Abstract of dissertation entitled

“Administration of oral sucrose to reduce immunization-induced pain and distress for infants one to eighteen months of age”

Submitted by

NGAI KA YAN

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The World Health Organization (WHO) recommends childhood immunization as one of the necessary preventive health measures to reduce the chance of contracting infectious diseases in children. Despite the proven benefits, immunization is associated with pain and management of immunization-induced pain has been neglected in current local practice.

Administration of oral sucrose is found to be an effective pain-relieving intervention during routine immunizations as evidenced by seven systematic reviews. This simple intervention is encouraged to be carried out during routine immunizations in community settings such as Maternal and Child Health Centres in Hong Kong. Evidence-based practice guidelines and implementation plans are set up in carrying out the new practice. Stakeholders are identified with communication strategies noted. In addition, pilot testing and evaluation are also necessary to improve the new practice. It is expected that the implementation of the intervention can bring about obvious
positive outcomes for infants, parents, nurses and the health care system by means of reducing infants’ pain and distress during routine immunizations.
Administration of oral sucrose to reduce immunization-induced pain and distress for infants one to eighteen months of age

by

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

August 2012
Declaration

I declare that the dissertation thereof 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 qualifications.

Signed .........................................................

Ngai Ka Yan
Acknowledgements

I would like to express my deepest gratitude to my supervisor, Dr. Marie Tarrant for her guidance, encouragement and timely response in the process of writing this dissertation.

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Especially, I would like to give my special thanks to my husband for his love and support throughout my work. Thank you for your understanding and encouragement whatever the situation.
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Chapter 1: Statement of the Problem

Introduction

Childhood immunization is one of the necessary preventive health measures to reduce the chance of contracting infectious diseases in children as recommended by the World Health Organization (2011). Most of the immunizations are administered by needle injections, invasive procedures that cause pain and distress. It is also a source of anxiety and distress for the children’s families and the health care providers responsible for the procedures. Untreated immunization-induced pain has immediate negative effects and long-term detrimental consequences including decreased immune response (Page, 2004), increased pain sensitivity (Taddio, Goldbach, Ipp, Stevens & Koren, 1995) and increased avoidance of health care in adulthood (Pate, Blount, Cohen & Smith, 1996). However, management of pain during routine immunizations has been neglected in local practice. Until new approaches for the administration of immunizations are developed, intervention should be introduced to reduce the associated pain and distress. Previous researchers found that administration of oral sucrose is an effective intervention to reduce pain for pre-term neonates during painful medical procedures (Stevens, Yamada & Ohlsson, 2005). Recently, it has been proposed that the intervention
could be applied to infants during routine immunizations. It is necessary to make efforts to minimize immunization-induced pain and distress for infants when evidence-based intervention is available. The purpose of this paper is to investigate the effectiveness of administration of oral sucrose to reduce immunization-induced pain and distress in infants and to develop evidence-based guidelines for the implementation of the innovation at a local Maternal and Child Health Centre.

**Background of the Problem**

**Immunization Programmes in Hong Kong**

In Hong Kong, childhood immunization programme was established in the 1950s. In 2006, the Scientific Committee on Vaccine Preventable Diseases of the Department of Health updated the recommendations on the local childhood immunization programme. Besides, Pneumococcal vaccine was introduced into the childhood immunization programme in 2009 (Department of Health, 2009b). Currently, the Hong Kong Childhood Immunization Programme is recommended to provide protection for infants and children from ten infectious diseases including tuberculosis, hepatitis B, diphtheria, pertussis, tetanus, poliomyelitis, pneumococcal infection, measles, mumps and rubella (Department of Health, 2009b). With the continued introduction of
new immunizations, infants need to receive thirteen recommended immunization injections from birth to eighteen months of age in Hong Kong (Department of Health, 2011a).

**Current Immunization Practice in Hong Kong**

The immunizations recommended in the programme are provided by thirty one Maternal and Child Health Centres of the Department of Health in Hong Kong. Parents can take their children to any Maternal and Child Health Centre to receive the recommended immunizations. Parents may also take their children to general practitioners for the immunizations. According to the Department of Health Annual Report 2007/2008, there were 70,394 registered births in Hong Kong in 2007 and about 83% of them received services from Maternal and Child Health Centres (Department of Health, 2009a). Infants receive eleven recommended immunization injections at six separate routine visits including one, two, four, six, twelve and eighteen months of visit at Maternal and Child Health Centres and they generally receive one to three immunization injections at every single routine visit (Department of Health, 2011a).

**Immunization-induced Pain and Distress**

Routine immunization is the most frequent painful medical procedure in
childhood (Schechter et al., 2007). Pain is defined as unpleasant sensory and emotional experience associated with acute or potential tissue damage by the International Association for the Study of Pain (IASP, 2011). Immunization evokes behavioural and physiological signs of distress for infants and it also causes distress for infants’ families and the health care providers.

**Affirming Needs**

Despite the proven benefits of immunization, childhood immunization is associated with pain and distress. Besides, families and health care providers generally have concerns about the pain associated with frequent and multiple immunization injections with the continued introduction of new immunizations (Gellin, Maibach & Marcuse, 2000; Woodin et al., 1995). However, immunization-induced pain remains untreated in local practice. Frontline nurses and doctors at Maternal and Child Health Centres always focus on educating parents and families about the reactions and aftercare of immunizations instead of pain-relieving measures. There is no specific guideline to tackle the pain associated with routine immunizations in our current practice. In fact, it is a professional and ethical decision to introduce effective pain-relieving intervention in routine immunizations for infants when evidence-based intervention is available.
Research Objectives and Questions

Objectives

1. To determine the effectiveness of administration of oral sucrose on immunization-induced pain and distress in infants one to eighteen months of age compared to placebo and no treatment groups.

2. To determine the acceptance of administration of oral sucrose as a pain-relieving intervention during routine immunizations for infants by nurses and parents.

Research Questions

1. How effective is the administration of oral sucrose intervention in comparison to no treatment and placebo groups on the reduction of immunization-induced pain and distress in infants one to eighteen months of age?

2. Does the administration of oral sucrose intervention reduce infant distress levels perceived by nurses?

3. Does the administration of oral sucrose intervention reduce infant distress levels perceived by parents?

PICO Components

Population: Infants one to eighteen months of age undergoing routine
immunizations.

**Intervention:** Administration of oral sucrose before routine immunizations.

**Comparison:** Current practice of no intervention and use of placebo.

**Outcome:** Pain and distress levels by behavioural indicators and pain assessment tools.

**Significance of the Problem**

Infants experience pain during medical procedures such as immunization may have significant short and long-term physiological, psychological and behavioural consequences. Page (2004) found that pain may lead to decreased immune system functioning. Besides, Ornstein, Manning & Pelphrey (1999) and Von Baeyer, Marche, Rocha & Salmon (2004) pointed out that infants have pain memory. The American Academy of Pediatrics & American Pain Society (2001) and Taddio et al. (1995) further pointed out that previous experience of pain increases infants’ pain sensitivity by means of longer crying time and higher pain scores when they face other painful procedures. Weisman, Bernstein & Schechter (1998) also found that infants react more intensely if they have undergone previous painful procedures with inadequate pain-relieving measures or analgesia. Furthermore, Pate et al. (1996) pointed
out that early exposure to painful medical procedures has been linked to higher levels of anxiety over medical procedures and avoidance of health care in adulthood. Obviously, parents and family members are often concerned about immunization-induced pain and distress in their infants. Meyerhoff, Weniger & Jacobs (2001) indicated significant parental concern over the pain associated with multiple immunization injections and pain is a source of distress especially for new parents. Similarly, anxiety and distress exist among health care providers responsible for the immunization procedures. Woodin et al. (1995) found that over half of physicians had strong concerns about three immunization injections at a single visit. Reis (1997) reported that doctors and nurses were six times less likely to give multiple immunization injections at a single visit. In all, minimizing pain during immunizations can reduce the associated distress during the procedures, prevent the development of subsequent health care avoidance behaviours and promote trust in health care providers through more positive experiences for the infants, their families and the health care providers.
Chapter 2: Review of Evidence

Selecting Studies for Review

**Inclusion criteria**

**Type of studies.** All randomized controlled trials using administration of oral sucrose as the intervention to manage pain and distress during routine immunizations for infants are included.

**Type of participants.** Studies must include term (gestational age ≥37 weeks) and healthy infants from one to eighteen months of age receiving routine immunizations.

**Type of intervention.** Administration of oral sucrose solution versus no intervention or placebo.

**Type of outcome measures.** Pain and distress levels measured by behavioural indicators and pain assessment tools.

**Exclusion criteria**

1. Studies solely conducted in hospital settings are excluded.

2. Studies solely comprising pre-term infants are excluded.

3. Studies not carried out during routine immunizations are excluded.

4. Studies involving a combination of interventions are excluded.
Search Strategies

Electronic searches of published literature were carried out via four electronic search databases on 10 July 2011: (1) CINAHL plus (1974 to 2011), (2) Cochrane, (3) OVID MEDLINE (1948 to June Week 5 2011) and (4) PubMed (see Table 1). Four key terms were used in the search strategies, (1) infant, (2) sucrose, (3) immunization or immunisation or vaccine or injection and (4) pain. The combination of key terms (1), (2), (3) and (4) yielded 88 copies of journals from the electronic searches. Limited to randomized controlled trial and those in English or Chinese, 29 copies of studies were retrieved. One study was produced by manual searches of reviewing reference lists of relevant studies. Therefore, the titles and abstracts of these 30 copies of studies were screened. Duplicated studies were eliminated and the studies were examined with reference to the inclusion and exclusion criteria. As a result, seven randomized controlled trials, which focused on the administration of oral sucrose in routine immunizations and its effect on pain and distress levels for infants were used for evaluation (see Figure 1).
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<tbody>
<tr>
<td>Search Date</td>
<td>10/7/2011</td>
<td>10/7/2011</td>
<td>10/7/2011</td>
<td>10/7/2011</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>1. Infant</td>
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<td>24961</td>
<td>875847</td>
<td>885036</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>2. Sucrose</td>
<td>2125</td>
<td>855</td>
<td>53243</td>
<td>57731</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>3. Immunization or Immunisation or Vaccine or Injection</td>
<td>39169</td>
<td>25374</td>
<td>507423</td>
<td>813257</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>4. Pain</td>
<td>120738</td>
<td>32219</td>
<td>373559</td>
<td>468013</td>
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</tr>
<tr>
<td>5. Combine 1 and 2 and 3 and 4</td>
<td><strong>19</strong></td>
<td><strong>9</strong></td>
<td><strong>29</strong></td>
<td><strong>31</strong></td>
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<td><strong>88</strong></td>
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<td>6. Limit to Randomized Controlled Trial</td>
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<td>8</td>
<td>11</td>
<td>12</td>
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<td>7. Limit to English or Chinese</td>
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<td>7</td>
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<tr>
<td>Topic Screened and Abstract Read</td>
<td><strong>1</strong></td>
<td><strong>7</strong></td>
<td><strong>10</strong></td>
<td><strong>11</strong></td>
<td><strong>1</strong></td>
<td><strong>30</strong></td>
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<tr>
<td>8. Eliminate Duplicates</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td></td>
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<tr>
<td>9. Eliminate solely for hospital setting</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>10. Eliminate combination of interventions</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Numbers of Final Selected Literatures</td>
<td><strong>1</strong></td>
<td><strong>4</strong></td>
<td><strong>1</strong></td>
<td><strong>0</strong></td>
<td><strong>1</strong></td>
<td><strong>7</strong></td>
</tr>
</tbody>
</table>
88 potentially relevant studies identified

56 were excluded (not randomized control trials)

3 were excluded (other languages used, not English or Chinese)

1 study from manual searches by reviewing reference lists of the relevant studies

30 studies were retained for title and abstract screening

18 studies were excluded (Duplicated reports)

5 studies were excluded (not fulfilling the criteria)
  • solely hospital setting
  • pre-term infants only
  • not carried out during routine immunizations
  • involving a combination of interventions

7 randomized control trials studies were selected for literature review

Figure 1
Flow Diagram of Included and Excluded Studies
Methods of the Review

Data Extraction

Seven research studies finally retrieved for evaluation were reviewed. Relevant data were extracted and tabulated systematically in the form of a table of evidence.

