td>
<td>++</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Taddio et al.</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>~11%</td>
<td>++</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Well covered (+++); Adequately Covered (++); Poorly Covered (+); Not Covered (–); Not Reported (NR); Not Applicable (NA)

Table 11: Overall quality assessment of the selected studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Bias Minimised</th>
<th>Direction of Bias</th>
<th>Effect due to Intervention</th>
<th>Results Applicable to Target Group</th>
<th>Overall Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassidy et al.</td>
<td>++</td>
<td>The presence of more skin reactions in the intervention group</td>
<td>Yes</td>
<td>Yes</td>
<td>High (++)</td>
</tr>
<tr>
<td>Halperin et al.</td>
<td>++</td>
<td>Two subjects (both placebo group) were excluded from analysis of pain</td>
<td>No</td>
<td>Yes</td>
<td>High (++)</td>
</tr>
<tr>
<td>Nilsson et al.</td>
<td>+</td>
<td>Pre-medications may have an influence on pain perception</td>
<td>No</td>
<td>Yes</td>
<td>Fair (+)</td>
</tr>
<tr>
<td>Chang et al.</td>
<td>+</td>
<td>18 patients were excluded from analysis</td>
<td>No</td>
<td>Yes</td>
<td>Fair (+)</td>
</tr>
<tr>
<td>O’Brien et al.</td>
<td>++</td>
<td>Lost to follow-up /a technical failure in collecting blood</td>
<td>No</td>
<td>Yes</td>
<td>High (++)</td>
</tr>
<tr>
<td>Taddio et al.</td>
<td>+</td>
<td>4 subjects deviating from the study protocol were excluded from analysis after randomisation</td>
<td>Yes</td>
<td>Yes</td>
<td>Fair (+)</td>
</tr>
</tbody>
</table>

- Would the placebo have any special smell from the coconut oil?
### Table 12. Internal validity of selected systematic review

<table>
<thead>
<tr>
<th></th>
<th>Addressed an appropriate and clearly focused question</th>
<th>A description of the methodology used is included.</th>
<th>Search is sufficiently rigorous to identify all the relevant studies.</th>
<th>Study quality is assessed and taken into account.</th>
<th>There are enough similarities between the studies selected to make combining them reasonable.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah et al.</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

### Table 13. Overall quality of systematic reviews

<table>
<thead>
<tr>
<th></th>
<th>How well was the study done to minimise bias?</th>
<th>Summary of the authors’ conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah et al.</td>
<td>+++</td>
<td>Topical local anaesthetic, and combined analgesic interventions were associated with reduced pain during immunisations and should be recommended for use in clinical practice.</td>
</tr>
</tbody>
</table>
Summary and synthesis

Analysis of interventions’ characteristics and effectiveness

In five selected studies (Cassidy et al., Chang et al., Halperin et al., Nilsson et al., Taddio et al.) and the systematic review, EMLA was used as an intervention to reduce routine immunisation/venepuncture pain for infants/children. EMLA (cream/patch) which contains 2.5% lidocaine and 2.5% prilocaine is used to create a temporary loss of feeling or numbness of small areas of skin (slightly larger than a two-dollar coin). Since EMLA should be applied at least 60 minutes before producing an anaesthetic effect, the documentation of application and removal times is observed in all five studies. EMLA has been approved and registered in many Western countries - Sweden, Canada, United Kingdom, United States etc. - as well as in Hong Kong (Reg No. HK-27892). Human clinical trials proved that EMLA can be used: (1) prior to receiving a needle or having blood taken, and only on healthy, unbroken skin; (2) prior to vaccination, only MMR, DTP, Hepatitis B, Hib (haemophilus influenza b) and BCG (Dohlwitz et al,1998; Halperin et al., 2002; Halperin et al., Taddio et al.) for infants > 3 months to 12 year-old children. But its use is not recommended in connection with any other vaccine until further clinical trials have been undertaken.

4% amethocaine gel is a relatively new topical anaesthetic which produces anaesthesia within 30-45 minutes and therefore may be more appropriate for use in out patient/ primary care settings (O’Brien et al.). It has also been approved and registered in overseas countries such as Australia, Canada, New Zealand and the United Kingdom, as well as in Hong Kong (Reg No.HK-45083). EMLA and amethocaine are equally effective in reducing the pain of needle puncture, but under some circumstances the use of amethocaine may be more flexible and user-friendly (Choy, Collier & Watson, 1999).
Summary of the evidence

Current methods of measuring infant/child pain include direct observation of behaviour, physiological responses or both (Cassidy et al., Halperin et al., Halperin et al., O’Brien et al., Shah et al., Taddio et al.). Research evidence shows that topical anaesthetics are associated with lower pain scores and less crying in infants and children. In addition, parents were willing and able to apply the cream/patch correctly before the child’s vaccination (Cassidy et al., Halperin et al., O’Brien et al., Parvez et al., 2010). Reduction of injection pain through the use of topical anaesthetics could have a positive effect on the immunisation programme by enhancing public acceptance of the procedure and increasing the proportion of infants immunised on schedule.

Implications for practice

The gap between the publishing of research and its translation into practice to improve health and patient care is a cause for concern in healthcare organisations and federal agencies (Melnyk & Fineout-Overholt, 2011). An intensive and comprehensive review of previous research evidence in a study on the pain of childhood vaccination by Taddio et al. (2010b) recommended that: ‘topical anaesthetics are effective for reducing vaccination pain’ (Grade A recommendation, based on level I evidence). Thus using topical anaesthetics to reduce the vaccination pain and distress of children in a maternal and child health centre setting has been considered, in order to achieve the best evidence of nursing care and improve care or health outcomes of immunisation.

