Assignment 2 : **Systematic/Integrative Approach to Reviewing Literature**

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Title: Sucrose

The ultimate goal of nursing is to deliver evidenced-based practice (EBP) that promotes high quality care that is safe and cost effective for all those involved (Burns, 2015). The aim of this systematic/integrated review is to assess the efficacy of oral sucrose solution as an intervention for reducing pain when given to infants and children prior to immunisations and will be conducted using a systematic approach.

Electronic databases and reference lists were searched using key terms. A total of 124 articles were retrieved, and this was reduced using inclusion and exclusion criteria to a total of 6 studies. These were assessed for methodological quality and rigour using the Joanna Briggs Institute (JBI) quality appraisal form. Three studies were accepted for the review.

The JBI data extraction was used to assist with date analysis and synthesis. The use of tables and charts will be provided to assist with data presentation and will also be discussed in narrative form. Finally, the results of the data extraction, analysis and synthesis will be discussed in relation to the wider context.

Although this review includes both infants and children for the purpose of this assignment they will be referred to as child unless there is a need for them to be separated.

Background

The development of vaccinations to prevent communicable diseases is considered one of the most significant achievements in medical history, increasing the average life span by 30 years (Schechter et al., 2007; Ulmer, Valley, & Rappuoli, 2006). Vaccinations date as far back as 1796, when Edward Jenner, first introduced a vaccine against small pox (Docherty, 1996). Today there are many vaccines available to reduce the burden of preventable diseases.

Increasing vaccine coverage continues to be an international concern for policy makers. The 'Global Vaccine Action Plan' 2011-2020, was developed by the World Health Organisation with the goal of providing vaccinations to all populations irrespective of where people live in an attempt to reduce morbidity and mortality (World Health Organization, 2013) Immunisation coverage is just as important at a local level with the NZ Government making immunisations a health target in July 2007, and one of the six National Health Targets in 2009. In 2016 the national target for 'Increased Immunisation' is set at 95% of infants to have completed their primary course of immunisations by the age of 8 months (Ministry of Health, 2011).

In 1960, the New Zealand (NZ) immunisation schedule commenced where infants received three publically funded doses of Tetanus, Diptheria and Pertussis in a single injection before the age of 6 months (Docherty, 1996). Today, children receive up to 9 injections by 4 years of age, with the potential of this being increased to 15, if the varicella and annual influenza vaccinations are given. Multiple injections can be given at each visit.

Immunising children is a common task in general practice and a clinical task that is generally carried out by the practice nurse and their role is pivotal in the national immunisation schedule being successful. Currently, the NZ immunisation schedule provides protection against 11 communicable diseases with the most recent introduction of the oral Rotavirus vaccine that was added in July 2014 and is given at 6 weeks, 3 months and 5 month concurrently with two injectable vaccines (Ministry of Health, 2014).

Jacobson et al. (2001) conducted a study to determine the magnitude of distress seen in children prior and during routine vaccinations. The results showed childhood vaccinations cause significant distress for children and was recorded as worse amongst the ages of 15-18 month and 4-6 year olds. Immunisations are the most frequent occurring

painful procedure in children and it is believed capable of creating a pain memory. potentially effecting how an individual engages in health care later in life (Schechter et al., 2007).

Systematic reviews have been completed assessing both pharmacological, non-pharmacological and combined interventions for reducing vaccine injection related pain (Harrison et al., 2015; Kassab, Foster, Foureur, & Fowler, 2012; Shah et al., 2015). Some of the interventions assessed are breastfeeding, topical anaesthetics, distraction, skin cooling techniques, oral analgesics, and the use of sweet solutions. The use of sweet solutions to reduce pain is not a new concept, with 'sugarball anaesthesia' being used as early as the 1940s in new born infants undergoing circumcision (Lewindon, Harkness, & Lewindon, 1998). Blass and colleagues (1989) published a study revealing that sweet solutions had a calming effect in infants in 1989, with further research occurring in 1991 claiming infants receiving 12% sucrose prior to a heel prick procedure cried 50% less than infants that received sterile water (Blass & Hoffmeyer, 1991).

The administration of sucrose is common practice in New Zealand Neonatal Intensive Care Units (NICU) as an intervention to reduce pain the neonate experiences (Heaton, Herd, & Fernando, 2007). It is NICU policy at the Southern District Health Board to give a 0.5ml dose of 66.7% strength sucrose, 1-2 minutes prior to any painful procedure including immunisations (Southern District Health Board, 2016). Although common practice in NICU's sucrose is not used in general practice.

Pain management is challenging and the Institute of Medicine states pain management in children is often absent (Thrane, Wanless, Cohen, & Danford, 2015). It is believed children may even experience pain to a greater extent than adults (Taddio, Ilersich, Ilersich, & Wells, 2014). Despite advancements in medical and nursing care, pain related to

immunisations continues to be underestimated and undertreated (Taddio et al., 2010).

Therefore the aim of this review is to assess available literature to determine if sucrose is effective in pain related to immunisations for infants beyond the neonatal period.

Aim/review question:

An important part of the review process is to ensure the review question is well formulated and focused as it underpins the steps of the process (Moule & Goodman, 2014). A foreground question addresses a specific question that can only be answered from reviewing current literature on a specific topic (Bettany-Saltikov, 2012) The primary aim of this review is to examine the international and national literature on the topic of using sucrose as pain relief for infants/children receiving vaccines.

The acronym PICO can be used when developing a review question when the purpose is to address interventions (Moule & Goodman, 2014). A PICO questions identifies four components – these being, population, intervention, comparison and outcome (Polit & Beck, 2017).