Quality Assessment

In quality assessment, section 1 (internal validity) and section 2 (overall assessment) of the methodology checklist for randomized controlled trials by the Scottish Intercollegiate Guidelines Network (SIGN, 2008) was used (see Appendix A). Quality assessment in deciding the level of evidence for studies was performed according to the recommendations of the level of evidence by SIGN (2008) (see Appendix B).

Data Synthesis

In data synthesis, useful information was retrieved and could be used to help in developing the evidence-based guideline.

Description of Studies

Characteristics of Included Studies

Demographics

A total of seven studies were identified for evaluation. All of the studies
were carried out to compare the effects of administration of oral sucrose and placebo or no intervention on the reduction of immunization-induced pain and distress in infants in community settings. The characteristics of the studies are outlined in Table 2. All the seven selected studies were randomized controlled trials (RCTs) and published in English (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). The year of publication ranged from 1995 to 2009. The studies were conducted in different countries including the United States (n=3) (Allen et al., 1996; Hatfield, 2008; Hatfield et al., 2008), Canada (n=1) (Barr et al., 1995), United Kingdom (n=1) (Ramenghi et al., 2002), Australia (n=1) (Lewindon et al., 1998) and Turkey (n=1) (Dilli et al., 2009), with diverse populations. Four out of the seven studies were funded. The study of Allen et al. (1996) was funded by the Maternal and Child Health Bureau and Administration on Developmental Disabilities. The study conducted by Barr et al. (1995) was funded by the Medical Research Council of Canada, Interservice Clubs Council Telethon Fund and Lewis Sessenwein Trust. The study of Hatfield (2008) and Hatfield et al. (2008) was funded by the Children’s Miracle Network and an American Nurses Foundation grant respectively.
Participants

Details of study participants are listed in Table 2. The seven studies covered a total of 879 infants. Sample size ranged from 57 to 285. In these seven RCTs, all samples were obtained by the convenience method and were randomly assigned to either the intervention group or control group if they were eligible for enrolment and written informed consent was available. The seven studies targeted participants with similar characteristics, healthy and full-term infants (gestation ≥37 weeks) (n=4) (Allen et al., 1996; Hatfield, 200; Hatfield et al., 2008; Ramenghi et al., 2002), healthy infants and children (n=2) (Barr et al., 1995; Dilli et al., 2009) and healthy and gestation ≥34 weeks infants (n=1) (Lewindon et al., 1998). The age of participants targeted varied among the studies from 2 to 4 months (n=4) (Barr et al., 1995; Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002), 2 to 6 months (n=1) (Lewindon et al., 1998), 2 weeks to 18 months (n=1) (Allen et al., 1996) and 6 to 48 months (n=1) (Dilli et al., 2009). All participants were obtained from different community settings including well-child unit (n=1) (Dilli et al., 2009), university-affiliated ambulatory paediatric clinic (n=3) (Allen et al., 1996; Hatfield, 2008; Hatfield et al., 2008), general paediatric practice (n=1) (Barr et al., 1995) and immunization clinic (n=2) (Lewindon et al., 1998; Ramenghi et
Outcome Measures

All the seven studies had clearly defined outcome measures. The effects of administration of oral sucrose were measured in terms of infant crying time in five studies (n=5) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Lewindon et al., 1998; Ramenghi et al., 2002). Three studies measured pain score (n=3) (Dilli et al, 2009; Hatfield, 2008; Hatfield et al., 2008). The study of Dilli et al. (2009) measured pain response in terms of Neonatal Infant Pain Scale (NIPS) score for infants of 6 to 12 months and Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS) for infants and children above 12 months of age. The NIPS is a valid and reliable pain measuring tool which consists of six categories including facial expression, cry, breathing pattern, arm and leg movements, and state of arousal, and is utilized for both full-term and pre-term infants under 12 months of age (Lawrence et al., 1993; Uyan, Bilgen, Topuzoglu, Akman & Ozek, 2008). The CHEOPS is another pain measuring tool which consists of six categories including cry, facial expression, verbal, torso, touch and legs, and is used for children above 12 months of age (McGrath et al., 1985; Suraseranivongse et al., 2001). Two studies (Hatfield, 2008; Hatfield et al., 2008) used the University of Wisconsin Children’s
Hospital (UWCH) Pain Scale, which is a validated pain measuring scale consisting of five categories including crying, facial expression, behavioural response, body movement and sleep to quantify acute behavioural pain response for pre- and nonverbal children less than three years old (Soetenga, Frank & Pellino, 1999). One study used the Oucher distress score rated by nurses and parents as one of the measure outcomes (n=1) (Lewindon et al., 1998). It is a visual analogue score from 0 to 100 used to measure the subjective distress level suffered by the infant during the procedure (Beyer, 1988). The details of the outcome measures of the studies are presented in Table 2.