Conclusion

In conclusion, health and medical care can be improved if pain management becomes a routine aspect of the delivery of vaccine. It is clear that current analgesic practices could be improved substantially if all those involved in immunisation (policy-makers, healthcare
professionals, parents etc.) participate in efforts to treat pain during childhood immunisation, for such a practice might enhance the positive experience of vaccination for children and their families. Other potential benefits include improved adherence to immunisation schedules and a substantial reduction in untreated pain - immunisation is at the core of healthcare, after all.
Chapter 3

Implementation potential

After critical appraisal of the six randomised controlled trials and the systematic review, the evidence-based findings recommend that topical anaesthetics are an effective intervention to minimise injection pain among healthy children. In spite of the literatures suggesting that many innovations are beneficial to clinical care and its outcomes, few of them are being implemented in clinical practice (Taddio et al., 2007; Christian, 2012). Moreover, as it takes an average of 17 years to bring research findings into practice, aggressive initiatives must be undertaken to reduce this large research-practice gap (Melnyk & Fineout-Overholt, 2011). In view of the health benefits of applying topical anaesthetics, it is clearly advisable to implement and co-opt this clinical procedure into the local setting. In order to facilitate practice with evidence, a comprehensive investigation should be carried out before its local launch. Prudent considerations are focused on the transferability, feasibility and cost-benefit ratio of the programme (Shepard et al., 1995).

Target setting and population

Proposed setting

The Maternal and Child Health Centres (MCHC) will be selected since nurses working in MCHCs are potential users of the guidelines. In the review of RCTs, the study settings included family physician clinics, urban and private GPs’ clinics and paediatric outpatient clinics in Canada and Sweden, and there is a similarity to local settings where healthcare services are provided by a dedicated team of medical and nursing professionals together with supporting staff from a cluster of 31 Maternal and Child Health Centres (MCHCs) and three Woman Health Centres (WHCs).
Philosophy of care

The mission of the Family Health Service (FHS) is to improve maternal and child health through providing evidence-based, quality-assured and cost-effective services to meet the changing needs of the community (FHS, 2012). The proposed intervention is based on the same philosophy of care of existing maternal and child health services, aiming to reduce immunisation pain among healthy children as well as the associated negative feelings experienced by their parents and families during the vaccination procedure.

Target population

In this translational nursing project, the proposed targets are healthy children aged between one and six years recommended to receive routine or catch-up immunisations at the Maternal and Child Health Centre, with the objective of reducing immunisation-induced pain. The recommended immunisation programme is set out in Appendix E. The target population is similar to the subjects in the review RCTs and systematic review in age, sex and health status. Basically, infants receive B.C.G. and the first dose of hepatitis B vaccine in hospital. Subsequent recommended immunisations will be at Maternal and Child Health Centres or private general practitioners or hospitals, from one month to eighteen months of age. Recommended immunisation by School Immunisation Teams will be carried out for primary students together with the health assessment programme provided by the Student Health Service, Department of Health.

Transferability of the findings

Fit of intervention in the proposed setting

In the previous chapter, seven studies were identified, published from 1994 to 2009, which are relevant to the management of immunisation pain by applying topical anaesthetics as
an intervention. The clinical settings in these published papers included family clinics, general practitioner clinics and out-patient clinics in Canada and Sweden, both well-developed and innovative countries. Hong Kong is one of the most developed territories in the Asian region and, as the proposed innovation is derived from the evidence generated in other developed countries, it is expected that the innovation will fit the local setting.

**Similarity of research to target population**

In the MCHCs, over 95% of the target population are healthy Chinese children up to six years old, while the participants in the reviewed studies were normal healthy children aged between six months and 12 years, with similar characteristics in age, sex and health status to those of the local target population in MCHCs, where the setting is similar to the general family physician clinics, urban and private GPs’ clinics and paediatric outpatient clinics in overseas countries, as described earlier.

**Similarity of organisational and administration support**

In the reviewed studies, organisational support was supplied by direct funding/grants from hospital, university or pharmacological companies, as well as administrative and organisational supports to carry out the randomised controlled trials. Thus, data can be collected and the outcomes of the studies can serve as evidence to confirm the hypothesis and the significance of the intervention through analysis and publication. As one of the leading services of the Department of Health, the Family Health Service (FHS) allows clients to improve their health through the provision of evidence-based and quality-assured service, together with partnership, innovation, flexibility and technology. In the light of such mutual commitment, the present proposed guideline is likely to be advocated by the FHS. In addition, the Department of Health (DH) is the major provider of immunisation services to safeguard the health of the
community. Over a million doses of vaccine are administered yearly by nurses, in Family, Student, Elderly and Travel Health Services. It is anticipated that the proposed guideline would be beneficial not only to normal healthy children, but also to those with ‘needle phobia’. Where logistical and financial factors permit such an approach, topical anaesthesia should certainly be considered.

**Feasibility**

**Sufficient number of targets**

Early in the 1950s, the DH was already providing a free comprehensive childhood immunisation programme to protect infants and children from serious infectious disease. Since then, the Hong Kong programmes have been extended to other at-risk groups, including people aged above 65, pregnant women, workers in the poultry trade and healthcare staffs. In 2008, the DH adopted a public-private partnership approach and introduced various vaccination subsidy schemes to eligible groups of citizens. According to *Health Facts of Hong Kong 2012*, the official estimate of immunisation coverage was 95%, including BCG, hepatitis B vaccine, DTaP-IPV vaccine as well as MMR. In one of my work centres, about 400 healthy infants and children receive vaccination every month, and about 20% of them are children aged 12 months or more. In this way, a majority of healthy children would be served if the intervention was launched in my centres as well as the other 30 MCHCs - even other possible departments in future.