The review question is: Is the use of oral sucrose immediately prior to administering immunisations effective in reducing pain in infants and children beyond the neonatal period?

PICO			
Population	Intervention	Comparison	Outcomes
Infants/children receiving immunisation	Oral sucrose/glucose	water/placebo or no intervention	crying time and/or Reduce behavioural response to pain

Inclusion and exclusion criterial were developed from the PICO table. These should be predetermined prior to undertaking the search and set the boundaries of the review (Bettany-Saltikov, 2012; Moule & Goodman, 2014) . Inclusion and exclusion criteria ensures the search is focused and reduce the potential for relevant evidence being missed (Moule & Goodman, 2014).

Inclusion criteria:

- Healthy children born at full term undergoing scheduled immunisations
- Receive oral sucrose prior to immunisations either by a dropper or syringe
- Primary study
- Randomised Controlled Trial study design
- Outcomes used in the study crying time and/or behavioural indicators, may include standardised/validated pain scores
- Research written in English

Exclusion criteria:

- Preterm infants
- If feeding while receiving vaccinations
- Sucrose combined with non-nutritive sucking
- Studies involving other painful stimuli e.g. heel pricks

- Studies only measuring physiological indictors as outcome measures, for example, heart rate, respiratory rate

Search strategy for identification of studies:

The aim of a search is to generate a comprehensive and unbiased list of primary research that are relevant to the research question (Moule & Goodman, 2014). This was conducted using a systematic approach with the use of appropriate key terms which increase the success of identifying the most relevant material.

Key terms were identified from the PICO table already completed. International spelling was considered in the search and the Boolean operators 'AND and OR' were applied. Some databases allow for international spelling, for example PubMed, but each data base was searched using different spelling to ensure no relevant material was excluded in the search.

<u>Key terms used:</u>

immunisations OR immunizations OR vaccin*
child* OR infant
sucrose OR sugar OR glucose
pain OR discomfort
Oral

The search strategy was conduction using a two stage approach. First, the databases Cumulative Index to Nursing and Allied Health Literature (CINAHL), Ovid, Web of science, PubMed and the Cochrane Collaborative Database were searched using the key terms listed above. (see appendix A for search results) There were no date or language restrictions applied to the search strategy as the initial number of articles retrieved were manageable for this review.

A total of 123 articles were returned. Of these, 69 were duplicates and removed from the search list. The remaining titles were verified against the inclusion and exclusion criteria and were rejected if criteria specifications were not met. Hard copies of full text articles were obtained for further assessment. Search criteria were also applied to the full text reports and those that did not meet the criteria were excluded. Reasons for study exclusion at this stage were due to inappropriate interventions, for example sucrose combined with non-nutritive sucking, not in the age range; neonates, or secondary research documents.

The second stage of the search process involved citation searching in the reference lists of the retrieved articles. Only one article was obtained that met the inclusion criteria. See Appendix B, for summary of search strategy using the PRISMA 2009 flow diagram.

The six studies that passed the inclusion criteria were then tested for methodological quality.

Methodological Quality Appraisal

Prior to the analysis of any evidence collected methodological quality of each article must be assessed. This determines the degree that researchers have conducted the study and their attempt at minimising any bias and error (Gerrish & Lacey, 2010).
Randomised controlled trials (RCT's) were chosen as the most effective way of accessing the effectiveness of sucrose. RCT's are viewed as the strongest methodology and are considered the gold standard for providing evidence when an intervention is being measured, as elements of bias can be limited in the quantitative design (Burns, 2015).

There are a number of tools available to conduct a quality appraisal however, the JBI critical appraisal tool, for experimental studies was

used here. This tool has ten questions evaluating for potential bias with a maximum score of 10. A rating of less than 7/10 was set for exclusion in to the review as these studies may be potential flawed. All six studies assessed were graded above this rating and the three most rigorous and recent studies were chosen. (see appendix C) Generally two reviewers would undertake this process separately to avoid subjectivity, however for the purpose of this assignment methodological validity has been assessed by one reviewer (Polit & Beck, 2017).

The three studies included in the review are:

Despriee, Å. W., & Langeland, E. (2016). The effect of sucrose as pain relief/comfort during immunisation of 15-month-old children in health care centres: A randomised controlled trial. *Journal of Clinical Nursing, 25*(3-4), 372-380.
Yilmaz, G., Caylan, N., Oguz, M., & Karacan, C. D. (2014). Oral sucrose administration to reduce pain response during immunization in 16–19-month infants: A randomized, placebo-controlled trial. *European journal of pediatrics, 173*(11), 1527-1532.
Curry, D. M., Brown, C., & Wrona, S. (2012). Effectiveness of oral sucrose for pain management in infants during immunizations. *Pain Management Nursing, 13*(3), 139-149.

Data Extraction

Data extraction was completed using the JBI-MAStARI data extraction form for experimental studies, see Appendix D. This data has then been summarised in the table below.