**Characteristics of Included Interventions**

**Interventions**

The intervention in the form of administration of oral sucrose was carried out with some differences among the studies. The details of the interventions of the studies are stated in Table 3. The amount and concentration of sucrose used varies among the studies, 3 continuous 0.25ml 50% (n=1) (Barr et al., 1995), 2ml 12% (n=2) (Allen et al., 1996; Dilli et al., 2009), 2ml 24% (n=2) (Hatfield, 2008; Hatfield et al., 2008), 2ml 25% (n=1) (Ramenghi et al., 2002), 2ml 50% (n=1) (Ramenghi et al., 2002) and 2ml 75% (n=1) (Lewindon et al., 2002).
Five out of the seven studies administered oral sucrose two minutes before immunization (n=5) (Allen et al., 1996; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002), while the others administered oral sucrose immediately before immunization (n=2) (Barr et al., 1995; Lewindon et al., 1998). All the studies administered oral sucrose solution by syringe or pipette (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). Two studies specified that the oral sucrose solution was applied onto the anterior part of the tongue (n=2) (Barr et al., 1995; Ramenghi et al., 2002), two studies applied it onto the surface of the tongue (n=2) (Hatfield, 2008; Hatfield et al., 2008) and the others stated that the oral sucrose solution as applied into the mouth only (n=3) (Allen et al., 1996; Dilli et al., 2009; Lewindon et al., 1998). Two studies inserted a pacifier immediately after administration of sucrose for both the intervention and control groups (n=2) (Hatfield, 2008; Hatfield et al., 2008). Measures for control groups varied a little between the studies. Five studies used water as a placebo for control (n=5) (Barr et al., 1995; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002), one study did not administer any solution and used standard practice as control (n=1) (Dilli et al.,
2009) and the remaining one used both water and no intervention as control (n=1) (Allen et al., 1996).
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants’ Characteristics</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al. (1996)</td>
<td>Infants: healthy &amp; term (gestation≥37 weeks)</td>
<td>N: 285</td>
<td>IG: 2 ml of 12% sucrose 2 minutes before immunization</td>
<td>Crying time: Audible distress vocalizations</td>
<td>Mean difference not mentioned clearly</td>
</tr>
<tr>
<td></td>
<td>Age: 2 weeks, 2 months, 4 months, 6 months, 9 months, 15 months &amp; 18 months</td>
<td>IG: ~95 CG(I): ~95 CG(II): ~95</td>
<td>CG(I): 2 ml of sterile water 2 minutes before immunization</td>
<td></td>
<td>Both sterile water group &amp; sucrose group cried significantly less than no intervention group (p&lt;0.05) for infants receiving one injection (2 week, 9 months &amp; 18 months of age)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG: ~95</td>
<td>CG(II): No intervention</td>
<td></td>
<td>No significant difference for infants receiving 2 injections (2 months, 6 months &amp; 15 months)</td>
</tr>
<tr>
<td>Barr et al. (1995)</td>
<td>Infants: healthy</td>
<td>N: 57</td>
<td>IG: 3 continuous 0.25 ml of 50% sucrose immediate before immunization</td>
<td>Percentage of time crying per period</td>
<td>1) Mean percentage of time crying during injection was similar (sucrose=84.2±3.8; water=84.1±4.0)</td>
</tr>
<tr>
<td></td>
<td>Age: 2 months &amp; 4 months</td>
<td>IG: 30</td>
<td>CG: 27</td>
<td>1) Injection (10 seconds) 2) Post-injection (60 seconds)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG: 27</td>
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## Table 2
### Characteristics of Included RCT Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants’ Characteristics</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilli et al. (2009)</td>
<td>Infants &amp; children: healthy</td>
<td>N: 88</td>
<td>IG(I): -</td>
<td>2 ml of 12% sucrose 2 minutes before immunization</td>
<td>6-12 months infants: 1) Median difference = -80 (sucrose=40; control=120) (p=0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IG(II):</td>
<td>Lignocaine cream</td>
<td>2) Median difference = -3 (sucrose=3; control=6) (p=0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CG: 30</td>
<td>No intervention</td>
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<tr>
<td></td>
<td>Age: 6-48 months</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>IG(I): -</td>
<td>2 ml of 12% sucrose 2 minutes before immunization</td>
<td>13-48 month old children: 3) Crying time significantly higher in IG(I) (p=0.002)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IG(II):</td>
<td>Lignocaine cream</td>
<td>4) Pain score (CHEOPS) significantly higher in CG than IG(I) (p=0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CG:</td>
<td>No intervention</td>
<td></td>
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<tr>
<td>Hatfield et al. (2008) Infants: healthy &amp; term</td>
<td>N: 40 2 months</td>
<td>IG: -</td>
<td>2 ml of 24% sucrose 2 minutes before immunization</td>
<td>Mean difference at 2 minutes = 0.14</td>
<td></td>
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<tr>
<td>(Gestation≥37 weeks)</td>
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<td></td>
<td>(test=4.54; control=4.39) (p=0.9588)</td>
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<td></td>
<td></td>
<td></td>
<td>CG: 20</td>
<td></td>
<td>&amp; 5 minutes = -2.74 (test=0.27; control=3.02) (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td>Age: 2 &amp; 4 months</td>
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<td></td>
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<td>IG: -</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IG: 38</td>
<td>2 ml of 24% sucrose 2 minutes before immunization</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IG:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CG: 45</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 2
Characteristics of Included RCT Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants’ Characteristics</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewindon et al. (1998)</td>
<td>Infants: healthy &amp; gestation ≥ 34 weeks</td>
<td>N:107</td>
<td>IG: 54</td>
<td>1) Crying time: First cry, sum total crying, start to finish crying</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age: 2 months, 4 months &amp; 6 months</td>
<td>IG: 54</td>
<td>IG: 2 ml of 75% sucrose before immunization</td>
<td>2) Oucher score rated by nurse</td>
<td>Mean difference of first cry=-13 (test=29; control=42) (p&lt;0.0003), sum total crying=-23 (test=36; control=59) (p&lt;0.000008) &amp; start to finish crying=-26 (test=43; control=69) (p&lt;0.00002)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG: 53</td>
<td>CG: 2 ml of sterile water before immunization</td>
<td>3) Oucher score rated by parent</td>
<td>2) Mean difference=-8 (test=35; control=43) (p&lt;0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3) Mean difference=-7 (test=47; control=54) (p&lt;0.1)</td>
</tr>
<tr>
<td>Ramenghi et al. (2002)</td>
<td>Infants: healthy &amp; term (Gestation≥37 weeks)</td>
<td>N: 184</td>
<td>IG(I): 46 IG(II): 45 IG(III): 46</td>
<td>Crying time</td>
<td>- Median difference of 2m group= -7.5 (25% sucrose=35; control=42.5), 3m group= 0.9 (25% sucrose=29.2; control=28.3) &amp; 4m group=-35.6 (25% sucrose=17.2; control=52.8)</td>
</tr>
<tr>
<td></td>
<td>Age: 2 months, 3 months &amp; 4 months</td>
<td>IG(III): 46</td>
<td>IG(I): 2 ml of 25% sucrose 1 minute before immunization</td>
<td></td>
<td>- Median difference of 2m group= -23.1 (50% sucrose=19.4; control=42.5), 3m group=-12.7 (50% sucrose=15.6; control=28.3) &amp; 4m group= -38.9 (50% sucrose=13.9; control=52.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG: 47</td>
<td>IG(II): 2 ml of 50% sucrose 1 minute before immunization</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IG(III): 2 ml Lycasin (40% hydrogenated glucose) 1 minute before immunization</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CG: 2 ml sterile water 1 minute before immunization</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N – Sample Size; IG – Intervention Group; CG – Control Group; NR – Not Reported
# Table 3
Characteristics of Interventions in the Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Intervention Components</th>
<th>Number of injections</th>
<th>Conducted by</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al.</td>
<td>RCT</td>
<td>IG - Administration of 2ml 12% sucrose by oral syringe 2 minutes prior to injection</td>
<td>1, 2 or 3 injections</td>
<td>Not stated</td>
<td>Cannot be calculated since mean difference not mentioned clearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG - Administration of 2ml sterile water by oral syringe 2 minutes prior to injection</td>
<td></td>
<td></td>
<td>Both sterile water group &amp; sucrose group cried significantly less than no intervention group (p&lt;0.05) for infants receiving one injection (2 weeks, 9 months &amp; 18 months of age)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No intervention - no administration of solution before injection</td>
<td></td>
<td></td>
<td>No significant difference for infants receiving 2 injections (2 months, 6 months &amp; 15 months)</td>
</tr>
<tr>
<td>Barr et al.</td>
<td>RCT</td>
<td>IG - Administration of 3 continuous 0.25ml 50% sucrose by pipette onto the anterior part of the tongue at 30-second intervals before injection</td>
<td>1 injection</td>
<td>Research assistant</td>
<td>↑ 0.12% of time crying during injection for IG than CG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG - Administration of 3 continuous 0.25ml water by pipette onto the anterior part of the tongue at 30-second intervals before injection</td>
<td></td>
<td></td>
<td>↓ 16.67% of time crying in the post-injection period for IG than CG (p&lt;0.05)</td>
</tr>
<tr>
<td>Dilli et al.</td>
<td>RCT</td>
<td>IG(I) - Administration of 2ml 12% sucrose by oral syringe 2 minutes before injection</td>
<td>1 or 3 injections</td>
<td>Not stated</td>
<td>6-12 month old infants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IG(II) - Administration of 1g of lidocaine-prilocaine to vaccination area 1 hour before injection</td>
<td></td>
<td></td>
<td>↓ 66.67% of crying time for IG(I) than CG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CG - No intervention</td>
<td></td>
<td></td>
<td>↓ 50% of pain score (NIPS) for IG(I) than CG</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13-48 month old infants &amp; children</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cannot be calculated since crying time &amp; pain score (CHEOPS) not mentioned clearly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Crying time &amp; pain score (CHEOPS) significantly higher in CG than IG(I) (p=0.001 &amp; p=0.002)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Intervention Components</td>
<td>Number of injections</td>
<td>Conducted by</td>
<td>Effect Size</td>
</tr>
<tr>
<td>--------------</td>
<td>--------</td>
<td>-------------------------</td>
<td>----------------------</td>
<td>--------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Hatfield</td>
<td>RCT</td>
<td>IG</td>
<td>3 injections</td>
<td>Not stated</td>
<td>† 3.19% of pain score for IG than CG at 2 minutes</td>
</tr>
<tr>
<td>(2008)</td>
<td></td>
<td>- Administration of 2ml 24% sucrose by syringe onto the surface of the tongue immediately followed by insertion of a pacifier 2 minutes before injection</td>
<td></td>
<td></td>
<td>† 90.7% of pain score for IG than CG at 5 minutes (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml 24% sterile water by syringe onto the surface of the tongue immediately followed by insertion of a pacifier 2 minutes before injection</td>
<td></td>
<td></td>
<td>† 60.60% of pain score for IG than CG at 2 minutes (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>† 31.09% of pain score for IG than CG at 5 minutes (p&lt;0.001)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>† 21% of pain score for IG than CG at 7 minutes (p&lt;0.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>† 78.55% of pain score for IG than CG at 9 minutes (p&lt;0.001)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Intervention Components</td>
<td>Number of injections</td>
<td>Conducted by</td>
<td>Effect Size</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------</td>
<td>-------------------------</td>
<td>---------------------</td>
<td>-------------------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Lewindon et al. (1998)</td>
<td>RCT</td>
<td>IG</td>
<td>2 injections</td>
<td>Single nurse practitioner</td>
<td>Crying time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml 75% sucrose solution by syringe before injection</td>
<td></td>
<td></td>
<td>- ↓ 30.95% of first cry for IG than CG (p&lt;0.0003)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml sterile water by syringe before injection</td>
<td></td>
<td></td>
<td>- ↓ 38.98% of sum total crying for IG than CG (p&lt;0.000008)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- ↓ 37.68% of start to finish crying for IG than CG (p&lt;0.00002)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Oucher score by nurse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- ↓ 18.60% of Oucher score by nurse for IG than CG (p&lt;0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Oucher score by parent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- ↓ 12.96% of Oucher score by parent for IG than CG (p&lt;0.1)</td>
</tr>
<tr>
<td>Ramenghi et al. (2002)</td>
<td>RCT</td>
<td>IG(I)</td>
<td>2 injections</td>
<td>Single operator</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml 25% sucrose by syringe for 1 minute onto the anterior part of the tongue 2 minutes before injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml 50% sucrose by syringe for 1 minute onto the anterior part of the tongue 2 minutes before injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml Lycasin (40% hydrogenated glucose) by syringe for 1 minute onto the anterior part of the tongue 2 minutes before injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Administration of 2ml sterile water by syringe for 1 minute onto the anterior part of the tongue 2 minutes before injection (a pacifier was allowed to be used after injection if parents requested)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results of Review

Effect of Interventions vs. Usual Care

Five out of the seven studies used infant crying time as the outcome measure and found a reduction in crying time to a certain degree with the intervention group (IG) compared with the control group (CG). Allen et al. (1996) did not mention the mean difference of crying time clearly in the report and thus the effect size cannot be calculated. However, it stated that the sterile water group and sucrose group cried significantly less than no intervention group (p<0.05) for infants receiving one injection (2 weeks, 9 months and 18 months of age). Barr et al. (1995) found 16.67% less crying time with the IG in the post-injection period. Dilli et al. (2009) found 66.67% less crying time with the IG for infants of 6 to 12 months and crying time significantly higher in CG than IG for infants above 12 months of age (p=0.002). Lewindon et al. (1998) found 30.95%, 38.98% and 37.68% less first cry, sum total crying and start to finish crying for the IG respectively. Ramenghi et al. (2002) stated 17.65% and 67.42% less crying time for infants of 2 months and 4 months of age in the IG of 2ml 25% sucrose, while 54.35%, 44.88% and 73.67% less crying time for infants of 2 months, 3 months and 4 months of age in the IG of 2ml 50% sucrose.
Three out of the seven studies used a pain score as the outcome measure and all of them showed a reduction in pain score with the IG compared with the CG. Dilli et al. (2009) used the Neonatal Infant Pain Scale (NIPS) and Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS) to rate the pain response for infants and children of 6 to 12 months and 13 to 48 months respectively. The study found a 50% lower pain score (NIPS) with the IG in infants of 6 to 12 months and a pain score (CHEOPS) significantly higher in the CG than the IG for infants and children above 12 months of age (p=0.001). The University of Wisconsin Children’s Hospital (UWCH) Pain Scale was used as outcome measures for the studies of Hatfield (2008) and Hatfield et al. (2008). Hatfield (2008) found a 90.7% lower pain score with the IG at 5 minutes after immunization injections. Hatfield et al. (2008) found a 60.60%, 31.09%, 21% and 78.55% lower pain score with the IG at 2, 5, 7 and 9 minutes after immunization injections respectively.

The study of Lewindon et al. (1998) used the Oucher distress score as one of the outcome measures. It stated an 18.6% and 12.96% lower Oucher distress score rated by nurses and by parents for the IG compared with the CG respectively. The details of the above effect size of the intervention are listed in Table 3.
Effective vs. Non-effective Interventions

One of the seven studies had two related intervention groups. Ramenghi et al. (2002) arranged two intervention groups with the use of different concentrations of sucrose, 2ml 25% and 2ml 50% of sucrose. The intervention group with a higher concentration of sucrose (2ml 50%) showed a greater reduction of crying time for infants in all the age groups including 2 months, 3 months and 4 months of age compared with the intervention group with 2ml 25% of sucrose. This implies that the concentration of sucrose used could be greater than 2ml 25% in order to reduce the crying time and the pain experienced by infants more significantly.

Quality Assessment

Quality assessment of the selected studies was done based on the critical appraisal tool, “SIGN 50: A guideline developer’s handbook” from the Scottish Intercollegiate Guidelines Network (2008). The methodology checklist for randomized controlled trials was used (see Appendix A). The internal validity of studies was evaluated according to ten aspects of their design and the details are presented in the Quality Assessment Table (Internal Validity) (see Table 4). The overall assessment of the studies was also conducted and presented in the Quality Assessment Table (Overall Assessment)
According to Appendix B of SIGN Levels of Evidence and Grades of Recommendations, the studies were classified into different levels of evidence. RCTs were classified as high quality (1++) if they fulfilled most or all of the criteria in the checklist and any unsatisfactory items were very unlikely to alter the conclusion of the studies. If the RCTs only fulfilled some of the criteria and those criteria that were not fulfilled or not adequately described were thought unlikely to alter the conclusions, they were classified as fair quality (1+). RCTs were classified as poor quality (1-) if they had few or no criteria fulfilled and the conclusions were thought to be likely or very likely to be adjusted. With reference to SIGN (2008), three out of the seven RCTs were rated as good quality (1++) (n=3) (Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002), while the others were rated as fair quality (1+) (n=4) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Lewindon et al., 1998) in the quality assessment. The details of quality assessment in section 1 (internal validity) and section 2 (overall assessment) are presented in Table 4 and Table 5 respectively. The strengths and limitations of the studies are discussed based on the methodology checklist for RCTs (SIGN, 2008) as follows.
Table 4
Quality Assessment Table of Selected RCTs (Internal Validity)

<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 for all sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al. (1996)</td>
<td>++</td>
<td>+</td>
<td>−</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>−</td>
<td>−</td>
<td>NA</td>
</tr>
<tr>
<td>Barr et al. (1995)</td>
<td>++</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>13.6%</td>
<td>−</td>
<td>NA</td>
</tr>
<tr>
<td>Dilli et al. (2009)</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>++</td>
<td>++</td>
<td>2.8%</td>
<td>−</td>
<td>NA</td>
</tr>
<tr>
<td>Hatfield (2008)</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>12.5%</td>
<td>++</td>
<td>NA</td>
</tr>
<tr>
<td>Hatfield et al. (2008)</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>17%</td>
<td>−</td>
<td>NA</td>
</tr>
<tr>
<td>Lewindon et al. (1998)</td>
<td>++</td>
<td>++</td>
<td>−</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>2.7%</td>
<td>−</td>
<td>NA</td>
</tr>
<tr>
<td>Ramenghi et al. (2002)</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>−</td>
<td>+</td>
<td>++</td>
<td>0%</td>
<td>+</td>
<td>NA</td>
</tr>
</tbody>
</table>