**Staffing support and consensus**

As the most valued of leading healthcare providers, healthcare professionals working in FHS are dedicated people, with a strong team spirit. However, some of them have been working in hospitals or similar services over a long period, over ten years in many cases. As a result, they may be more reluctant to change and to adopt innovations. Friction may be encountered if nurses
arrange for children to receive topical anaesthetics before immunisation, while medical doctors may be reluctant to prescribe such anaesthetics. Staff education and dissemination of the relevant information is therefore advisable to overcome such problems and achieve the right consensus and support. After setting up the translational nursing proposal, a working group will be established, comprising mainly nursing staff but with a medical representative, a clinical psychologist and administrative representatives. Working group members should share their ideas freely within group meetings and arrange the processes of implementation and evaluation in advance.

**Implementation and evaluation processes**

A Gantt chart has been developed to outline the whole project process - preparation, submission for approval, implementation and evaluation processes of the proposed innovation (Table 14).

After preparing the proposal, a working group will be organised to execute the project within two months, with subsequent submission of the proposal for the approval of the Department of Health, an interval of three months, while staff training and equipment preparation will be launched within one month. A pilot study will be carried out before the implementation period (Ahlers-Schmidt et al., 2012). The interim steps will take five to six months and the final process of evaluation (short and long run) will take another month or so after the analysis of data.
**Table 14.** A Gantt chart for monitoring process

<table>
<thead>
<tr>
<th>Process</th>
<th>Month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Jan</td>
</tr>
<tr>
<td>1. Preparation of proposal &amp; setting up working group</td>
<td></td>
</tr>
<tr>
<td>2. Submission of proposal</td>
<td></td>
</tr>
<tr>
<td>3. Waiting for approval</td>
<td></td>
</tr>
<tr>
<td>4. Staff training &amp; equipment preparation</td>
<td></td>
</tr>
<tr>
<td>5. Pilot study</td>
<td></td>
</tr>
<tr>
<td>6. Implementation</td>
<td></td>
</tr>
<tr>
<td>7. Evaluation</td>
<td></td>
</tr>
</tbody>
</table>
Cost-benefit ratio of the innovation

Potential risks

There is no potential risk in the case of this intervention according to the RCTs and Shah et al’s systematic review. Only minor local reactions, itching and skin pallor, were reported, and only by a minority of the study subjects.

Potential benefits to clients

The RCTs and systematic review clearly recognised that parents and other family members revealed great concern and anxiety about the pain induced by immunisation. In my work department, most immunisation-related conflicts and complaints, according to daily observation and past experience, are mainly related or directly due to such associated anxiety or negative feelings. With the continuing introduction of new programmes, infants/children need to receive multiple immunisation injections at a single visit. Support is likely to be gained for the innovation by illustrating the potential benefits of reduced pain.

To convey the benefits to the proposed target population, implementation of the proposed innovation should be executed in advance. Nursing staff may encounter slightly increased workloads, but the core benefits for children, family members and nurses will become apparent in due course, since conflicts and complaints will be reduced in the long run. And positive commendations from parents will be likely to raise nurses’ morale.

Risks of maintaining current practice

Children, parents and medical staff will continue to experience distress at immunisation-induced pain if we still neglect people’s negative feelings. Furthermore, it may cause anxiety before any medical procedure, needle fears and healthcare avoidance behaviour. It is therefore expected that a positive experience during vaccination is an essential element in minimising pain
during injections and strengthening trust in healthcare providers, and that this can be achieved if the innovation is launched.

**Skills available to implement intervention**

Most of the staff working in Family Health Service MCHCs are already well trained to administer immunisation with competence and quality assurance. The skill of applying a topical anaesthetics is easy to learn. As a single-dose product that is easy to apply, the EMLA patch may have a role as a convenient form of analgesic prior to immunisation. Moreover, with its ease of application, very limited instruction of healthcare provider or parent is required.

**Material costs of the innovation**

Material costs come mainly from the items consumed in the intervention, i.e. EMLA patches, in addition to the preparation of related information leaflets and evaluation forms (Taddio et al., 2013). A budget estimate of the material costs of the proposed intervention appears in Figure 2. The purchase price (private only) of EMLA cream with six tegaderm inside is HK$120 (information from Pharmacy, Hospital Authority Hospital). The cost is therefore HK$20 per patch (single dose), giving a total material cost for every 160 children each month of HK$3,200 (Figure 2).

**Non-material costs of the innovation**

In addition to the material cost, there are certain non-material costs (Figure 3.) incurred in adopting the proposed intervention, inevitable with a standardised protocol and additional informative leaflets to facilitate and streamline education (Taddio et al.). Health education may decrease negative client feelings towards injection and avoidable complaints can be diminished, with daily operation expected to be carried out in a cost effective manner.
### Budget of material costs for every 160 eligible children

<table>
<thead>
<tr>
<th>Material</th>
<th>Cost</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. EMLA patches</td>
<td>HK$20 per patch (single dose)</td>
<td>$3,200</td>
</tr>
<tr>
<td></td>
<td>Estimate: 160 x $20 = $3,200</td>
<td></td>
</tr>
<tr>
<td>2. Leaflets &amp; copies of protocol and evaluation forms</td>
<td>HK$0.5 per page</td>
<td>$800</td>
</tr>
<tr>
<td></td>
<td>Photocopying fees: 1,600 x $0.5 = $800</td>
<td></td>
</tr>
</tbody>
</table>