Study	Participants	Procedures	Interventions	Outcomes	Metric	Results
Despriee, A & Langeland, E. 2016	114 15 month infants In Norway	1 injection	2ml 30% sucrose 2ml sterile water	Duration of crying – from time needle withdrawn	Duration of crying (DOC) reported in Mean and Standard Deviation (SD) Mann-Whitney U test – measure differences of DOC between groups Chi-square test - pacifier and gender Cohen's d – number needed to measure differences between groups	**Duration of Crying**: (*p ≤ 0.001)* between sucrose and sterile water
Yilmaz et al. 2014	537 16-19 month infants In Turkey	2-3 injections given simultaneously	2ml 75% sucrose (n=179) 2ml 25% sucrose (n=179) 2ml sterile water (n=179)	Crying time – from time needle inserted & CHEOPS	Crying time reported in Mean and SD CHEOPS reported as >4 = pain ANOVA Chi-squared	**Crying time:** 75% sucrose compared to 25% sucrose & sterile water (*p < 0.001)* 75% sucrose compared to 25% sucrose (*p < 0.001)*

						CHEOPS 75% sucrose vs 25% & control (*p < 0.001)* 75% sucrose compared to 25% sucrose (*p < 0.001)* 51% infants pain > than cut off score of 4
Curry et al. 2012	109 2, 4 & 6 month infants In United States	? number of injections	2ml 75% sucrose 2ml 50% sucrose 2ml sterile water	Crying time – from start of injection FLACC	Both crying time and FLACC scores reported in Mean, SD and p values.	Comparing all treatment groups (*p* = 0.24) Comparing age groups (*p* = 0.942) Comparing developmental groups (*p* = 0.35)

Data Analysis/Synthesis

Traditionally a meta-analysis of RCT's would be conducted using a statistical computer programme so that studies can be grouped to calculate an effect size providing information on relationships between variables and estimate the magnitude across the studies (Polit, 2014).

Due to the authors limitations a true analysis has not been conducted and the data analysis will be provided in narrative form with the use of tables and charts.

Sample

The three studies included 760 children attending clinics for routine immunisations, aged two to 19 months, investigating the effect of sucrose prior to vaccines. See Table 1 and 2 for distribution of sample sizes and ages. The majority of the children were 16-19 month age group, see (table 2). The studies were conducted in Norway, Turkey and United States.

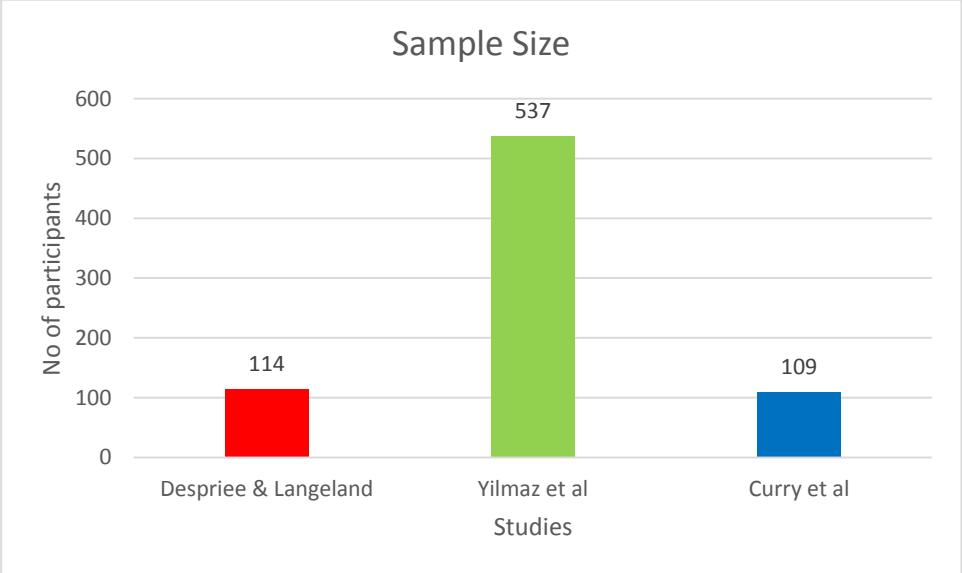

Table 1

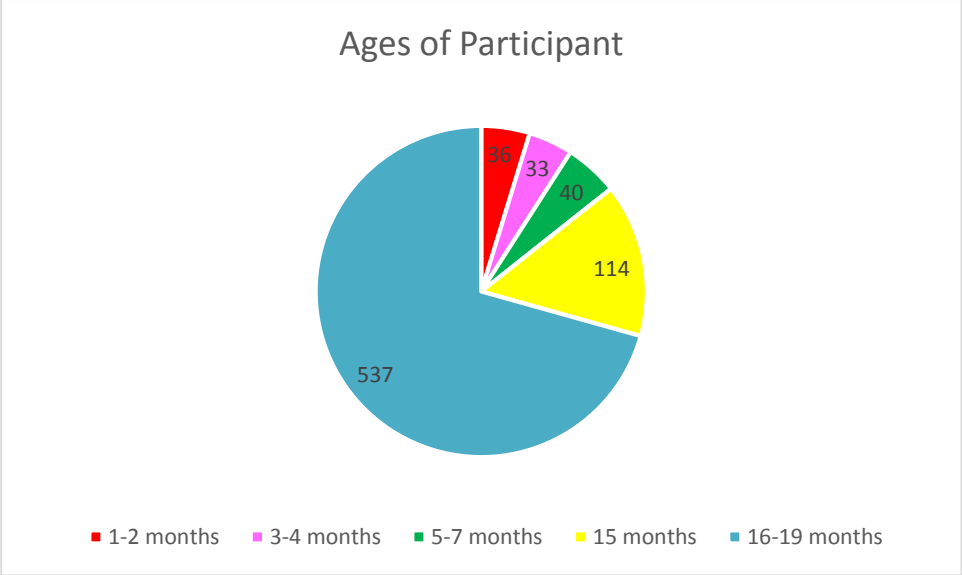

Table 2

Sucrose – concentration, volume and timing

All studies used sterile water as the control and sucrose concentrations ranged from 25% to 75%. Table 3 states the numbers in each intervention groups when studies were combined. Two studies Yilmaz et al (2014) and Curry et al (2012) used two different strengths, compared to the control while Despriee and Langeland (2016) used the one strength, being 30%. The volume of solution given was 2ml in all three studies, Yilmaz et al (2014) and Curry et al (2012) administered the solution 2 minutes prior to the procedure and Despriee and Langeland (2016) 1-2 minutes.