Well covered (+++); Adequately addressed (++); Poorly addressed (+); Not addressed (−); Not reported (NR); Not applicable (NA)
<table>
<thead>
<tr>
<th>Study</th>
<th>Bias Minimized</th>
<th>Direction of Bias</th>
<th>Effect due to Intervention</th>
<th>Results Applicable to Target Groups</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al. (1996)</td>
<td>+</td>
<td>Sample size, drop-out rate and results not mentioned in detail</td>
<td>Yes</td>
<td>Yes</td>
<td>1+</td>
</tr>
<tr>
<td>Barr et al. (1995)</td>
<td>+</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1+</td>
</tr>
<tr>
<td>Dilli et al. (2009)</td>
<td>+</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1+</td>
</tr>
<tr>
<td>Hatfield (2008)</td>
<td>++</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1++</td>
</tr>
<tr>
<td>Hatfield et al. (2008)</td>
<td>++</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1++</td>
</tr>
<tr>
<td>Lewindon et al. (1998)</td>
<td>+</td>
<td>No control of the use of a pacifier which may have effects on the outcomes (although the utilization rate of a pacifier was low)</td>
<td>Yes</td>
<td>Yes</td>
<td>1+</td>
</tr>
<tr>
<td>Ramenghi et al. (2002)</td>
<td>++</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1++</td>
</tr>
</tbody>
</table>
Strengths

All the seven selected studies were RCTs and they addressed appropriate and clearly focused questions which focused on the administration of oral sucrose and its effects on infants’ immunization-induced pain and distress (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). The studies randomly allocated subjects to the intervention and control group except for the study of Barr et al. (1995). Adequate concealment allocation methods such as use of coded identical containers were used in most of the studies (n=4) (Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002). Double blinding for treatment allocation was applied and therefore neither the investigator nor participants were aware of the treatment allocation in all seven studies (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). The intervention and control groups were similar at the beginning of the trials for most of the studies (n=5) (Allen et al., 1996; Barr et al., 1995; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998). The only difference between intervention and control groups was the intervention under investigation for all studies (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield,
2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). All the outcomes of the studies were measured in a standard, valid and reliable way by means of objective infants crying time and/or pain assessment tools (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). Data were collected from a single site (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002).

Limitations

The study of Allen et al. could not be analyzed thoroughly due to insufficient details of dropout rate and results in the report. The dropout rates of these seven studies varied from 0% to 17%. Three studies had more significant dropout rates (>10%) (n=3) (Barr et al., 1995; Hatfield, 2008; Hatfield et al., 2008). Most of the studies did not have intention to treat analysis which ensure the initial treatment intent and avoid the effects of dropout and crossover (n=5) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield et al., 2008; Lewindon et al., 1998). The study of Lewindon et al. did not control the use of a pacifier and the sucking action may induce additional effects on the outcomes.
Summary and Synthesis

With reference to the results of the critical review of the selected literature, a beneficial effect by reducing immunization-induced pain and distress was demonstrated in the intervention of administration of oral sucrose. The evidence suggested that it can be considered to be introduced as a pain-relieving intervention in routine immunizations in Maternal and Child Health Centres as there is no related intervention in current practice. Besides, some useful information was retrieved through the critical appraisal to help develop an evidence-based guideline.

Characteristics of Interventions Reviewed

Dosage and concentration of sucrose. The dosage and concentration of sucrose used varied among the studies, from 3 continuous 0.25ml 50% to 2ml 75%. The study of Ramenghi et al. (2002) arranged two intervention groups with the use of different concentrations of sucrose, 2ml 25% and 2ml 50%. The intervention group with a higher concentration of sucrose (2ml 50%) showed a greater reduction of crying time for infants in all the age groups which implies that the higher concentration of sucrose used reduced the pain experienced by infants in terms of crying time more significantly. It is recommended 2ml 50% of oral sucrose could be used for the intervention.
**Time to administer sucrose.** Most studies administered oral sucrose two minutes before immunization (n=5) (Allen et al., 1996; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002). Two studies administered oral sucrose immediately before immunization (n=2) (Barr et al., 1995; Lewindon et al., 1998). A systematic review which targeted the effects of oral sucrose for hospitalized neonates undergoing painful medical procedures found the optimal time to administer oral sucrose was two minutes before painful procedures (Stevens et al., 2005). Besides, most of the selected studies also administered oral sucrose two minutes before immunization and showed significant pain reduction. Therefore, it is recommended that oral sucrose could be administered two minutes before immunization.

**Administration method.** All the included studies used a syringe or pipette to administer oral sucrose solution (n=7) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008; Lewindon et al., 1998; Ramenghi et al., 2002). It is recommended that oral sucrose solution should be administered by syringe or pipette since it is the most common and convenient method.

**Administration technique.** Two studies stated that oral sucrose solution was applied onto the anterior part of the tongue (n=2) (Barr et al., 1995;
Ramenghi et al., 2002), two studies applied it onto the surface of the tongue (n=2) (Hatfield, 2008; Hatfield et al., 2008) and the others stated that oral sucrose solution was applied into the mouth (n=3) (Allen et al., 1996; Dilli et al., 2009; Lewindon et al., 1998). It is recommended that oral sucrose solution should be applied onto the anterior part of the tongue for best stimulation of taste perception and sucking (Ramenghi, Wood, Griffith & Levene, 1996; Tatzer, Schubert, Timischl & Simbruner, 1985).

**Intervention Effectiveness**

All the seven RCTs showed the effectiveness of the intervention in reducing pain and distress for infants during routine immunizations. The effect size of the studies in the reduction of crying time and pain score ranged from 16.67% to 73.67% and 21% to 90.7% respectively.

**Summary of the Evidence**

Seven RCTs published from 1995 to 2009 were reviewed. The included studies involved a total of 879 healthy infants recruited from different community health care settings. All the studies aimed at evaluating the effectiveness of administration of oral sucrose with regard to reduction of immunization-induced pain. Three RCTs (Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002) were rated as good quality (1++) and the other four
RCTs were rated as fair quality (1+) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Lewindon et al., 1998) in quality appraisal with reference to SIGN (2008). After reviewing the literature, evidence showed that the administration of oral sucrose can reduce immunization-induced pain and distress for infants. All the studies showed a reduction in crying time or pain score for the intervention group. Five out of the seven studies demonstrated a reduction in crying time for the intervention group with an effect size ranging from 16.67% to 73.67% (n=5) (Allen et al., 1996; Barr et al., 1995; Dilli et al., 2009; Lewindon et al., 1998; Ramenghi et al., 2002). Three studies showed a reduction in pain score for the intervention group with an effect size ranging from 21% to 90.7% (n=3) (Dilli et al., 2009; Hatfield, 2008; Hatfield et al., 2008). Besides, administration of oral sucrose as a pain-relieving intervention is acceptable to most parents and nurses. The study of Lewindon et al. (1998) stated an 18.6% and 12.96% lower Oucher distress score rated by nurses and by parents for the intervention group respectively.

**Implications for Practice**

Childhood immunization is associated with pain and distress. However, there is no specific guideline to tackle immunization-induced pain in our current practice. From the literature review, evidence shows that the
administration of oral sucrose is an effective intervention for reducing pain and distress in infants during routine immunizations. With the evidence-based benefits of the intervention and the feasibility and acceptability of its procedures and equipment needed, it is important to introduce this intervention into practice. Therefore, a comprehensive evidence-based clinical guideline should be established to enhance the implementation of the innovation in practice.
Chapter 3: Implementation Potential

The review suggested that the administration of oral sucrose is an effective intervention to reduce immunization-induced pain and distress for infants. In this chapter, the potential of implementing the intervention in one of the Maternal and Child Health Centres of the Department of Health in Hong Kong was explored. The transferability of the findings from the reviewed studies and the feasibility of launching the innovation are discussed. Besides, the cost-benefit analysis of the innovation is discussed.

Target Population and Setting

Proposed Setting

The proposed setting is one of the Maternal and Child Health Centres of the Department of Health located in the New Territories. There are thirty one Maternal and Child Health Centres in Hong Kong. They promote the holistic health and wellbeing of children under six years old by providing an Integrated Child Health and Development Programme which includes health and developmental surveillance, parenting education and immunization services. The immunization service is one of the key services of Maternal and Child Health Centres and is provided to protect infants and children from infectious diseases in Hong Kong.
Target Population in the Proposed Setting

The target population in the proposed setting is infants one to eighteen months of age who receive routine recommended immunizations at a Maternal and Child Health Centre. The recommended schedule of the childhood immunization programme is attached in Appendix C. Generally, infants receive Bacillus Calmette-Guérin (B.C.G.) and the first dose of Hepatitis B Vaccine in hospital. Infants receive recommended immunizations from either Maternal and Child Health Centres or general practitioners from one month to eighteen months of age. As children grow up and attend primary school, they receive other recommended immunizations at primary schools by the School Immunization Team of the Department of Health. The proposed nursing intervention targets infants from one to eighteen months of age who receive routine recommended immunizations at the Maternal and Child Health Centre with the objective to reduce the immunization-induced pain and distress during routine immunizations. Although the vaccination coverage in Hong Kong is overall high, a very small number of parents bring their children to Maternal and Child Health Centres for vaccination beyond the scheduled time as recommended by the Hong Kong Childhood Immunization Programme (Department of Health, 2011a). Therefore, an age cut-off of twenty four
months is set for the intervention if the infants receive vaccination beyond the recommended scheduled time.

**Transferability of the Findings**

**Fit of Intervention in the Proposed Setting**

In Hong Kong, infants generally receive recommended immunizations in community health care settings including Maternal and Child Health Centres and general practitioners. The proposed innovation will be carried out in one of the Maternal and Child Health Centres and it is similar to the settings of the reviewed studies. In the reviewed studies, the study settings were community health care settings including well-child units, university-affiliated ambulatory paediatric clinics, general paediatric practices and immunization clinics located in the United States, Canada, United Kingdom, Australia and Turkey. Both of the proposed setting and the settings from the reviewed studies are community health care settings which provide recommended immunizations to infants. Therefore, the proposed intervention fits the proposed setting.

**Similarity of Research Population to Target Population**

In the reviewed studies, most of the participants were Caucasian infants in Western countries. The target population of this guideline is infants attending the Maternal and Child Health Centre and the majority of infants
attending the proposed setting are Chinese infants. Since infants of different ethnicity also experience pain and distress during immunizations, the target population will also benefit from the proposed intervention. The age group of the research population of the reviewed studies is infants and children from two weeks to forty eight months of age. Generally, infants receive recommended immunizations from one to eighteen months of age at Maternal and Child Health Centres in Hong Kong as recommended by the Hong Kong Childhood Immunization Programme. Besides, an age cut-off of twenty four months is set for the proposed intervention if the infants receive the vaccination beyond the recommended scheduled time. Therefore, the age group of the target group fits the research population of the reviewed studies. On the other hand, the reviewed studies targeted participants with similar characteristics, either healthy infants and children, healthy and full-term infants or infants that are healthy with a gestation $\geq 34$ weeks. Similarly, infants attending and receiving routine immunizations at the Maternal and Child Health Centres are generally healthy infants or those without significant illness. In all, the target population of the proposed setting is similar to the characteristics of the participants of the reviewed studies and the findings from the reviewed studies are transferable to the guideline of the proposed
intervention.