### Budget of non-material costs for every 160 eligible children

<table>
<thead>
<tr>
<th>Personnel</th>
<th>Cost</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Nursing staff responsible for client education</td>
<td>Salary ~ HK$30,000/month ~$173/hour</td>
<td>$2,335.5</td>
</tr>
<tr>
<td></td>
<td>Hours invested: 5 minutes x 160 = 13.5 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimate cost: $173 x 13.5 = $2,335.5</td>
<td></td>
</tr>
<tr>
<td>2. Nursing staff responsible for administration procedures</td>
<td>Salary ~ $30,000/month ~$173/hour</td>
<td>$2,335.5</td>
</tr>
<tr>
<td></td>
<td>Hours invested: 5 minutes x 160 = 13.5 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimate cost: $173 x 13.5 = $2,335.5</td>
<td></td>
</tr>
<tr>
<td>3. Nursing staff responsible for evaluation</td>
<td>Salary ~ $35,000/month ~$202/hour</td>
<td>$2,727</td>
</tr>
<tr>
<td></td>
<td>Hours invested: 5 minutes x 160 = 13.5 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimate cost: $202 x 13.5 = $2,727</td>
<td></td>
</tr>
</tbody>
</table>
Chapter 4

Evidence-based practical guidelines

Overview of guidelines

Title

The title is ‘Evidence-based clinical guidelines for applying topical anaesthetics to reduce injection pain in healthy children.

Aim

The aim of the guidelines is to provide an evidence-based clinical protocol for nursing staff to practise pain-relieving intervention for children receiving immunisation, by means of topical anaesthetics administered via EMLA patches.

Objectives

The objectives of this guideline are:

♦ To summarise the clinical evidence for promoting evidence-based pain-relieving intervention for healthy children when they are receiving routine immunisations.

♦ To formulate clinical instructions for practising pain-relief intervention, i.e. application of EMLA patches, based on the best evidence available.

♦ To reduce the anxiety and distress experienced by parents and families during routine immunisation.

Target group
The target population consists of healthy children from one to two years of age undergoing routine immunisation. Children older than two but under six will also be included if they receive immunisation outside the recommended schedule.

**Interventions and practices considered**

Intervention of applying topical anaesthetics, i.e. EMLA patches, before routine immunisation is considered for implementation.

**Outcomes considered**

Major outcomes are reductions in:

1. Pain scores;
2. Parent reports of children’s distress;
3. Nurse’s reports of child distress.

**Recommendations**

Recommendations were derived from the seven reviewed studies in accordance with levels of evidence and grades of recommendations established by the Scottish Intercollegiate Guidelines Network (SIGN) (2008) (see Appendix D). Recommendations in this guideline were generated according to the best available evidence, and only grade A recommendations are included.

**Recommendation 1.0 – Who should be administered topical anesthetics?**

♦ All healthy children from 12 months to 12 years old should be given topical anaesthetics on their skin prior to immunisation.

♦ 4 – 6 years (Cassidy et al.) (1++)

♦ 12 months (Halperin et al.) (1+++), O’Brien et al.) (1++
♦ 5 – 15 years (Nilsson et al.) (1+)

♦ 3 – 10 years (Chang et al.) (1+)

♦ 4 – 6 months (Taddio et al.) (1+)

♦ 0 – 18 years (Shah et al.) (1++)

**Recommendation 2.0 - When to apply topical anaesthetics.**

♦ Topical anaesthetics should be applied 30 to 60 minutes before vaccination

♦ 60 to 120 minutes (Cassidy et al.) (1++); (Halperin et al.) (1++); (Nilsson et al.) (1+);

   (Chang et al.) (1+); (Taddio et al.) (1+)

♦ 30 minutes (O’Brien et al.) (1++)

♦ 30 to 60 minutes (Shah et al.) (1++)

**Recommendation 3.0 - Dosage of anaesthetic**

♦ EMLA cream (5%-1g) (2.5% lidocaine & 2.5% prilocaine)

   (Cassidy et al.) (1++); (Halperin et al.) (1++); (Nilsson et al.) (1+); (Chang et al.) (1+);

   (Shah et al.) (1++) and (Taddio et al.) (1+)

♦ 4% 1g amethocaine gel (O’Brien et al.) (1++)

**Recommendation 4.0 - Administration method**

♦ Apply topical anaesthetic to skin in a patch-form or with a dressing.

   (Cassidy et al.) (1++); (Halperin et al.) (1++); (Nilsson et al.) (1+);
(Chang et al.) (1+); (Shah et al.) (1++) and (Taddio et al.) (1+) and (O'Brien et al.) (1++)

**Recommendation 5.0 - Administration technique**

♦ Apply EMLA patch to the injection site, i.e. upper part of thigh or mid-deltoid muscle with easy technique.

**Summary**

Reducing pain at the time of injection by the application of topical anaesthetics, and encouraging parents to use this intervention during vaccination of their children should be recommended for clinical practice *(grade A recommendation, based on level I evidence).*
Chapter 5

Implementation plan

Introduction

Previous chapters have maintained that, despite global advances in vaccines, pain associated with immunisation is usually neglected or undertreated among healthy children although pharmacotherapy has been found to be effective in reducing iatrogenic pain from clinical procedures such as vaccination or injection (Taddio et al.). Evidence-based clinical guidelines are promising tools for filling such gaps in research-evidence practice. In order to facilitate the implementation plan from the development phase to service provision, an evidence-based protocol, a communication plan and a pilot test are key components.

Plan for communication with potential users

Stakeholders

The proposed innovation will be launched in a part-time Maternal and Child Health Centre situated in the Kowloon peninsula. The senior administrative, medical and nursing staff in the head office of the Family Health Service and Public Health Nursing Division are influential stakeholders, since their support and endorsement are of great value the implementation (Christian 2012; Taddio et al.). In order for frontline staff serving in daily centres to adhere to the guidelines, the medical officer-in-charge, nursing officer-in-charge and nursing officers in MCHC will act as managing supervisors. It can be expected that some staff will be in favour of the innovation and that others will oppose it, and the role of the nursing officer is therefore vital. The other stakeholders are the healthy children themselves and their parents since their feedback and suggestions will also contribute to the innovation (Taddio et al.).