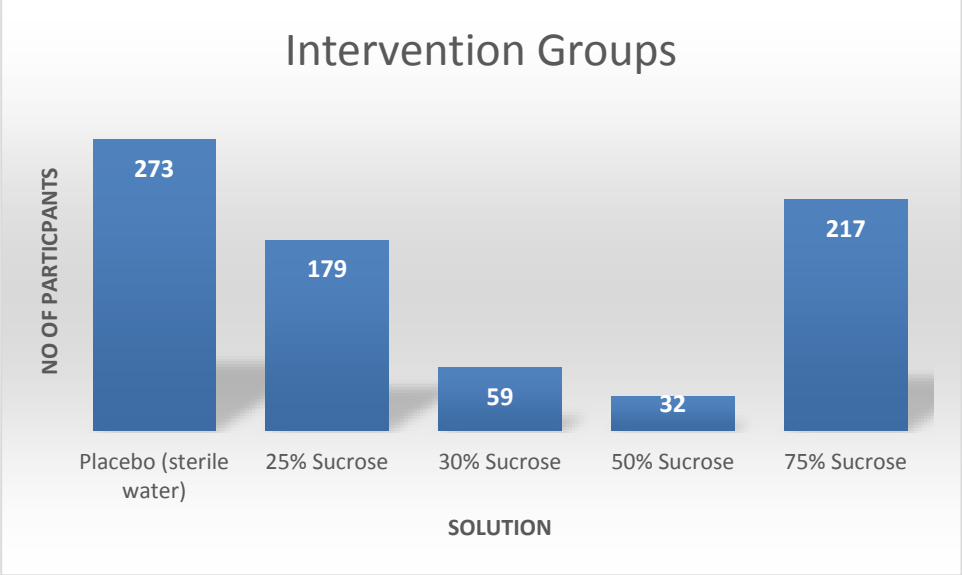

Table 3

Number of injections

In all three studies children received a different number of injections. In Despriee and Langelands (2016) study one injection was given, Yilmaz et al. (2014) two-three and in Curry et al. (2012) the number of injections administered is not stated.

Crying time and Behavioural scale

All three studies used crying time as the primary outcome measure, however all differed in the technique used to measure crying time. Despriee and Langelands (2016) used a stop watch, Yilmaz et al. (2014) used the second hand on a wrist watch and Curry et al. (2012) watched a video at a later date to record the time. Yilmaz et al. (2014) and Curry et al. (2012) recorded crying time from the time the needles was inserted compared to Despriee and Langelands (2016) who measured crying time from the time the needle was withdrawn.

While Despriee and Langeland (2016) only used crying time as the outcome measure, Yilmaz et al. (2014) and Curry et al. (2012) used both crying time and behavioural scales, being the Children' Hospital of Eastern Ontario Pain Scale (CHEOPS) Yilmaz et al. (2014) and the

Face, Legs, Activity, Cry, Consolability scale or FLACC scale Curry et al. (2012).

Results

Administration of sucrose prior to injections resulted in reduced crying time in two of the studies, Despriee and Langeland (2016) and Yilmaz et al. (2014) when compared to sterile water. Curry et al. (2012) study showed no significant difference in crying time in the three treatment groups, with lower mean crying times recorded in the treatment group receiving sterile water. The same study revealed no significant difference when crying times were compared across ages and developmental groups.

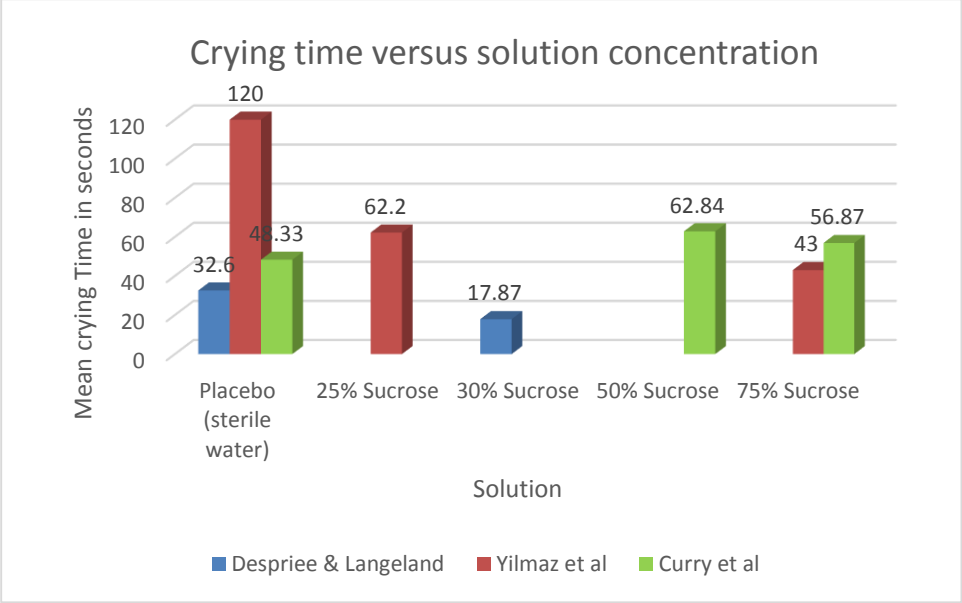

Table 4

It is evident from table 4, there is a 13.87 second mean difference between the two studies, in the 75% sucrose concentration group. Both Yilmaz et al. (2014) and Curry et al. (2012) started recording the crying time when the needle was inserted, however the measurement instruments used were different. Yilmaz et al. (2014) recorded the

procedure on video and then analysed crying time at a later date, the researcher was blinded to the child's intervention group. Six different research assistants in Curry et al. (2012) study were responsible for recording crying time using the second hand on a wrist watch. This may account for the difference as the potentially for bias to occur with this method would be much higher.