**Philosophy of Care**

Implementation of the innovation of administration of oral sucrose aims to reduce the pain and distress in infants and reduce the associated anxiety and distress experienced by their parents and families during the immunization procedures. The proposed intervention enhances a high-quality client-centred service which meets the philosophy of care of the Department of Health and the Maternal and Child Health Centres. The vision of the Department of Health is “… providing quality client-oriented service” (Department of Health, 2011b) and the missions of Maternal and Child Health Centres include “continuously upgrade our service through fostering innovation …” and “provide cost-effective service to meet the changing needs of our clients” (Department of Health, 2011c). In the proposed setting, health care professionals have mostly adopted the vision and missions at work and are willing to introduce new innovations aiming to provide quality client-centred service. The shared philosophy of care also enhances the implementation potential of the proposed innovation in the Maternal and Child Health Centre.

**Sufficient Number of Clients**

The Hong Kong Childhood Immunization Programme has been
established for many years in Hong Kong. Parents can take their children to any Maternal and Child Health Centre to receive the recommended immunizations. Parents may also take their children to general practitioners for the immunizations. According to the Department of Health Annual Report 2007/2008, there were 70,394 registered births in Hong Kong in 2007 and about 83% of them received services from Maternal and Child Health Centres (Department of Health, 2009a). In fact, most of them receive services including immunization service at Maternal and Child Health Centres. Another study conducted in 2006 found that 87.3% of the immunizations were given by Maternal and Child Health Centres, excluding B.C.G. and the first dose of Hepatitis B Vaccine which were given at the time of birth in hospitals (Wu, Chan, Kung, Lau & Choi, 2006). Therefore, the practice and quality of care of the service department affect most infants in Hong Kong. In my Maternal and Child Health Centre, there are around 1,200 to 1,500 infants receiving vaccinations every month. As a result, thousands of infants and their families will benefit from the proposed intervention when it is launched in my centre.

**Implementation and Evaluation Time**

The Gantt chart for adopting the proposed innovation is shown in Table 6. At the beginning, a working group will be set up and the proposal will be
prepared. This first step will take about two months. The next necessary step of obtaining approval from the Department of Health will take around three months. After obtaining the approval, committee meetings and protocol development will take around two months. Staff training and equipment preparation will take around one month. The implementation of the intervention will last for three months. The evaluation will last for a one-month period for data entry and analysis.

Feasibility

Freedom to Implement

It is feasible to implement the proposed innovation in my practice. However, it is necessary to seek approval from the head of service before implementation. It is not likely to be difficult to gain support for the innovation from the head of service by illustrating the potential benefits. Related supporting documents including evidence of the efficacy of the proposed intervention and its cost-benefits analysis will be provided for the consideration of approval. After getting the approval from the head of service, the details of the proposed innovation can be planned and nurses can carry out the innovation accordingly. On the other hand, the innovation can be terminated if it is considered to be undesirable by nursing staff.
<table>
<thead>
<tr>
<th>Phase</th>
<th>Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10 11 12</td>
<td></td>
</tr>
<tr>
<td>Setting up of working group/Preparation of proposal</td>
<td></td>
</tr>
<tr>
<td>Obtain approval</td>
<td></td>
</tr>
<tr>
<td>Committee meetings/Protocol development</td>
<td></td>
</tr>
<tr>
<td>Staff training/Equipment preparation</td>
<td></td>
</tr>
<tr>
<td>Implementation</td>
<td></td>
</tr>
<tr>
<td>Evaluation</td>
<td></td>
</tr>
</tbody>
</table>
Interference with Current Functions

The implementation of the proposed intervention will probably interfere with some current staff functions. Immunization nurses at the Maternal and Child Health Centre generally complete the whole immunization procedures within two to four minutes in a busy clinical environment. The proposed intervention involves an additional procedure of administration of oral sucrose solution into infants’ mouths by syringe before administration of the immunization injection. Although this simple procedure only takes seconds to complete, a two-minute wait period is suggested for the effect of oral sucrose to take hold before the immunization injection. Besides, related education and explanation is needed during nurse interviews. The intervention will increase some workload of nursing staff.

Administration/ Organizational Support

The administration does support the innovation. Although Maternal and Child Health Centres have not yet introduced pain-relieving interventions during routine immunizations, the Department supports and introduces new interventions and programmes which have been proven through research to improve the service and meet clients’ needs from past experience. Besides, nurses in my centre are open to learning new knowledge and skills, and adapt
well to new interventions and programmes. We have meetings every Wednesday to discuss clients’ needs and related improvement measures in order to improve the quality of care. With the continued introduction of new immunizations, infants need to receive multiple immunization injections at a single visit. From past experience and daily observation, parents and families show great concern and anxiety about immunization-induced pain. Besides, it is found that some conflicts and complaints are related to the concern over immunization-induced pain. Support is likely to be gained for the innovation by illustrating the potential benefits of reducing the immunization-induced pain and distress of infants and the associated anxiety and distress experienced by their parents and families.

**Consensus among Staff**

The efficacy of administration of oral sucrose for pain relief before immunization for infants has been scientifically supported. Although it may cause some extra workload for the nursing staff during the implementation process, it can be offset by the clinical benefits. Besides, the nursing staff working at the Maternal and Child Health Centre have strong team spirit and consensus among them is high. It is proposed that a working group can be established to facilitate the implementation of the proposed intervention. The
team members of the working group will include a doctor, a nursing officer and two nurses including the proposer of the intervention.

**Friction among Staff**

Support from both nurses and doctors for the innovation is essential before any implementation of intervention. In fact, the routine immunization procedure has been implemented for a long period of time and there is a lack of training and information related to pain-relieving interventions during immunization provided by the department. Therefore, frontline staff are generally not equipped with related up-to-date knowledge. Fortunately, new interventions and programmes such as education on consumption of iodine-rich food for antenatal clients to prevent hypothyroidism of infants and the Comprehensive Child Development Scheme have been introduced in the department and the acceptance of the new innovations in my centre is good from past experience. However, some staff may have different viewpoints and opinions on the proposed intervention. Therefore, a two-week enquiry period will be arranged to tackle the potential frictions and collect comments during the two-month period of committee meetings and protocol development.

**Skills Available to Implement Intervention**

In Maternal and Child Health Centres, interviewing nurses are
responsible for providing education on the type of immunization, examination of any contraindication to immunization, and on reaction and aftercare for immunization. Client education related to the innovation will also be incorporated into the nurse interviews. After the nurse interviews, immunization nurses will be responsible for the immunization procedures. For the proposed intervention, immunization nurses need to administer oral sucrose solution into infants’ mouth by syringe. Before the introduction of Diphtheria, Tetanus, acellular Pertussis and Inactivated Poliovirus Vaccine (DTaP-IPV), immunization nurses also need to administer Oral Polio Vaccine (OPV) into infants’ mouth by syringe using a similar technique. The proposed intervention only involves a simple procedure and special training for the administration method is not needed for the nursing staff. At the beginning, a briefing about the innovation will be provided. A guideline with relevant photos and videos of the administration method and procedures will be used for staff training. Guidelines will be set and nursing staff will be allowed to carry out or terminate the innovation if it is considered undesirable.

**Equipment Available to Implement Intervention**

In this proposed nursing intervention, oral sucrose solution, syringes and educational leaflets will be the main commodities used. The new item needed
is oral sucrose solution and it can be obtained from the pharmacy. Any new
inventory needed should be informed to and approval obtained from the
pharmacy. Besides, 3ml syringes are supplied by the Consumable Unit and an
extra amount of syringes can be ordered for the innovation depending on
centre needs. Related educational leaflets will be designed by the working
group. On the other hand, evaluation forms and two timers are needed for the
evaluation. Evaluation forms will be prepared by the working group and the
timers are already available at the centre.

**Evaluation Tools Available**

An assessment form with the case number of the infant, the date of birth
of the infant, the date of visit, the types of immunization given, the crying time,
the pain score, the parent report of infant distress and the nurse report of infant
distress after immunization will be used for recording and evaluation (see
Appendix D). For the primary outcome measures, both the crying time and the
pain score will be measured. The crying time, defined as the total crying time
within three minutes from the moment of needle insertion, will be recorded.

For the pain score, the University of Wisconsin Children’s Hospital (UWCH)
Pain Scale which is a validated pain measuring scale for pre- and non-verbal
children under three years old will be used (Soetenga et al., 1999). It consists
of five categories including crying, facial expression, behavioural response, body movement and sleep to quantify acute behavioural pain responses. Each category is correlated with a rating from 0 to 5. The mean value of the ratings of the five categories provides an overall score for the level of observed behavioural pain, with higher scores representing greater pain (see Appendix E). For the secondary outcome measures, both the parent report of infant distress and the nurse report of infant distress will be measured. A 100mm Visual Analogue Scale (VAS) will be used to measure the parent and nurse ratings of distress level suffered by the infant during the immunization procedures.

**Cost-Benefit Analysis of the Innovation**

**Potential Risks**

The reviewed research studies actually showed that administration of oral sucrose can reduce immunization-induced pain and distress effectively and pointed out that such perceivable risks are purely theoretical rather than actual risks in reality. Harrison (2008) further pointed out that the administration of oral sucrose does not impose any potential risks on infants. However, some of the nurses and families may perceive that the innovation could potentially increase the infants’ risk of hyperglycaemia and dental caries. In fact, a study
conducted by Stevens et al. (2005) found that there was no difference in blood glucose level between sucrose and water control groups. Besides, the innovation is unlikely to increase the risk of the development of dental caries since the small volumes of sucrose solution administered for pain reduction is comparably less than the volume and sugar content of some commonly administered medications such as antipyretics (Lewindon et al., 1998). Therefore, the target population of healthy infants will not be exposed to any potential risks during the implementation of the innovation.

**Potential Benefits**

With the continued introduction of new immunizations, there have been a rising number of immunizations for infants in Hong Kong. Previous research studies found that untreated immunization-induced pain has profound effects on infants’ physical, psychological and behavioural development (Page, 2004; Taddio et al., 1995; Pate et al., 1996). The proposed pain-relieving innovation can reduce the corresponding profound effects of untreated pain. Besides, infants are very important for their parents and families. Parents and families also experience anxiety and distress due to the pain experienced by their infants during routine immunizations. To reduce the pain and distress experienced by infants and the associated anxiety and distress experienced by
their parents and families, implementation of an evidence-based pain-relieving intervention is necessary. To pass on the benefits to the proposed target population, the implementation of the proposed innovation should be taken in advance. Initially, the proposed intervention may increase the workload of nursing staff. However, the benefits of the innovation to the infants, families and nurses will become apparent later. Reduction of pain for infants during immunizations can reduce conflicts related to the concerns of immunization-induced pain and appreciations from the families help to raise nurses’ morale in work. As a result, the proposed innovation can be beneficial to infants, families and health care providers.

**Risks of Maintaining Current Practice**

Without the introduction of the proposed innovation, infants will run the risk of suffering from the detrimental effects of untreated pain including decrease of the immune response (Page, 2004), increase of pain sensitivity (Taddio et al., 1995) and increase of avoidance of health care in adulthood (Pate et al., 1996). In our current practice, parents and families are informed with the information about the reaction and aftercare of immunizations by interviewing nurses but is inadequate. Parents and families feel anxious and distressed as their infants suffer from immunization-induced pain without any
pain-relieving measures. Besides, health care providers are under stress when there are conflicts related to the concerns of immunization-induced pain from parents and families.

**Material Cost of the Innovation**

Material costs are mainly spent on the items used in the intervention including oral sucrose solution and syringes. Other expenses include preparation of related educational leaflets and evaluation forms. On the other hand, two timers which are already available in the centre, are needed for the evaluation of the crying time. The budget estimation of the material cost of adopting the proposed intervention is attached in Table 7 and the total estimated material cost for every 1,000 eligible clients is $2,400.