Communication process
To go through the implementation plan, nursing best-practice champions have a multi-dimensional role that is well suited to navigating the complexities of a dynamic health system to create positive change (Ploeg et al., 2010). A proposal with a table of evidence arguing the necessity of change in practice, a protocol covering implementation potential, barriers, feasibility, cost effectiveness, budget plan and timeline of the proposed innovation will be prepared and submitted to the Senior Nursing Officer and Senior Medical Officer at head office for an advance sight. If permission is granted, a summary of the proposal will be presented at the next senior staff meeting.

A working group will be established consisting of a medical doctor, a nursing officer and a registered nurse/the proposer. Information about the innovation will be discussed and shared among the working group by the proposer (Graydon et al., 1993). Concerns about pain from immunisation will be discussed, as well as the inadequacy of current practice. The evidence for the guidelines and effectiveness of topical anaesthetics in reducing pain will also be examined. There will not be an immense impact on existing routine immunisation practice, while the stakeholders and working group members are urged to accept and support the proposed innovation.

With approval received from the Head Office, subsequent communications and liaison with frontline colleagues will be processed. Frontline staff can be guided through open discussions held during lunch hour meetings or any other formal or informal meetings, in order to convey the benefits of the innovation and to increase colleagues’ motivation to change. Since they will implement the proposed innovation directly to children, they should be familiar with the innovation in accordance with the guidelines (Melnyk & Fineout-Overholt).

Communication methods
It is advisable that regular meetings, telephone conversations or internet communications be conducted among representatives of the working group together with the Research Team in Head Office, so that the study’s progress will be followed in the course of regular departmental meetings.

A full briefing for frontline colleagues will be conducted two or three weeks in advance of implementation of the guidelines, whose procedures, with related photographs, will be featured in staff training and will be distributed to all frontline doctors and nurses in the centre. A copy of the guidelines will be displayed in the injection, Nursing Officer’s, Medical Officer’s and interviewing rooms. Furthermore, posters will be used to introduce the launch of the innovation, and put up in the waiting hall, the injection room and the Health Education Corner. Educational leaflets will be provided to parents for their information. Common concerns about topical anaesthetics will be explained in the leaflets in order to support its benefits. It is suggested that at least one experienced nurse will be assigned to immunisation duty at every infant session during the pilot and implementation periods of the innovation (Muller et al., 2010).

**Sustaining the change process**

The nursing officer will guide and sustain the change by creating a supportive environment and cohesive team functioning during the handover time in the first fortnight of the pilot phase before the implementation itself (Barrett et al., 2009). Reminders about using the innovation will be posted in the waiting area for frontline staff, and for publicity purposes. During the implementation period, the nursing officer/proposer will act as a supervisor to assess whether frontline colleagues adhere to the compliance properly to achieve the sustainability of the implementation guidelines. The nursing officer of the working group will take the role of an auditor able to sit in and observe the process and check that the guidelines are being applied with
a satisfactory compliance level. An evaluation will be carried out at week two of pilot in order to assess the immediate impact - health status, staff commitment to action, satisfaction/acceptance etc. - of applying topical anaesthetics to children undergoing the routine immunisation procedure.

**Pilot testing**

A thorough pilot testing of every aspect of the innovation should be carried out in order to test its feasibility and identify potential barriers prior to full-scale launching of guidelines. The pilot should act as a rehearsal of the implementation so that the dynamics, logistics and characteristics of the guidelines can be fine-tuned and the preliminary data can be evaluated after collection.

A pilot study covering 20 healthy children aged one year and above will be carried out in one of the part-time Maternal and Child Health Centres in Kowloon. The whole pilot plan will last two to three weeks. The innovation guidelines, administration methods and procedures, relevant photos etc. will be provided for staff training before launching the pilot. Consent forms and educational leaflets will be prepared for the recruitment procedure and for client education. Outcome measurements such as pain scores and local reactions will be recorded on the data collection form (see Appendix F). Nurse and parent reports of any child distress will be acquired by means of questionnaires (see Appendices G & H).

Similarly, a questionnaire will be distributed to nurses and parents for evaluation of their satisfaction levels in respect of the innovation (see Appendices I & J). The smoothness of procedures and administration techniques of nursing staff will be monitored to check whether they can administer the topical anaesthetics (EMLA patches) properly in line with the guidelines. Resource and process monitoring is crucial and must be done from pilot to implementation as
well as during the evaluation period. Evaluation of and amendments to the guidelines will be carried out accordingly after data from the pilot test is available.
Chapter 6
Evaluation plan

Intervention outcomes and their measurements

To justify the effectiveness of the innovation/guideline, an outcome evaluation is featured, with monitoring of the process itself, clients’ involvement, clinical settings, expenses and data collection as well as the standards being maintained. It is anticipated that continuous monitoring will be a vital tool in making decision to balance the effectiveness of the innovation.