There is a wide range between the mean crying times in the sterile water group, 32.6 – 120 seconds. There are a number of possible explanations for this, the commencement of recording crying time and the number of injections the child received. The children in Yilmaz et al. (2014) study received 2-3 injections compared to Despriee and Langeland (2016) study who received one. The number of injections administered in Curry et al. (2012) study were not stated making it difficult to compare. Finally, the sample sizes in studies Despriee and Langeland (2016) & Curry et al. (2012) were considerable smaller than in Yilmaz et al. (2014).

Seventy five percent sucrose concentration was used in 2 of the studies and the other concentrations were unable to be pooled together due to no cross over into the other studies. With the data available, mean crying times were calculated and are provided in table 5. It appears the 30% sucrose concentration group had a considerably reduced crying time compared to the other groups, however children only received one injection and crying time recording commenced when the needle was removed making it difficult to compare to the other studies without a bias occurring and as such, a misinterpretation of the efficacy of the solution.

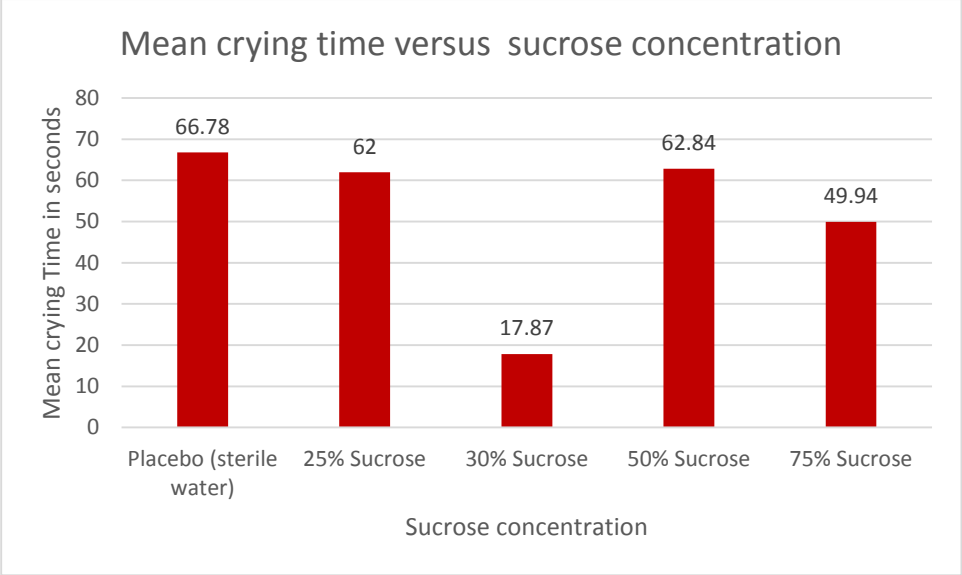

Table 5

The scales used to measure behavioural outcomes, the CHEOPS and FLACC tools are validated as accurate and sensitive pain measures that were originally developed to measure post-operative pain in children (McGrath, 1987; Voepel-Lewis, Shayevitz, & Malviya, 1997). Both scales are dependent of the observations and expertise of the recorder (McGrath, 1987). FLACC scores were recorded, 3 minutes before and 3 minutes after injections were given, results showed no significant difference between all 3 treatment groups, (p = 0.942), and no significant difference across developmental groups (p =0.697). CHEOPS scale recorded p values of $p<0.001$ when comparing across all three intervention groups and $p<0.001$ when 75% and 25% were compared. The CHEOP scores in table 6 show the effect sucrose has in reducing CHEOPS scores particularly, in children that had the 75% concentration, however it is not stated when the CHEOPS scores were recorded.

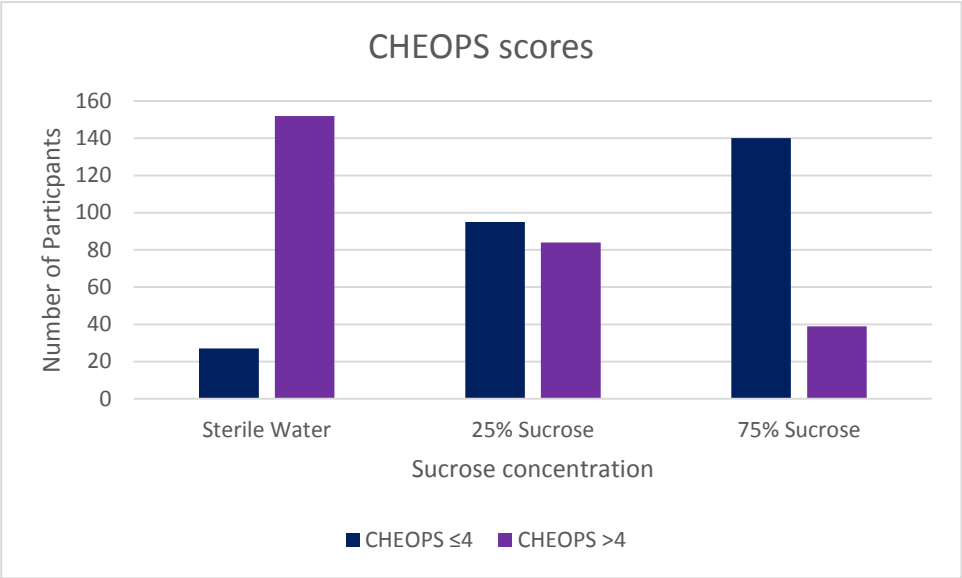

Table 6

Discussion

The findings of this review suggest that sucrose may have an effect on pain related to immunisations but due to there being a number of variances in methodology of the studies it is difficult to confidently initiate a change in current practice.