**Non-material Cost of the Innovation**

In addition to the material cost, there are some non-material costs involved in adopting the proposed innovation. Nursing staff need to spend extra time on client education, administration procedure and evaluation. Client education will be incorporated into the nurse interviews and educational leaflets will be used to facilitate the education. The procedure of administration of oral sucrose will be carried out by immunization nurses and it will be incorporated into the immunization procedure. Administration of oral
sucrose will be started at the beginning of the immunization procedure. The
immunization nurses can make use of the time to perform “3 Checks 5 Rights”
and position preparation during the two-minute interval after administration of
the sucrose solution for the effect of oral sucrose to take hold. In this situation,
the additional time needed for interviewing nurses and immunization nurses to
conduct client education and administration procedures can be shortened and
the related costs can be reduced. It is estimated that two minutes of additional
time is needed for client education and the administration procedure for each
client respectively. On the other hand, a maximum of three minutes will be
used for the evaluation of each client. The budget estimation of the
non-material costs for adopting the proposed intervention is attached in Table
8 and the total estimated non-material cost for every 1,000 eligible clients is
$18,656.
Table 7
Budget Estimation of Material Costs for Every 1,000 Eligible Clients

<table>
<thead>
<tr>
<th>Materials</th>
<th>Cost</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Oral sucrose solution</td>
<td>Oral sucrose solution: $25/50ml (25 dose)</td>
<td>$1,000</td>
</tr>
<tr>
<td></td>
<td>Estimated cost: $1 per dose X 1,000 clients</td>
<td></td>
</tr>
<tr>
<td>2. Syringes</td>
<td>3ml syringe: $100/100 syringes</td>
<td>$1,000</td>
</tr>
<tr>
<td></td>
<td>Estimated cost: $1 per one X 1,000 clients = $1,000</td>
<td></td>
</tr>
<tr>
<td>3. Educational leaflets &amp; Evaluation forms</td>
<td>Photocopy fee: $400/1,000 leaflets + 1,000 evaluation forms</td>
<td>$400</td>
</tr>
<tr>
<td></td>
<td>Estimated cost: $0.40 per set X 1,000 clients = $400</td>
<td></td>
</tr>
</tbody>
</table>

Table 8
Budget Estimation of Non-material Costs for Every 1,000 Eligible Clients

<table>
<thead>
<tr>
<th>Non-material</th>
<th>Cost</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Nursing staff responsible for client education</td>
<td>Salary: <del>$28,000/month (</del>$160/hour)</td>
<td>$5,328</td>
</tr>
<tr>
<td></td>
<td>Hours invested: 2 minutes X 1,000 clients = 33.3 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimated cost: $160 X 33.3 = $5,328</td>
<td></td>
</tr>
<tr>
<td>2. Nursing staff responsible for administration procedure</td>
<td>Salary: <del>$28,000/month (</del>$160/hour)</td>
<td>$5,328</td>
</tr>
<tr>
<td></td>
<td>Hours invested: 2 minutes X 1,000 clients = 33.3 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimated cost: $160 X 33.3 = $5,328</td>
<td></td>
</tr>
<tr>
<td>3. Nursing staff responsible for evaluation</td>
<td>Salary: <del>$28,000/month (</del>$160/hour)</td>
<td>$8,000</td>
</tr>
<tr>
<td></td>
<td>Hours invested: 3 minutes X 1,000 clients = 50 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimated cost: $160 X 50 = $8,000</td>
<td></td>
</tr>
</tbody>
</table>
Chapter 4: Evidence-based Practical Guidelines

Overview of Guidelines

Guideline Title

The guideline title is “Administration of oral sucrose to reduce immunization-induced pain and distress for infants one to eighteen months of age”.

Aim of Guidelines

The aim of the guidelines is to provide practical clinical guidelines for nursing staff to carry out pain-relieving intervention of administration of oral sucrose for infants during routine immunizations.

Objectives of Guidelines

The guidelines have three main objectives: first, to promote evidence-based pain-relieving intervention of administration of oral sucrose for infants during routine immunizations; second, to reduce pain and distress for infants during routine immunizations; and finally, to reduce the anxiety and distress experienced by parents and families during routine immunization procedures.

Target Group

The target population is healthy infants one to eighteen months of age.
undergoing routine immunizations. Infants under twenty four months of age are included if they receive the vaccination beyond the recommended scheduled time.

**Interventions and Practices Considered**

Intervention of administration of oral sucrose solution before routine immunizations is considered for implementation.

**Major Outcomes Considered**

The major outcomes considered include reduction in infant crying time; reduction in pain score; reduction in parent report of infant distress; and reduction in nurse report of infant distress.

**Recommendations**

Recommendations were derived from the seven reviewed studies, and based on levels of evidence and grades of recommendations by the Scottish Intercollegiate Guidelines Network (SIGN) (2008) (see Appendix B). Recommendations in this guideline were developed based on the best available evidence and only grade A recommendations were included in this guideline.

Recommendation 1.0 – Who should be administered oral sucrose solution?

- All healthy oral feeding infants not more than twenty four months of age
should be administered oral sucrose solution.

- 2 weeks to 18 months (Allen et al., 1996) (1+)
- 2 months to 4 months (Hatfield, 2008; Hatfield et al., 2008, Ramenghi et al., 2002) (1++) and (Barr et al., 1995) (1+)
- 2 months to 6 months (Lewindon et al., 1998) (1+)
- 6 months to 48 months (Dilli et al., 2009) (1+)

Recommendation 2.0 - Time to administer oral sucrose

- Eligible infants should be administered oral sucrose solution not less than two minutes before administration of immunization.
- 2 minutes before administration of immunization (Hatfield, 2008; Hatfield et al., 2008) (1++) and (Allen et al., 1996; Dilli et al., 2009) (1+)

Recommendation 3.0 - Dosage and concentration of oral sucrose solution

- 2ml of 50% oral sucrose solution is suggested to be used.
- 2ml of 50% oral sucrose solution (Ramenghi et al., 2002) (1++)

Recommendation 4.0 - Administration method

- A syringe is suggested to be used for administration of oral sucrose solution.
- Syringe (Hatfield, 2008; Hatfield et al., 2008; Ramenghi et al., 2002)
Recommendation 5.0 - Administration technique

- Oral sucrose solution is suggested to be applied into the mouth, preferably applied onto the surface of the anterior part of the tongue.

- Onto the anterior part of the tongue (Ramenghi et al., 2002) (1++) and (Barr et al., 1995) (1+)

- Onto the surface of the tongue (Hatfield, 2008; Hatfield et al., 2008) (1++)

- Into the mouth (Allen et al., 1996; Dilli et al., 2009; Lewindon et al., 1998) (1+)
Chapter 5: Implementation Plan

The literature review showed that the administration of oral sucrose is an effective intervention to reduce pain and distress for infants during immunization. To ensure successful implementation of the evidence-based practical guideline, it is essential to establish a well-designed implementation plan which covers stakeholder identification and communication strategies. It is also important to perform pilot testing before full implementation of the guideline in order to test its feasibility (Melnyk & Fineout-Overholt, 2011).

Communication Plan

Stakeholders

Ploeg, Davies, Edwards, Gifford & Miller (2007) suggested that leadership support from administrators is necessary for guideline implementation. The headquarters of the Family Health Service of the Department of Health is responsible for the arrangement and allocation of resources, manpower and budget for the service needs of the Maternal and Child Health Centres. It also plays a decisive and managerial role in carrying out new innovations and programmes. It sets standardized guidelines and protocols, and makes continuous changes for improvement through ongoing evaluation. Therefore, senior administrators of the headquarters are important
stakeholders and it is necessary to seek their support for the successful implementation of the innovation.

The innovation will be carried out in one of the Maternal and Child Health Centres located in the New Territories. In the Maternal and Child Health Centre, centre administrators and frontline staff are vital stakeholders for the success of the innovation. Centre administrators including medical officer in-charge, nursing officer in-charge and nursing officers are responsible for the management of daily centre operations and ensuring that frontline staff work in compliance with the established guidelines and protocols. Frontline staff including doctors, registered nurses and enrolled nurses are also the main stakeholders as they are the ones who directly deliver the services according to the standardized guidelines and protocols. Therefore, it is important to gain their understanding, acceptance and support.

In addition, infants and parents attending the centre are also stakeholders as they are the recipients of the health care service. They are welcomed to give constructive feedback and suggestions in relation to the innovation.

In all, the key stakeholders include senior administrators of the headquarters, centre administrators and frontline staff in the centre and infants and parents attending the centre. In order to communicate with all the
identified stakeholders effectively, the communication process should be well-planned and tailored communication strategies should be established for different stakeholders (Ploeg et al., 2007).

**Communication Process**

The communication process will involve three steps including setting up a working group, getting approval from the headquarters and seeking cooperation with centre administrators and frontline colleagues.

Firstly, a working group with a doctor, a nursing officer, a registered nurse and the proposer will be formed. The proposer of the innovation will share the information of the innovation among the working group. The concern of immunization-induced pain, inadequacy of current practice and evidence on the effectiveness of administration of oral sucrose to reduce pain during immunization will be shared. It is aimed to gain the support and consensus among the working group in order to promote the innovation further to the identified stakeholders.

Secondly, it is necessary to obtain approval and support from the headquarters in order to initiate the innovation. Senior administrators in the headquarters are the key persons to decide whether the innovation can be carried out or not. The idea of the innovation will be introduced and the
proposal of the innovation will be sent to the senior administrators of the headquarters. The proposal which includes the rationale behind introducing the innovation with evidence from the reviewed literature, potential benefits and budget plan will be prepared by the working group. Also, it is important to emphasize the potential benefits of the innovation for the clients and the service. On the other hand, the fact that the implementation of the innovation will not lead to great impacts on current routine practice will be explained in order to persuade them to accept and support the proposed innovation. Open discussions will be held to present the details of the innovation, understand the senior administrators’ interest, collect feedback and comments, and build trust with them.

After obtaining the approval and support of the senior administrators of the headquarters, the next step of communicating and seeking cooperation with frontline colleagues will be conducted. Since they will directly implement the proposed intervention to the clients, they should understand, accept and support the innovation. During lunch hour meetings, the evidence-based findings and beneficial effects of the innovation will be explained firstly. Also, it is necessary to explain their roles in the implementation of the innovation. Lancaster (1999) pointed out that change of practice may stimulate a range of
responses among colleagues and these responses may be stimulating, neutral or frightening. In fact, some colleagues may show resistance to the new practice since they may not understand the benefits of the change and feel anxious about their roles in implementing the innovation. Open discussions will be held and colleagues will be encouraged to voice their concerns and perceived barriers in carrying out the new innovation (Lancaster, 1999). Barriers will be identified and solutions will be discussed together during lunch hour meetings. Finally, the evidence-based practical guidelines will be explained in detail and a video of administration method and procedures will be used for staff training to ensure that everyone is on the right track and the innovation will be implemented smoothly.

**Communication Strategies**

Successful implementation of an innovation needs collaboration of stakeholders, and therefore tailored and effective communication strategies must be established (Polit & Beck, 2012).

To initiate the innovation, it is necessary to gain support from the headquarters. The working group will discuss the innovation with the senior administrators of the headquarters. The current practice will be introduced. It is suggested that the representatives of the working group will meet the senior
administrators regularly. The aims of the meetings are to decide when and how to start the innovation, to allocate and arrange resources, and to examine the results of the innovation under evidence-based support. Also, the representatives of the working group will report the progress and obstacles to the headquarters regularly. On the other hand, the senior nursing officer of each service region and the nursing officer in-charge from each centre will meet together every two months. During the meetings, the progress of the innovation will be discussed. In addition, the senior nursing officer visits the centre every three months. Discussions can also be held individually as needed. Barriers can be identified and solutions can be worked out accordingly.