Client outcomes

The primary outcome is to reduce immunisation-induced pain and distress in healthy children aged one year or more through applying topical anaesthetics (EMLA patches). The level of pain will be measured by the Modified Behavioural Pain Scale (MBPS) (range of scores 0 to 10) (see Appendix F). The MBPS is a well-validated pain measurement scale that examines facial expression (range 0-3), crying (range 0-4) and body movement (range 0-3) by assigning each form of behaviour a score, and summing up to give a total score per phase, i.e. before and after immunisation (Cassidy et al., Halperin et al., O’Brien et al.). The minimum score is 0 and the maximum 10 of the three behavioural measurements. The MBPS will be used to score pre- and post-vaccination pain for each procedure. In addition, a 10cm unmarked Visual Analogue Scale (VAS) (range 0-10cm) will be used to measure children’s distress during routine immunisation. On the VAS, a score of 0 denotes no pain, and 10cm denotes maximal pain. A questionnaire will be distributed to parents or caregivers after immunisation asking them to rate the children’s level of distress on VAS. A similar questionnaire will be distributed to the nurse performing the procedure to rate children’s levels of distress immediately after immunisation (see Appendices G & H). The evaluation nurse will use a ruler (cm) to measure the length of marking on unmark-VAS (both parent and nurse’s markings) and write the result on the form.
The secondary outcome, local skin reaction after removal of the anaesthetic, will be measured on a four-point scale (none/ mild/ moderate/ severe). Other outcomes, such as the number of complaints/special requests concerning routine immunisation, e.g. a request to separate two simultaneous vaccinations into two visits, will be recorded at the same time. In addition, a self-reported survey (see Appendices I & J) will be conducted on a four-point Likert scale - 1 (strongly disagree) to 4 (strongly agree) - to show staff and parent satisfaction rates with the innovation.

Other outcomes

The provider outcomes are concerned with utilisation rates and costs of the innovation. The total number of cases where implementation is associated with the innovation as well as the number of eligible cases will be captured to calculate percentages and levels of utilisation. The material and manpower used will be reflected in the actual expenses spectrum, which will be reviewed in the eighth after the commencement of the innovation.

Nature and number of clients involved

Eligibility criteria

The inclusion and exclusion criteria of the targets will be identical to those mentioned in Chapter 2. All healthy children aged one year or more receiving routine scheduled immunisations at the Maternal and Child Health Centre are eligible for the innovation.

Sample size calculation

Halperin et al. reported that the mean pain score (MBPS) after vaccination was 7.1 for the control group and 6.6 for the intervention group, and O’Brien et al. that the MBPS within 15 seconds of vaccination was 5.3 for the control group and 4.8 for the intervention group. Taddio et al. reported the MBPS was 8 for the control group and 7 for the intervention group. Cassidy et
al. found that an intervention effect size of 0.45 was clinically important. From the results of these three studies and taking a conservative estimate, it is considered that an effect size of 0.5 in the MBPS pain score proves the effectiveness of the intervention. Assuming the effect size $d$ to be 0.5 with an $sd/sigma$ of 2, a power of 0.8 and alpha at 0.05, the estimated sample size will be 128, according to a statistical software calculation (Java Applets for Power and Sample Size). With reference to the Hong Kong Childhood Immunisation Programme, the participants will be divided into two age groups, one year and one and half or older, for evaluation. The first group includes children of one receiving MMR and PCV-13. The second group includes children of one and half or older receiving booster DTaP-IPV. Multiple vaccines will be given sequentially without any special calming time as routine practice. One single dose of topical anaesthetic (EMLA patch) will be applied on left/right anterior thigh (vastus lateralis) for MMR only, as the effect of EMLA on the immune response to any other vaccine such as PCV is still unknown, so it cannot be used for PCV-13 vaccination at present. For the older group of children a single dose of EMLA-patch will be applied on the deltoid before immunisation, in line with our usual practice. Assuming a ~5% drop-out and ~5% defaulter or refusal rate daily, the estimated sample size will be 140, 70 children aged one (MMR group) and 70 aged one and half or more (DTaP-IPV group).

Since there are around 800 eligible participants each year in one part-time MCHC in Kowloon, the time needed to recruit 140 subjects will be about 10 weeks. However, it is difficult to achieve long-term outcomes and costs within a short period. At least 20 weeks will therefore be preferred for the implementation phase (Deogaonkar et al., 2012).
**Data analysis**

**Data collection**

Because of the time lag in the topical anaesthetic becoming effective, usually 30-60 minutes (Cassidy et al. Halperin et al. O'Brien et al.), it is anticipated that minor logistic adjustments will need to be made before starting the pilot and implementation phase. It may be feasible to allocate eligible children, aged one year or older, to the early appointment time slot in morning or afternoon sessions before receiving the routine immunisation in order to facilitate the smoothness of clinical setting. If the parents or caregivers agree to the innovation, details and instructional leaflets will be provided for their reference. The primary and secondary outcomes, such as pre-vaccination and post-vaccination pain scores (MBPS) and local reactions, will be measured and entered on the data record form (see Appendix F) by the evaluation nurse once the injection procedure is completed. Additionally, the injection nurse will be asked to indicate the perceived child distress level during immunisation in a questionnaire (see Appendix G). Similar questionnaires will be distributed to the parents or caregivers after the procedures and they will be asked about perceived child distress (VAS) during immunisation (see Appendix H). Parents/caregivers will be asked to return the completed questionnaires to a data “collection box” in the waiting area before they leave the Centre.

Other long-term outcomes, complaints related to immunisation and cost, should be recorded from the beginning of the pilot until the end of the implementation phase. Meanwhile, staff and parent satisfaction and utilisation rates will be collected in weeks 8, 12, 16 and 20 to assess the efficiency and sustainability of the innovation (Shah et al., Taddio et al.).

**Data evaluation**
Before evaluation, data will be entered into a computer database and analysed by one of the working group or research team members in head office who has been trained on SPSS software. One sample paired t-test will be used to determine if there has been any pain score (MBPS) difference between the pre- and post-vaccination procedures. This test is used to check whether the difference between a pair of variables (before and after pain scores) measured in each individual is, on average zero or not, which can be done by calculating the difference between pre- and post- MBPS scores. The sample population mean pain score (MBPS) after the introduction of the innovation will be compared with the known mean already outlined before, i.e. 6.6 in the general population (Halperin et al.). A correlation analysis of MBPS and VAS will also be done to determine any association between pain and distress levels. All output results with a p-value <0.05 will be regarded as statistically significant.