There is a large degree of heterogeneity between the studies making it difficult to accurately compare results. Firstly, the differing concentrations of the sucrose solutions across the studies. The recording of crying time commenced at different times, and the tools used to measure time differed in all three studies. One study used the second hand of a wrist watch which doesn't allow for any distractions or mistakes as there was only one opportunity to gather the data. There was a different number of injections given, with one study giving no indication how many injections were administered. Finally, the uneven distribution of age groups represented in the review. All these factors must be taken into consideration making it impossible not to interpret the results with some caution.

The findings of this review suggest sucrose is ineffective in infants aged 2 to 6 months. These results are inconsistent with the results of published systematic reviews. Kassab et al. (2012) systematic review results revealed a reduction of crying time in infants between one month to one year of age when administered a sweet tasting solution prior to a needle related procedure.

Each country has a specific immunisation schedule and the NZ immunisation schedule is considerably different from those countries included in the review. The introduction of the rotavirus contains 71.5% sucrose (Taddio et al., 2015) and potentially have an effect on injection related pain. Taddio et al (2015) recent study compared sucrose to the oral rotavirus vaccine in reducing crying time and assessing pain scales. Although their results did not show any significant effect, the sucrose solution used was 24% concentration which is considerably less than the sucrose concentration in the rotavirus solution and the results from this review would indicator the stronger solution of sucrose is more effective.

Pain related to immunisations is distressing for children, their caregivers and for those administering the vaccines (Taddio et al., 2010). The NZ immunisation Schedule has been part of NZs health care delivery system for over 55 years, however there appears to be no progress in reducing pain associated to injections. This is hard to comprehend despite the advances in the health care of children over this same time period.

Up until recently parents were encouraged to give children paracetamol prior to receiving their vaccinations however, this is now discouraged due to the interference with the immune response of some common childhood vaccines (Taddio et al., 2010). In the past children have received lolly pops post immunisations, this is now not considered to be socially acceptable due to the increasing concerns of childhood obesity and dental problems seen in NZ children (Kelly & Swinburn, 2015).

Recent recording of the national target for immunisation was verified at 93.7% for the 2015/16 period by the Ministry of Health (Ministry of Health, 2016). Practice nurses play a vital role in delivery of immunisations and all barriers that may prevent or delay parents bringing their children in for immunisations need to be considered to ensure this target is reached. As many as 10% avoid immunisations due to needle fears (Taddio et al., 2009) and there is evidence to suggest needle phobias develop in childhood (Hamilton, 1995).

A large part of the practice nursing role is health promotion and education. The concept of introducing what may be perceived as a 'sugary treat' prior to immunisations for pain can only become part of common practice if there is robust research to support this change. Despite the minimal volume and frequency of sucrose being used in practice it would have to be considered carefully to ensure caregivers bringing their children in for immunisations are not receiving confusing messages about sugar.

Limitations

There are several limitations of this review. Firstly, the restriction of only 3 studies being selected therefore the potential for study bias may exist. There are a number of differences in mode and methodology between the three studies making it difficult to collate data to provide strong evidence. In addition, the majority of the children in the reviewed studies were in the age group 15-19 months, making it difficult to confidently determine the effect of sucrose in the children outside this age range.

Further Research

The results from this review prevents the reviewer drawing a definitive conclusion of the efficacy of sucrose used in reducing pain associated with immunisations and further research is needed. There appears to be no current research carried out in New Zealand on this topic and it would be valuable to conduct a study including infants receiving vaccines from 6 weeks to four years. Although Taddio et al (2015), has already compared the effect of sucrose with the oral rotavirus vaccine, potential future studies could use a higher concentration solution of sucrose and definitive parameters for measured responses. Pain caused by immunisations continue to be distressing for all those involved and it is essential simple and effective ways of alleviating pain related to immunisations are explored.

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Appendix A

Search using key terms

CINHAL		
Search N#	Search items – key terms	Search results
1	Immunisation OR immunization OR vaccin*	37,803
2	Child* OR infant	414,833
3	Sucrose OR sugar OR glucose	38,320
4	Pain OR discomfort	141,014
5	Oral	59,967
6	1 AND 2 AND 3 AND 4 AND 5	21

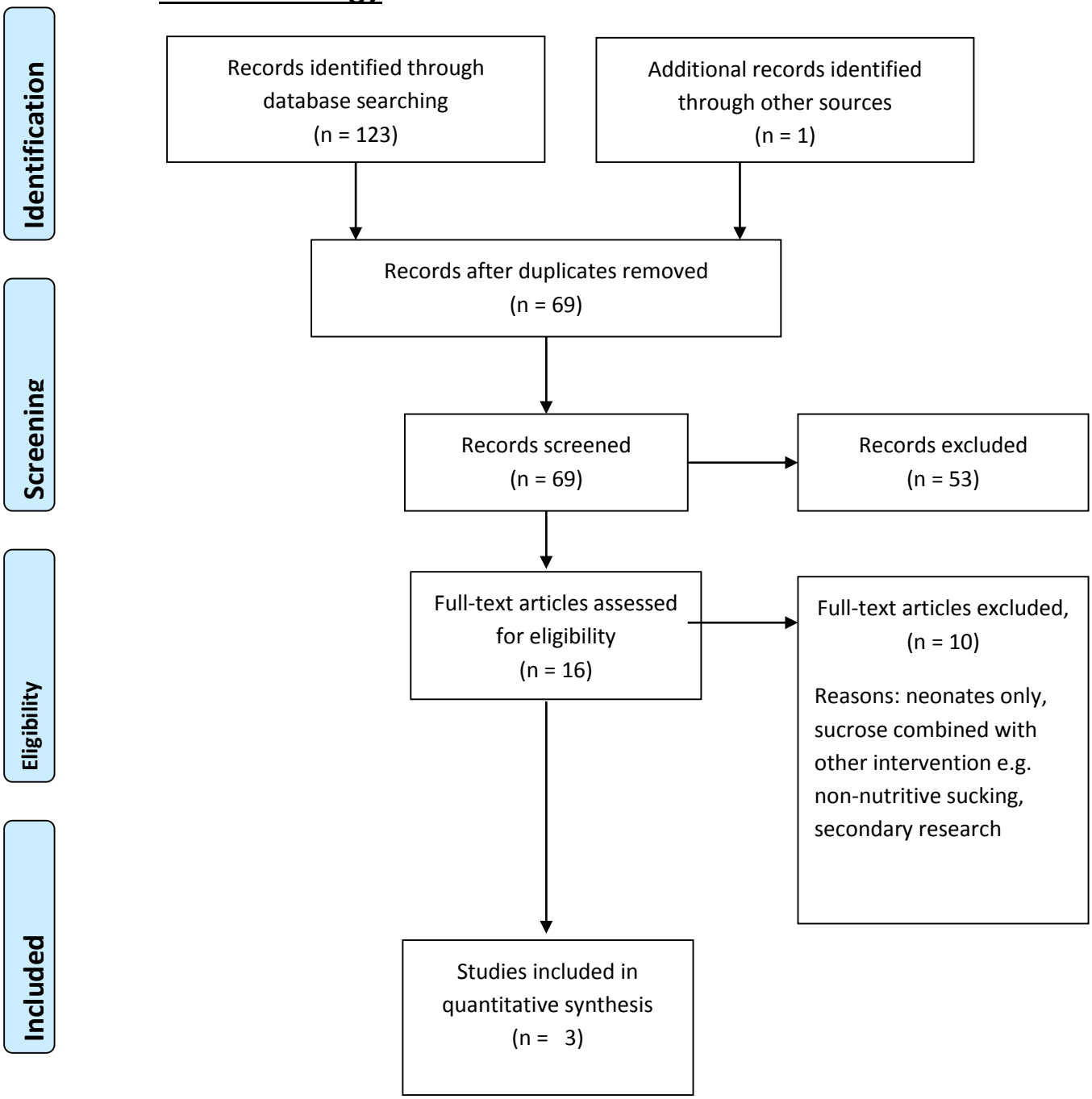
PUBMED		
Search N#	Search items – key terms	Search results
1	Immunisation OR immunization OR vaccin*	385,766
2	Child* OR infant	2,654,504
3	Sucrose OR sugar OR glucose	1,579,098
4	Pain OR discomfort	664,377
5	Oral	910,536
6	1 AND 2 AND 3 AND 4 AND 5	30

OVID		
Search N#	Search items – key terms	Search results
1	Immunisation OR immunization OR vaccin*	364,826
2	Child* OR infant	2,531,212
3	Sucrose OR sugar OR glucose	551,816
4	Pain OR discomfort	549,939
5	Oral	523,714
6	1 AND 2 AND 3 AND 4 AND 5	26

WEB OF SCIENCE		
Search N#	Search items – key terms	Search results
1	Immunisation OR immunization OR vaccine*	308,689
2	Child* OR infant	1,574,926
3	Sucrose OR sugar OR glucose	642,661
4	Pain OR discomfort	452,204
5	Oral	461,815
6	1 AND 2 AND 3 AND 4 AND 5 AND 6	46

Appendix B

Search Strategy



Appendix C

Quality Appraisal Table

Quantitative Assessment Form (Randomised Controlled Trial) – Joanna Briggs Institute

	Despriee & Langeland 2016	Lewindon et al 1998	Yilmaz at el 2014	Curry et al 2012	Thyr et al 2007	Ramenghi et al 2002
Q1	Yes	Yes	Yes	Yes	Yes	Yes
Q2	Yes	Yes	Yes	Yes	Yes	Yes
Q3	No	Yes	Yes	Yes	No	No
Q4	Yes	Unclear	Yes	No	Yes	Unclear
Q5	Yes	Yes	Yes	Yes	Unclear	Yes
Q6	Yes	Unclear	Yes	Yes	Unclear	Yes
Q7	Yes	Yes	Yes	Yes	Yes	Yes
Q8	Yes	Yes	Yes	Yes	Yes	Unclear
Q9	Yes	Yes	Yes	Yes	Yes	Yes
Q10	Yes	Yes	Yes	Yes	Yes	Yes
Total	9	8	10	9	7	7

Appendix D

Data Extraction Form

ARTICLE 1
Author: Despriee & Langeland
Journal: Journal of Clinical Nursing
Year: 2016

Study Method: RCT

Participants
Setting: 3 Norwegian health clinics
Population: infants receiving 15 month immunisation
Sample size: 114

Interventions Given 1-2 min before immunisation, not stated how administered
Intervention 1 2ml 30% sucrose (n=59)
Intervention 2 2ml sterile water (n=55)

Clinical outcome measures

Outcome Description	**Scale/Measure**
Duration of crying (DOC)	Stop watch Measured from when needle was removed until crying stopped Mean and Standard Deviation (SD) Mann-Whitney U Test – to measure differences of DOC between groups Chi-square test – measure impact on pacifier and gender Cohen's d test – number needed to measure needed to measure differences between groups

Study results

Outcome – Duration of crying	**Intervention**	**Intervention**
(*p ≤ 0.001)*	30% sucrose vs sterile water	

Authors Conclusion:

- Hypothesis rejected, therefore there is a significant difference in crying time between infants who have 15 month immunisations and receive sucrose and those that do not.
- Introduce into practice prior to giving immunisations

Reviewers Comments:

- Single blinded, parents blinded
- Small sample size – between medium and large effect
- Ethical approval ✓
- 7 public health nurses trained in management of sucrose and use of stop watch
- Not clear if nurse giving vaccine was also the one recording duration of crying
- Stop watch used for measuring duration of crying, potential for bias as dependent on reaction time of user
- Nurse or parent administered sucrose
- No statistical significance between pacifier use ($p = 0.976$) and gender ($p = 0.602$)
- One injection only

ARTICLE 2

Author: Yilmaz, Caylan, Oguz Karacan
Journal: European Journal of Pediatrics
Year: 2014

Study Method: RCT

Participants

Setting: Well child clinic in department of paediatrics in Turkey
Population: Healthy infants aged between 16-19 months receiving immunisations
Sample size: 537

Interventions Given 2 minutes before vaccination, administered via syringe
Intervention 1 2ml 75 sucrose (n=179)
Intervention 2 2ml 25% sucrose (n=179)
Intervention 3 2ml sterile water (n=179)

Clinical outcome measures

Outcome Description	**Scale/Measure**
Primary Outcome - Crying times	Mean, SD and *p* values ANOVA test to test for differences of means Chi-square used to compared rates between groups Primary researcher measured off video recording, not state what instrument used to measure outcome Measured from insertion of needle
Pain behaviour	Children's Hospital of Eastern Ontario Pain Scale (CHEOPS scale) 6 categories of pain behaviour – cry, facial expression, verbal, torso, touch, and legs. All forms filled out by same paediatrician. Above 4 indicates pain, highest score=13 Not clear when CHEOPS score was recorded

Study Results

Outcome – crying time	**Intervention**	**Intervention**
(*p < 0.001)*	75% sucrose compared to 25% & control groups	
(*p < 0.001)*	75% vs 25%	

Outcome – CHEOPS scores	**Intervention**	**Intervention**
(*p* < 0.001)	75% sucrose vs 25% & control	
(*p* < 0.001)	75% sucrose compared to 25% sucrose	
51% infants pain > than cut off score of 4		

Authors Conclusion:

- Limiting measures to crying time, using behavioural pain responses may have strengthened results
- Sucrose may be preferred than other pain measures when administering 16-19 month immunisations

Reviewers Comments:

- 694 recruited and randomised, 537 analysed, excluded as parent consent not gained and infant didn't meet inclusion criteria
- Ethical approval ✓
- Double blinded

- Large sample size
- Infant held over shoulder
- Pacifier (n=5) or pre paracetamol (n=8)
- Oral OPV given first ? have effect on results not directly related to sucrose
- 2-3 injections, 2 in each deltoid, at same time
- Crying time measured from when needle inserted

ARTICLE 3

Author: Curry, Brown & Wrona
Journal: Pain Management Nursing
Year: 2012

Study Method: RCT

Participants

Setting: 3 ambulatory paediatric clinics
Population: infants who presented for routine immunisations at 2, 4 or 6 months of age
Sample size: 109

Interventions 2 minutes prior to immunisation, administered via syringe
Intervention 1 2ml 75% sucrose (n=38)
Intervention 2 2ml 50% sucrose (n=32)
Intervention 3 2ml sterile water (n=39)

Clinical outcome measures

Outcome Description	**Scale/Measure**
Crying time	Mean, SD and *p* values Measured in seconds using second hand on wrist watch Measured from when needle was inserted by 6 research assistants
Measure pain based on behaviour	Mean, SD and *p* values FLACC scale – 5 categories of pain behaviour: facial expression, position of legs, activity of the child, presence/character or cry and consolability. Range is 0-10, No score given for when infant does experience pain. 3 minutes before and 3 minutes after administration of immunisations for comparisons

Study Results

Outcome – Crying time	**Intervention**	**Intervention**
Comparing treatment groups 56.87 sec (mean) 62.84 sec (mean)	 75% sucrose 50% sucrose	

48.33 sec (mean) (p = 0.24)	Sterile water	
Comparing ages groups (p = 0.942)		
Across developmental age (p = 0.35)	No difference across all treatment groups	
Outcome – FLACC score	**Intervention**	**Intervention**
(p = 0.942)	No difference across all treatment groups	
Across developmental age (p= 0.697)	No difference across all treatment groups	

Authors Conclusion:

- No significant difference crying time or FLACC if sucrose used pre vaccination
- Difficult to measure leg activity if legs swaddled by parents
- Second FLACC score recorded 3minutes post injections, ?too long as 2 minute peak time for sucrose
- Further research required with more rigor, larger sample size, single data collector and use video tape
- ?Consoling measures (rocking, patting back, holding against parents chest) have effective in reducing crying times and FLACC post vaccination (p=0.029)

Reviewers Comments:

- Small sample size – between medium and large effect
- Ethical approval ✓
- Double blinded
- 6 research assistants
- Infant sitting on parent lap

- Infants temperament asked, ?related to parents coping skills, 7 crying before injections done
- Pacifier (n=18) or pre paracetamol (n=18)
- Data collected by multiple research assistants in multiple clinic
- Stop watch used for measuring duration of crying, potential for bias as dependent on reaction time of user
- Number of injections not stated