To enhance the smooth running of the innovation, a briefing on the innovation will be conducted for frontline colleagues one month before implementation. The evidence-based practical guideline will be introduced to frontline colleagues in lunch hour meetings. Guidelines with relevant photos and a video of the administration method and procedures will be used for staff training. The guideline will be distributed to all the frontline doctors and nurses in the centre. A copy of the guidelines will be kept in the treatment room, the nursing officer room and the medical officer rooms. Communication is the backbone of effective change and therefore open communication should
be maintained so that questions, concerns and ideas can be addressed accordingly (Lancaster, 1999). In addition, the guidelines will be reviewed and updated by the working group. There are twenty nurses in the centre. Fifteen nurses have worked in Maternal and Child Health Centres for more than five years and they have the experience of administering OPV which involves a similar technique of administration of oral sucrose. Therefore, it is suggested that at least one experienced nurse be assigned to the duty of immunization in every infant session during the implementation period of the innovation.

Furthermore, posters will be used to introduce the launch of the new innovation in the centre and its benefits with evidence from the literature. Posters will be put up in the waiting hall, the treatment room and each of the nurse interviewing rooms. In order to help clients to have a better understanding of the innovation, educational leaflets will also be used during client education. Common myths and misunderstandings about the administration of oral sucrose will be included in addition to the benefits of the intervention.

**Sustaining the Change Process**

During the implementation period, the innovation proposer and the working group will act as coordinator. In order to sustain the implementation
of the evidence-based practical guidelines, an audit will be performed to assess frontline colleagues’ compliance with the guidelines and the nursing officer of the working group will take on the role of auditing. The nursing officer can sit in and observe if the staff follow the guidelines or not. In addition, active listening and open communication is necessary during the time of change (Marquis & Huston, 2012). Any difficulties in following the guidelines and possible solutions will be discussed during weekly lunch hour meetings. Furthermore, the outcomes of the innovation include infants’ crying time, pain score, parent report of infant distress and nurse report of infant distress will be obtained for the evaluation of the effectiveness of the intervention.

**Pilot Testing**

A pilot test should be carried out before full implementation of the new innovation in order to test its feasibility and identify potential barriers (Melnyk & Fineout-Overholt, 2011). Findings of the pilot test can provide opportunities for refinement of the evidence-based practical guidelines before full implementation.

The pilot study participants will be healthy oral feeding infants not more than twenty four months of age and their parents who attend the Maternal and Child Health Centre for routine scheduled immunization. The working group
will coordinate the pilot test and it will comprise two infant sessions. A total of twenty infants will be recruited in two infant sessions. The evidence-based practical guidelines with relevant photos and video of administration method and procedures will be used for staff training. Consent forms and educational leaflets will be prepared for the recruitment procedure and client education. Intervention outcomes including infant crying time and pain score will be measured and recorded in the data collection form and pain scale (see Appendices D and E). Parent report of infant distress and nurse report of infant distress will be obtained with the use of questionnaires (see Appendices F and G). In addition, questionnaires will be given to both parents and nursing staff in order to invite them to give comments and express opinions on the innovation (see Appendices H and I).

The process and outcomes will be evaluated in the pilot test. The process evaluation includes smoothness of the procedures, nurses’ administration technique, parents’ feedback and nurses’ responses, and use of resources will be conducted. All the procedures starting from the recruitment process will be observed to see whether the procedures can run smoothly or not. The administration technique of nursing staff will be assessed to see whether they can administer the oral sucrose solution in a proper way as the guidelines
prescribe. The nursing officer of the working group will be responsible for auditing the staff and giving comments and instructions to them as necessary. In addition, parents will be invited to fill in a satisfaction questionnaire and make comments regarding the adequacy of the explanation given by nurses, the appropriateness of the educational leaflets, the arrangement of the intervention and their satisfaction with the intervention (see Appendix H). Similarly, a satisfaction questionnaire will be distributed to nurses to evaluate the logistics and their satisfaction with the innovation (see Appendix I). Also, nurses will be invited to give feedback and their opinions. The logistics and the identified problems will be discussed and solved together during lunch hour meetings. Furthermore, resources will be monitored to see whether they can meet the demands or not. Evaluation and improvement will be made accordingly after gathering the data from the pilot test. On the other hand, the primary outcome of the innovation is to reduce immunization-induced pain and distress in infants. Therefore, infants’ crying time, pain score, parent report of infant distress and nurse report of infant distress will be measured to test the efficiency and effectiveness of the intervention. Finally, the findings and a formal report of the pilot study will be reported and submitted to the senior administrators of the headquarters.
Chapter 6: Evaluation Plan

In order to determine the effectiveness of the innovation in the proposed setting, it is essential to conduct an outcome evaluation and the evaluation plan is outlined as follows. The evaluation plan illustrates how the innovation will be evaluated with regard to its effectiveness regarding the intervention outcomes and outcome measurements. The nature and number of clients involved will be calculated. Also, the method of data analysis and criteria for its effectiveness will also be discussed.

Intervention Outcomes and Outcome Measurements

Client Outcomes

The primary client outcome is to reduce the immunization-induced pain and distress in infants. The level of pain and distress of infants will be measured by the crying time and pain score of infants after immunization. The infant crying time is defined as the total crying time within the first three minutes after administration of immunization and it will be recorded in the data collection form (see Appendix D). For the pain score, the University of Wisconsin Children’s Hospital (UWCH) Pain Scale which is a validated pain measuring scale for pre- and non-verbal children under three years old will be used (Soetenga et al., 1999). It consists of five categories including crying,
facial expression, behavioural response, body movement and sleep. Each category is correlated with a rating from 0 to 5 to quantify the acute behavioural pain response. The mean value of the ratings of the five categories represents the level of observed behavioural pain (see Appendix E). The pain score will be measured two minutes after administration of immunization. The secondary client outcome is the infant distress level perceived by the parent and the nurse. Parent report of infant distress and nurse report of infant distress will be measured by means of a 100mm VAS. A simple questionnaire will be distributed to the parent or caregiver and nurse after the immunization procedures, and they will be asked to mark their perceived infant distress level after immunization on the VAS (see Appendices F and G). All the above findings will be recorded on the data collection form (see Appendix D).

**Health Care Provider and System Outcomes**

In order to evaluate the effectiveness of the innovation in the context of the proposed health care setting, it is also necessary to evaluate the client satisfaction, the staff satisfaction, the utilization of innovation and the costs. The level of client and staff satisfaction with the innovation will be measured by means of satisfaction questionnaires (see Appendices H and I). The satisfaction questionnaires consists of ten statements, and parents and nurses
will be asked to state their opinion by using a 4-point Likert scale ranging from “strongly disagree” to “strongly agree”. In addition, the utilization of the innovation will be measured. The total number of cases with implementation of the innovation and the total number of eligible cases will be recorded in order to calculate the percentage of utilization and indicate the level of utilization of the innovation. On the other hand, the actual expenses due to the materials and manpower used will be calculated. The expenses will be reviewed one month after the beginning of the innovation.

**Nature and Number of Clients Involved**

**Eligibility Criteria**

Healthy oral feeding infants not more than twenty four months of age who receive routine scheduled immunizations at the Maternal and Child Health Centre are eligible for the innovation.

**Sample Size Calculation**

The study of Lewindon et al. (1998) found that the mean crying time within three minutes after immunization for infants of the control group was 59 seconds. In addition, Ramenghi et al. (2002) found that the crying time reduced by 44.9% to 73.7% when 2ml of 50% oral sucrose was administered to infants among different age groups including two months, three months and
four months. As the guidelines include a greater range of age groups and the results may vary between different age groups, it is considered that a 30% reduction in crying time proves its effectiveness and it is assumed that the mean of the population to be sampled is 30% less than the known value. Therefore, we assume the known value to be 59, the mean of the population to be sampled to be 41 and the sigma (standard deviation of the sampled population) to be 30, with the power set at 0.8 and alpha at 0.05. By means of statistical software calculation, the sample size needed is 22. On the other hand, Hatfield (2008) found the mean pain score two minutes after immunization for infants of the control group to be 4.39 out of 5. Hatfield et al. (2008) found that the pain score of the intervention group reduced by 21% to 78.6% when it was measured at different times after the immunization injection. It is considered that a 20% reduction in pain score proves its effectiveness and it is assumed that the mean of the population to be sampled is 20% less than the known value. Therefore, we assume the known value to be 4.39, the mean of the population to be sampled to be 3.5 and the sigma (standard deviation of the sampled population) to be 1, with the power set at 0.8 and alpha at 0.05. The sample size required is 10 by means of statistical software calculation. With reference to the Hong Kong Childhood
Immunization Programme (Department of Health, 2011a), the participants will be divided into three age groups: one month, two to twelve months and eighteen to twenty four months, for the evaluation (see Appendix C). The first group includes infants one month of age who received Hepatitis B Vaccine only. Infants of two to twelve months of age who receive multiple vaccines (two to three vaccines) which include DTaP-IPV, Pneumococcal vaccine and Measles, Mumps, Rubella (MMR) Vaccine are put into the second age group. Multiple vaccines will be given sequentially without special calming time as routine practice and only a single dose of oral sucrose solution will be administered before the first immunization injection. The third group includes infants eighteen to twenty four months of age who receive DTaP-IPV only. Assuming a drop-out rate of 10%, 25 samples in each of the age groups will be needed. Therefore, a total of 75 participants including 25 infants one month of age, 25 infants two to twelve months of age and 25 infants eighteen to twenty four months of age will be needed. It is estimated that sufficient samples will be obtained within 1 week.

Data Analysis

Data Collection

In daily practice, nurses discuss the issue of immunization with parents or
caregivers during nurse interviews. If the infant is fit for routine immunization and is eligible for the innovation, the nurse will introduce the innovation with the help of the educational leaflet and invite the parents or caregivers to receive the innovation. The number of cases that receive the intervention will be recorded and it will be compared with the total number of eligible cases in order to show the utilization rate of the innovation. If the parents or caregivers choose to receive the innovation, details of the innovation and the educational leaflets will be provided for their reference. The nurse responsible for the evaluation will measure and record the crying time and pain score of the infant after immunization. Questionnaires will be distributed to the parents or caregivers after the immunization procedures and they will be asked about their perceived infant distress during immunization and satisfaction level with the innovation (see Appendices F and H). The immunization nurse will be asked to mark the perceived infant distress level during immunization on the questionnaire (see Appendix G). In order to assess the health care providers’ satisfaction level, staff satisfaction questionnaires will also be distributed and comments will be collected for further improvement (see Appendix I).

**Data Evaluation**

The objective of the evaluation is to determine if the primary client
outcomes including infant crying time and pain score are changed by the implementation of the innovation. Statistical analysis will be carried out using the Statistical Package for the Social Sciences (SPSS) version 20.0 (SPSS, 2011). The outcome data will be entered in the SPSS database. The means of infant crying time and pain score will be calculated respectively. Also, the infant crying time and pain score after the introduction of the intervention will be compared with the known means already outlined before. Since they involve comparing a single sample with the known parameters of the corresponding population, z-test can be used for data analysis. There are two types of z-test: one-tailed and two-tailed. The two-tailed z-test is a non-directional, population parameter and sample means are significantly different from each other (Osborn, 2008). Since we wish to know whether the innovation will change the infant crying time and pain score after administration of oral sucrose, two-tailed z-test will be used. As a result, two-tailed one sample z-test will be performed to compare the infant crying time and the pain score under the current and new practice.

Criteria for Effectiveness

Primary Client Outcomes

As discussed in the section on sample size calculation, it is considered
that the infant crying time should be reduced by more than 30% which means a reduction of eighteen seconds in crying time to prove its effectiveness. For the pain score, it is considered that it should be reduced by more than 20% which means a reduction of 0.88 points in pain score to prove its effectiveness.