Criteria for effectiveness

Client outcomes

A crucial part of the evaluation is to determine if the innovation should be adopted. The working group members will hold an evaluation meeting with SNO, SMO and Head Office members at the end of the evaluation period. During the meeting, they will need to discuss the results of data analysis. It is expected that, in respect of the pain score, an effect size of 0.5 for the innovation will be obtained when compared with that of current practice, which means that a reduction of 0.5 points in the (MBPS) pain score represents the effectiveness of the innovation.

Other outcomes

The satisfaction rates of parents and nurses are also taken into account in deciding on the effectiveness of the innovation (Kennedy, Basket & Sheedy, 2011). It is considered to be effective if 70% of parents and nursing staff ‘strongly agree’ or ‘agree’ on the overall satisfaction.
level. The utilisation rate should be over 80% and the actual costs should be similar to those in the budget estimate.

**Conclusion**

In conclusion, the randomised controlled trials and review clearly support the proposition that topical anaesthetics, i.e. EMLA-patches, form an effective, simple and practical innovation to reduce immunisation-induced pain and distress among healthy children. Parents are willing to accept the administration of topical anaesthetics to their children’s skin before needle procedures if instructed how to do so. Such an innovation provides obvious positive outcomes for children, parents, nurses and the healthcare system generally, and should be advocated particularly in the case of children with behavioural problems such as autism, Asperger’s syndrome (AS), attention deficit hyperactivity disorder (ADHD) etc., since such children are more likely to have needle phobia/anxiety. To carry out the innovation at the Maternal and Child Health Centre successfully and launch its implementation with clear instructions, it should be well-planned and evidence-based, and so guidelines must be developed accordingly. Before implementation, it is necessary to communicate with the stakeholders, and a pilot test should be carried out in order to test the feasibility and make further improvements. Finally, the effectiveness of the innovation should be assessed according to the evaluation plan. It is expected that the introduction of topical anaesthetics for immunisation into our clinical area will be beneficial for children, parents and nurses, as well as for our healthcare system – the Family Health Service - where ‘care and respect, professionalism, partnership, evidence-based and quality assurance, communication and sustaining improvement’ are our core values.
### CDC Recommended Immunisation Schedule for Persons Aged 0 to 6 Years – United States, 2012

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age</th>
<th>Birth</th>
<th>1 month</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>15 months</th>
<th>18 months</th>
<th>19-23 months</th>
<th>2-3 years</th>
<th>4-6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B¹</td>
<td>HepB</td>
<td></td>
<td>HepB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus²</td>
<td>RV</td>
<td></td>
<td>RV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, tetanus, pertussis³</td>
<td>DTaP</td>
<td></td>
<td>DTaP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae type b⁴</td>
<td>Hib</td>
<td></td>
<td>Hib</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal⁵</td>
<td>PCV</td>
<td></td>
<td>PCV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated poliovirus⁶</td>
<td>IPV</td>
<td></td>
<td>IPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IPV</td>
<td></td>
<td></td>
<td>IPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Influenza (yearly)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MMR</td>
<td></td>
<td></td>
<td>MMR</td>
<td>VAR</td>
<td>VAR</td>
</tr>
<tr>
<td>Varicella⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VAR</td>
<td></td>
<td></td>
<td>VAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A¹⁰</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dose 1¹⁰</td>
<td></td>
<td></td>
<td>HepA series</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal¹¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MCV4 — See footnote¹¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Hepatitis A should be administered at the same time as hepatitis B vaccine.
² DTaP: Diphtheria and tetanus toxoids, acellular pertussis conjugate vaccine.
³ Hib: Haemophilus influenzae type b conjugate vaccine.
⁴ PCV: Pneumococcal conjugate vaccine, 7-valent.
⁵ IPV: Inactivated poliovirus vaccine.
⁶ Influenza: Influenza vaccine, any licensed formulation.
⁷ MMR: Measles, mumps, and rubella vaccine.
⁸ Varicella: Varicella vaccine.
⁹ Hepatitis A vaccine should be administered at the same time as hepatitis B vaccine.
¹⁰ Dose 1 of hepatitis A vaccine should be administered at the same time as DTaP vaccine.
¹¹ Meningococcal: Meningococcal conjugate vaccine, 4-valent.
Appendix B. SIGN Methodology Checklist: Randomized Controlled Trials

**Study identification** *(Include author, title, year of publication, journal title, pages)*

<table>
<thead>
<tr>
<th>Guideline topic:</th>
<th>Key Question No:</th>
</tr>
</thead>
</table>

**Before** completing this checklist, consider:

- Is the paper a **randomized controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+

- Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

**Reason for rejection**: Reason for rejection: 1. Paper not relevant to key question □ 2. Other reason □ (please specify):

**Checklist completed by:**

<table>
<thead>
<tr>
<th><strong>Section 1: Internal validity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In a well conducted RCT study...</strong></td>
</tr>
<tr>
<td>1.1</td>
</tr>
<tr>
<td>1.2</td>
</tr>
<tr>
<td>1.3</td>
</tr>
<tr>
<td>1.4</td>
</tr>
<tr>
<td>1.5</td>
</tr>
<tr>
<td>1.6</td>
</tr>
<tr>
<td>1.7</td>
</tr>
<tr>
<td>1.8</td>
</tr>
<tr>
<td>1.9</td>
</tr>
<tr>
<td>1.10</td>
</tr>
</tbody>
</table>
## Section 2: OVERALL ASSESSMENT OF THE STUDY