Other Outcomes

The levels of parent satisfaction and staff satisfaction are also taken into account to decide the effectiveness of the innovation. It is considered to be effective if 70% of the parents and nursing staff “strongly agree” or “agree” on the overall satisfaction level. For the utilization of innovation, 80% of the utilization rate constitutes evidence of the effectiveness of the innovation.

Conclusion

To conclude, evidence from the reviewed literature clearly supports the fact that the administration of oral sucrose is effective and feasible in reducing immunization-induced pain and distress in infants. This simple and safe practice can bring about obvious positive outcomes for infants, parents, nurses and the health care system. It is worth implementing the innovation for infants in light of the cost and benefit analysis performed. In order to carry out the innovation at the Maternal and Child Health Centre successfully and guide the implementation with clear instructions, the implementation of the innovation
should be well-planned and evidence-based guidelines need to be developed accordingly. Before the implementation of the innovation, it is necessary to communicate with the stakeholders. A pilot test should be carried out in order to test the feasibility and make further improvements. Lastly, the effectiveness of the innovation should be assessed according to the evaluation plan. It is expected that the implementation of the administration of oral sucrose will be beneficial to the infants, parents, nurses and the Maternal and Child Health Centre by means of reduction of infants’ pain and distress during routine immunizations.
### Methodology Checklist 2: Controlled Trials

**SIGN**

**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>

**SECTION 1: INTERNAL VALIDITY**

**In a well conducted RCT study...**  
**In this study this criterion is:**

<table>
<thead>
<tr>
<th>1.1</th>
<th>The study addresses an appropriate and clearly focused question.</th>
<th>Well covered</th>
<th>Adequately addressed</th>
<th>Poorly addressed</th>
<th>Not addressed</th>
<th>Not reported</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>The assignment of subjects to treatment groups is randomised</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.3</td>
<td>An adequate concealment method is used</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.4</td>
<td>Subjects and investigators are kept ‘blind’ about treatment allocation</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.5</td>
<td>The treatment and control groups are similar at the start of the trial</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.6</td>
<td>The only difference between groups is the treatment under investigation</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>1.9</td>
<td>All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
<tr>
<td>1.10</td>
<td>Where the study is carried out at more than one site, results are comparable for all sites</td>
<td>Well covered</td>
<td>Adequately addressed</td>
<td>Poorly addressed</td>
<td>Not addressed</td>
<td>Not reported</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
### SECTION 2: OVERALL ASSESSMENT OF THE STUDY

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

2.2 If coded as +, or – what is the likely direction in which bias might affect the study results?

2.3 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?

2.4 Are the results of this study directly applicable to the patient group targeted by this guideline?

### SECTION 3: DESCRIPTION OF THE STUDY (The following information is required to complete evidence tables facilitating cross-study comparisons. Please complete all sections for which information is available). PLEASE PRINT CLEARLY

3.1 **Do we know who the study was funded by?**

- □ Academic Institution  
- □ Healthcare Industry  
- □ Government  
- □ NGO  
- □ Public funds  
- □ Other

3.2 **How many centres are patients recruited from?**

3.3 **From which countries are patients selected? (Select all those involved. Note additional countries after “Other”)**

- □ Scotland  
- □ UK  
- □ USA  
- □ Canada  
- □ Australia  
- □ New Zealand  
- □ France  
- □ Germany  
- □ Italy  
- □ Netherlands  
- □ Scandinavia  
- □ Spain  
- □ Other:

3.4 **What is the social setting (ie type of environment in which they live) of patients in the study?**

- □ Urban  
- □ Rural  
- □ Mixed

3.5 **What criteria are used to decide who should be INCLUDED in the study?**

3.6 **What criteria are used to decide who should be EXCLUDED from the study?**

3.7 **What intervention or risk factor is investigated in the study? (Include dosage where appropriate)**

3.8 **What comparisons are made in the study (ie what alternative treatments are used to compare the intervention with). Include dosage where appropriate.**

3.9 **What methods were used to randomize patients, blind patients or investigators, and to conceal the randomization process from investigators?**

3.10 **How long did the active phase of the study last?**
### 3.11 How long were patients followed-up for, during and after the study?

### 3.12 List the key characteristics of the patient population. Note if there are any significant differences between different arms of the trial.

### 3.13 Record the basic data for each arm of the study. If there are more than four arms, note data for subsequent arms at the bottom of the page.

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
<th>Arm 4</th>
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<td><strong>With outcome:</strong></td>
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<td><strong>Primary outcome?</strong></td>
<td><strong>Primary outcome?</strong></td>
<td><strong>Primary outcome?</strong></td>
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</table>

### 3.14 Record the basic data for each IMPORTANT outcome in the study. If there are more than four, note data for additional outcomes at the bottom of the page.

<table>
<thead>
<tr>
<th>Outcome 1</th>
<th>Outcome 2</th>
<th>Outcome 3</th>
<th>Outcome 4</th>
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<td><strong>P value</strong></td>
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<tr>
<td><strong>Primary outcome?</strong></td>
<td><strong>Primary outcome?</strong></td>
<td><strong>Primary outcome?</strong></td>
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</tbody>
</table>

### 3.15 Notes. Summarise the authors conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question. *(Much of this is likely to be contributed by GDG members).*
Appendix B - SIGN Levels of Evidence and Grades of Recommendations

LEVELS OF EVIDENCE

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
   High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
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

GRADES OF RECOMMENDATIONS

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+
### Appendix C – Hong Kong Childhood Immunization Programme

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunization Recommended</th>
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</table>
| Newborn | B.C.G. Vaccine  
            | Hepatitis B Vaccine – First Dose                           |
| 1 month | hepatitis B vaccine – Second Dose                           |
| 2 months| DTaP-IPV Vaccine – First Dose  
            | Pneumococcal Vaccine – First Dose                          |
| 4 months| DTaP-IPV Vaccine – Second Dose  
            | Pneumococcal Vaccine – Second Dose                          |
| 6 months| DTaP-IPV Vaccine – Third Dose  
            | Pneumococcal Vaccine – Third Dose  
            | Hepatitis B Vaccine – Third Dose                            |
| 1 year  | MMR Vaccine (Measles, Mumps, Rubella) – First Dose  
            | Pneumococcal Vaccine – Booster Dose                         |
| 1 1/2 year | DTaP-IPV Vaccine – Booster Dose                           |
| Primary 1 | MMR Vaccine (Measles, Mumps, Rubella) – Second Dose  
            | DTaP-IPV Vaccine – Booster Dose                            |
| Primary 6 | dTap-IPV Vaccine – Booster Dose                           |

(Department of Health, 2011a)
Appendix D – Data Collection Form

Date: ____________

Infant No.: ____________ Date of Birth: ____________ Age: ____________

Types of Immunization given
- [ ] Hepatitis B Vaccine
- [ ] DTaP-IPV Vaccine
- [ ] Pneumococcal Vaccine
- [ ] MMR (Measles, Mumps, Rubella) Vaccine

Crying Time: ____________ (maximum of 3 minutes)
(total crying time within 3 minutes from the moment of needle insertion)

Overall Pain Score: ____________ (measure at 2 minutes after immunization)
(refer to University of Wisconsin Children’s Hospital Pain Scale)

Parent Report of Infant Distress: ____________
(refer to Parent Report of Infant Distress 100mm Visual Analogue Scale)

Nurse Report of Infant Distress: ____________
(refer to Nurse Report of Infant Distress 100mm Visual Analogue Scale)

Name and Signature of Nurse: ________________
## Appendix E – University of Wisconsin Children’s Hospital (UWCH) Pain Scale

### University of Wisconsin Children’s Hospital (UWCH) Pain Scale

<table>
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</table>

<table>
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<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td><strong>Vocal/ Cry</strong></td>
<td>No cry</td>
<td>Occasional whimpers</td>
<td>Moaning, gentle cry, or whimpering</td>
<td>Consistent cry that increases in volume and duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Facial</strong></td>
<td>Smiling, calm, relaxed</td>
<td>Neutral expression, frowning, occasional grimace</td>
<td>Occasional tense expression, slightly negative expression (e.g. grimace), brow bulge, shallow nasolabial furrow</td>
<td>Marked distress. Brow bulge, eyes squeezed shut, open mouth, taut tongue, deepening of nasolabial furrow</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Behavioral</strong></td>
<td>Neutral, moves easily, interact with people or environment, strong rhythmic suck on pacifier</td>
<td>Easy to console with holding, position change, or sucking; winces when touched/moved</td>
<td>Consoles with moderate difficulty; sucks for very short periods, followed by crying; cries out when oved/touched</td>
<td>Inconsolable; absent or disorganized sucking; high pitched cry or scream when touched or moved</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Body Movement/ Posture</strong></td>
<td>Normal motor activity, baseline muscle tone</td>
<td>Fidgeting; mild hypertonicity above baseline</td>
<td>Moderate agitation or moderate immobility; intermittent flexion; moderate hypertonicity above baseline</td>
<td>Thrashing, flailing, incessant agitation or strong voluntary immobility; pronounced flexion; strong hypertonicity above baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
<td>Sleeping quietly with easy respirations; normal sleep/ rest periods</td>
<td>Restless while asleep</td>
<td>Sleep periods shorter than normal, awakes easily, sleeps intermittently</td>
<td>Unable to sleep or sleeping for prolonged periods of time interrupted by jerky movements</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Overall Score (Mean value of ratings of five categories): __________**

(Soetenga, Frank & Pellino, 1999)
Appendix F – Parent Report of Infant Distress Questionnaire

Infant no.: ________________

Parent Report of Infant Distress

Please mark a cross to indicate the distress level suffered by the baby during the immunization procedures.

No distress                              Distress as bad as possible
Appendix G – Nurse Report of Infant Distress Questionnaire

Infant no.: ______________

Nurse Report of Infant Distress

Please mark a cross to indicate the distress level suffered by the baby during the immunization procedures.

No distress                                      Distress as bad as possible

Name and Signature of Nurse: ______________
# Appendix H - Parent Satisfaction Questionnaire

<table>
<thead>
<tr>
<th>Questions</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The explanation provided by the nurse is easy to understand</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2. The explanation provided by the nurse is adequate</td>
<td></td>
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<tr>
<td>3. The nurses are knowledgeable and helpful in answering the enquiries about the intervention</td>
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<tr>
<td>4. The educational leaflet is easy to understand</td>
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<tr>
<td>5. The educational leaflet is informative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. The intervention is properly arranged</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7. The intervention is beneficial to the babies</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>8. The intervention is helpful to relieve your anxiety and distress level during immunization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. The data collection form is easy to use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Overall, you are satisfied with this intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any other comments or suggestions on this intervention?

_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________
# Appendix I - Staff Satisfaction Questionnaire

<table>
<thead>
<tr>
<th>Questions</th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The guidelines is easy to understand</td>
<td></td>
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<tr>
<td>2. The video used for training is useful</td>
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<tr>
<td>3. There is adequate training time before implementation</td>
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<td></td>
<td></td>
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<tr>
<td>4. The intervention is properly arranged</td>
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<tr>
<td>5. The intervention is beneficial to the babies</td>
<td></td>
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<td></td>
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<tr>
<td>6. The intervention is helpful to relieve the anxiety and distress of</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>parents during immunization</td>
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<tr>
<td>7. There are enough equipment for use</td>
<td></td>
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<tr>
<td>8. The workload is affordable</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>9. The data collection form is easy to use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Overall, you are satisfied with this intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any other comments or suggestions on this intervention?
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

References


trial of sucrose by mouth for the relief of infant crying after immunisation.

*Archives of Disease in Childhood*, 78, 453-456.


Systematic Reviews, 2 (2005).