<table>
<thead>
<tr>
<th>2.1</th>
<th>How well was the study done to minimise bias? Code ++, +, or -</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2</td>
<td>Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?</td>
</tr>
<tr>
<td>2.3</td>
<td>Are the results of this study directly applicable to the patient group targeted by this guideline?</td>
</tr>
<tr>
<td>2.4</td>
<td><strong>Notes.</strong> Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.</td>
</tr>
</tbody>
</table>
### Methodology Checklist: Systematic Reviews and Meta-analyses

**Study identification** *(Include author, title, year of publication, journal title, pages)*

<table>
<thead>
<tr>
<th>Guideline topic</th>
<th>Key Question No</th>
</tr>
</thead>
</table>

**Before** completing this checklist, consider:

1. Is the paper a systematic review or meta-analysis? IF NO REJECT (give reason below). IF YES CONTINUE.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not a systematic review/meta-analysis [ ] 2. Paper not relevant to key question [ ]

3. Other reason [ ] (please specify):

Checklist completed by:

### Section 1: Internal validity

**In a well conducted systematic review**

<table>
<thead>
<tr>
<th>In this study this criterion is:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well covered</td>
</tr>
</tbody>
</table>

1. **The study addresses an appropriate and clearly focused question.**

2. **A description of the methodology used is included.**

3. **The literature search is sufficiently rigorous to identify all the relevant studies.**

4. **Study quality is assessed and taken into account.**

5. **There are enough similarities between the studies selected to make combining them reasonable.**

### Section 2: Overall assessment of the study

1. **How well was the study done to minimise bias?**
   
   Code ++, +, or –

2. **Notes.** Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question.
Appendix D.

SIGN Levels of Evidence and Grades of Recommendations

1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+ Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++ High quality systematic reviews of case control or cohort or studies
2+ Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3 Non-analytic studies, e.g. case reports, case series

4 Expert opinion

A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good practice points

☑ Recommended best practice based on the clinical experience of the guideline development group
## Hong Kong Childhood Immunisation Programme

<table>
<thead>
<tr>
<th>AGE</th>
<th>Immunisation RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>B.C.G. Vaccine</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B Vaccine - First dose</td>
</tr>
<tr>
<td>1 month</td>
<td>Hepatitis B Vaccine - Second dose</td>
</tr>
<tr>
<td>2 months</td>
<td>DTaP-IPV Vaccine - First Dose</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal Vaccine - First Dose</td>
</tr>
<tr>
<td>4 months</td>
<td>DTaP-IPV Vaccine - Second Dose</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal Vaccine - Second Dose</td>
</tr>
<tr>
<td>6 months</td>
<td>DTaP-IPV Vaccine - Third Dose</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal Vaccine - Third Dose</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B Vaccine - Third Dose</td>
</tr>
<tr>
<td>1 year</td>
<td>MMR Vaccine (Measles, Mumps &amp; Rubella) - First Dose</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal Vaccine - Booster Dose</td>
</tr>
<tr>
<td>1 1/2 year</td>
<td>DTaP-IPV Vaccine - Booster Dose</td>
</tr>
<tr>
<td>Primary 1</td>
<td>MMR Vaccine (Measles, Mumps &amp; Rubella) - Second Dose</td>
</tr>
<tr>
<td></td>
<td>DTaP-IPV Vaccine - Booster Dose</td>
</tr>
<tr>
<td>Primary 6</td>
<td>dTap-IPV Vaccine - Booster Dose</td>
</tr>
</tbody>
</table>
Appendix  (F) Data Collection Form

Types of vaccine given

□DTaP-IPV vaccine

□MMR vaccine

Local reaction: □None □Mild □Moderate □Severe

Parameters:
(1) facial expression: (0-3)
(2) crying: (0-4)
(3) movements: (0-3)

Pre-vaccination pain score/total score of three parameters: ____________
(assessed within 5 seconds of vaccination, refer to Modified Behavioural Pain Scale_MBPS)

Post-vaccination pain score/total score of three parameters: ____________
(assessed within 15 seconds of vaccination; refer to Modified Behavioural Pain Scale_MBPS)

Appendix G. Nurse’s report of child distress questionnaire

Nurse’s report of child distress

(Please mark a cross [ ] to indicate the distress level suffered by the children during the immunisation procedure)

No distress                                                                 Distress as bad as possible

Nurse’s report of child distress: __________
Appendix H. Parent’s report of child distress questionnaire

**Parent’s report of child distress**

(Please mark a cross [X] to indicate the distress level suffered by the children during the immunisation procedure)

No distress

Distress as bad as possible

Parent’s report of child distress: __________
Appendix I. Nurse satisfaction survey

<table>
<thead>
<tr>
<th>Questions (Please tick the appropriate answer)</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Agree strongly</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I think this innovation can reduce childhood immunisation pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I think this innovation does not place any burden on nurses in routine immunisation procedures.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. I think this innovation can introduce positive feelings among parents/care givers towards immunisation procedures.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. I think I am competent to apply topical anaesthetics.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Overall, I support this innovation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any other suggestions concerning this innovation?

______________________________________________________________

Thank you for your comments
Appendix J. Parent satisfaction survey

<table>
<thead>
<tr>
<th>Questions (Please tick the appropriate answer)</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Agree strongly</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The explanation provided by the nurse is adequate.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. The educational leaflet is easy to understand.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. The innovation is beneficial to the child.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. The innovation is helpful to relieve anxiety and distress during immunisation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Overall, I support this innovation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any other suggestions concerning this innovation?

__________________________________________________________

Thank you for your comments
References:


