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Systematic Review of Pertussis Immunisation Among Asians

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SYSTEMATIC REVIEW OF PERTUSSIS IMMUNISATION AMONG ASIANS

1. Introduction

This paper presents the results of a systematic review conducted in 2011 on pertussis and immunisation among Asians. There has been little research into immunisations and pertussis among Asians in New Zealand which requires an assessment of attitudes of Asians towards childhood immunisations and pertussis epidemiology in a global setting.

2. Aim

The aim of this article was to systematically review literature relating to childhood immunisation and pertussis among the Asian population. It was hypothesised that there would generally be positive attitudes to immunisations among Asians.

3. Methods

A systematic review of all available literature was conducted on pertussis and immunisation among the Asian population. The search was done in accordance to guidelines developed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).¹

3.1 Criteria for Study Selection

In order to limit the search results, focus was placed on studies done at a national population level, strategies to improve immunisation coverage and efficacy of vaccines, rather than purely bio-medical papers. Exclusion criteria included limiting the search to full-text availability, human participants and English language. The studies needed to involve some aspect of immunisation for pertussis in an Asian sub-population. No time constraint was placed on the search. Articles that were opinion pieces, religious and philosophical commentaries were excluded from the review. The PRISMA guidelines were followed as closely as possible in order to keep biases to a minimum.

3.2 Search Strategy

The key words used for the review were immun*, vaccine* AND whooping cough or Bordetella pertussis OR B pertussis AND Asia*. The electronic search was conducted in four databases: Medline, CINAHL, Embase and Cochrane Database of Systematic Reviews in June 2011. Articles were imported to the referencing software programme Endnote X4. The programme detected

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2 duplicate records which were then deleted. Further papers were sourced through hand searching the
3 reference lists of articles.
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6 All the results obtained from the search were screened for relevance by title. The abstracts of those
7 records which passed the initial screening were reviewed using the study criteria to determine
8 whether full-text articles were required for further evaluation. Full text screening was then conducted
9 on the remaining articles which passed the secondary screening using an eligibility checklist (Table
10 0.1: Checklist for full text screening).
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14 **Table 0.1: Checklist for full text screening**
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16 **4. Results of the Systematic Review**

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18 Results of the systematic search are presented in this section and cover areas regarding
19 epidemiology of pertussis, vaccine effectiveness studies which took place in Asian regions, and
20 strategies that can be employed in order to increase immunisation coverage for DTaP in Asia.
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23 *4.1 Study Selection*

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25 The results of the search are shown in Figure 0.1. There were 206 articles retrieved in the initial
26 search. Abstracts of 206 articles were screened of which 50 full-text articles were reviewed. From the
27 50 articles, 14 studies met the inclusion criteria for the systematic review.
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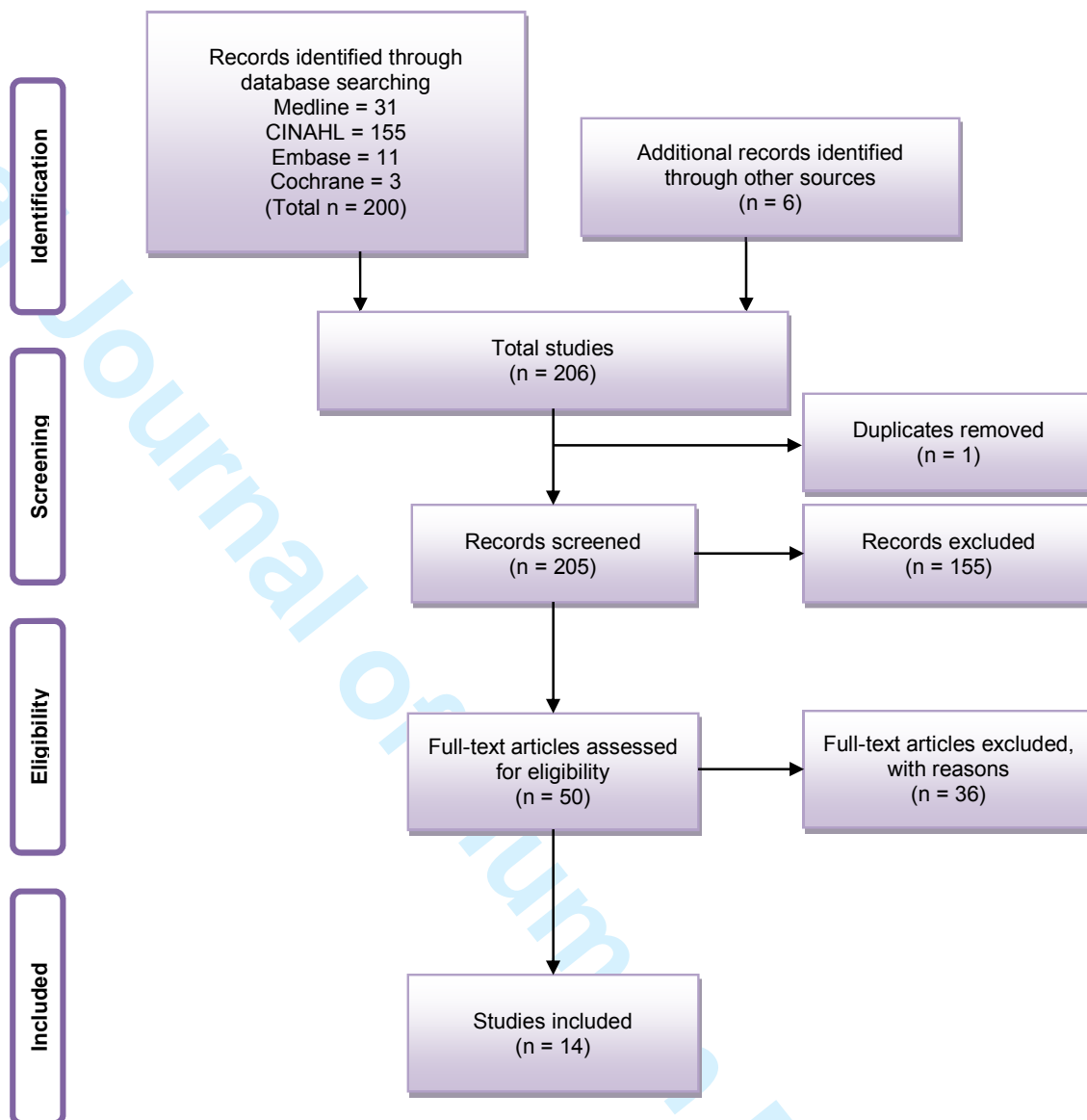


Figure 0.1: Flow chart following PRISMA guidelines for article selection.

These 14 remaining articles were then critically appraised on the basis of reliability, validity and generalisability (Table 0.2: Measure for quality rating of selected articles). The checklist was constructed specifically for the review in accordance with PRISMA guidelines and referred to throughout both screening processes. (Liberati et al., 2009, Moher et al., 2009) This was done in order to ensure biases were kept to a minimum and a sound and reproducible method could be developed. A quality rating overall score of high, moderate or low was given to the studies once the reliability, validity and generalisability had been assessed.

Table 0.2: Measure for quality rating of selected articles

Reasons for excluding 36 articles after full text screening were recorded and are presented in table 5.3. The studies remaining in the review were placed in a summary table recording study type, participants involved, year of publication and quality score.

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2 **Table 0.3: Reason for exclusion of articles after full text screening**

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4 **Table 0.4: Types of studies included in systematic review**

5 An evidence table (Table 5.5) was produced according to study type, participants involved, year of
6 publication and quality score. All articles which passed the full text eligibility were included as part of
7 the review (N = 14).
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Table 0.5: Table of studies included in review



4.2 Analysis of the Studies

The 13 studies covered issues relating to:

1. The epidemiology of pertussis.(Singh and Lingappan, 2006, Bokhari et al., 2011, Nishi et al., 1990, Wilder-Smith et al., 2007)
2. Vaccine effectiveness studies which took place in Asian regions.(Shek et al., 2003, Okada et al., 2009, Nakano, 2011)
3. Strategies that can be employed in order to increase immunisation coverage for DTaP in Asia.(Singh and Lingappan, 2006, Healy et al., 2011, Poovorawan, 1997, Usman et al., 2011, Robinson et al., 2001, Andersson et al., 2009, Pandey et al., 2007, Chandir et al., 2010)

4.2.1 Epidemiology of Pertussis among Asians

There has been a noticeable shift in the burden of pertussis from infants to adolescent and adults.(Singh and Lingappan, 2006) This shift may be due to waning immunity from childhood immunisation as well as better diagnostic tools, making it easier to detect the disease. These age groups then become the source of infection and a considerable threat to susceptible infants. Of major concern is the fact that symptoms of pertussis are easily misdiagnosed or remain undiagnosed in adults and adolescents. A 2006 report reviewed pertussis in the South-East Asian region and impact of the changing epidemiology of pertussis on this particular region.(Singh and Lingappan, 2006) The number of pertussis cases declined dramatically between 1980 and 1990 in South East Asia. Correspondingly, it was during this decade that the immunisation coverage rate increased from 7 to 70%.(Singh and Lingappan, 2006) It was observed that in 2004, the South East Asian region reported a decline in the number of pertussis cases despite a low immunisation coverage rate and a surge in rates of the disease globally.(Singh and Lingappan, 2006) However, it remains unclear whether this reduction was due to an actual decline in disease burden or undiagnosed cases due to the shift in epidemiology to older age groups, as data for this geographical region is patchy.(Singh and Lingappan, 2006) The report highlighted the need for a proper surveillance system in the South East Asian region in order to accurately track and understand the true burden of pertussis and its epidemiology.

Problems with reporting true burden of disease was also highlighted in a Pakistani study comparing the two strains, *Bordatella pertussis* and *Bordatella parapertussis*, which cause whooping cough.(Bokhari et al., 2011) Although the aim of the study was to find out the incidence of infections caused by the strain, it also highlighted the lack of an adequate surveillance system in monitoring pertussis in Pakistan. This could be due to misdiagnosis of whooping cough among older age groups.(Bokhari et al., 2011) It is essential for health professionals to have the necessary knowledge to be able to pick up suspected whooping cough cases and get them tested. Furthermore, results showed that infection through *Bordatella parapertussis* was more common than *Bordatella pertussis* which was an unexpected finding.(Bokhari et al., 2011) However, a major limitation of the study was the fact that the *Bordatella pertussis* cultures were more likely to perish due to the time taken to

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3 travel to the laboratories. This is another reason that can cause true disease rates to be severely
4 underestimated.(Bokhari et al., 2011)
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7 A Japanese study carried out in 1990 aimed to understand immunisation practices among a
8 representative sample of mothers of school children.(Nishi et al., 1990) At the time of the study, the
9 DTP vaccine was administered three times starting at the age of three months, followed by a booster
10 injection before school entry. The study was questionnaire based and required participants to report
11 their children's immunisation records from the official maternal and child health handbook. The results
12 of the study showed that final immunisation coverage rates for DTP were high. Over 90% of children
13 were immunised and this was comparable to BCG and polio vaccines. However, timeliness was
14 extremely poor, with only half the proportion of children being immunised at 24 months for DTP than
15 other vaccines.(Nishi et al., 1990) The median age for receipt of the first DTP vaccine was found to be
16 22 months based on the participants' responses. This finding is of major concern as pertussis is a
17 disease that is most severe in infants. Therefore, infants should be immunised against the disease as
18 soon as possible and primary series of vaccination should be completed before 12 months of
19 age.(Nishi et al., 1990) This study was useful in highlighting immunisation practices among the
20 Japanese population and shows that this particular sample was extremely delayed in immunising their
21 children against pertussis. Disease outbreaks may still occur in such settings, as there would be a
22 large proportion of infants who are left unimmunised for a long period of time. On the other hand, it is
23 important to note that this study was carried out in the early 1990s and practices may now have
24 changed and timeliness may also have improved.
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33 A questionnaire based study was conducted in Singapore travellers' health and vaccination centre to
34 investigate attitudes and knowledge of 184 adult travellers regarding pertussis and adult booster
35 doses.(Wilder-Smith et al., 2007) Eighty per cent of participants were of Singaporean ethnicity. Upon
36 analysis of the responses, it was found that Western travellers were seven times more likely to be
37 aware of pertussis booster injections than Asian travellers. This was a statistically significant
38 finding.(Wilder-Smith et al., 2007) Furthermore, Western travellers were also significantly more likely
39 than Asian travellers to know whether or not their child had received immunisation against
40 pertussis.(Wilder-Smith et al., 2007) Participants in the study had a carefree attitude towards
41 pertussis in comparison to diphtheria and tetanus. This attitude was reflected in practice as only 3% of
42 participants had received a combined booster for diphtheria, tetanus and pertussis whereas 33% had
43 received a booster immunisation for tetanus.(Wilder-Smith et al., 2007) The survey demonstrated a
44 lack of awareness concerning adult pertussis boosters. Knowledge among the participating travellers
45 was poor, and lack of knowledge was independent of educational level as well as professional
46 background.(Wilder-Smith et al., 2007) The study highlighted the dangers of lack of awareness on
47 pertussis booster doses among Asians, as international travel among this group is sharply
48 increasing.(Wilder-Smith et al., 2007) It is therefore important to raise awareness regarding pertussis
49 and immunisations against the disease within this population and to stop its spread to other
50 populations.
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4.2.2 Vaccine Use

Use of whole cell pertussis vaccines declined after concerns were raised regarding adverse reactions and some serious but rare neurological damage.(Shek et al., 2003) This led to formulation of acellular pertussis vaccines which use only highly purified parts of the pertussis bacterium. A single-blinded randomised controlled trial was carried out to compare reactogenicity of acellular and whole cell pertussis among Singaporean infants.(Shek et al., 2003) At the time of the study, whole cell pertussis vaccines were in routine use in Singapore. A total of 177 infants received either the acellular or whole cell pertussis vaccines which were administered at three, four and five months of age. Parents were then required to keep a record of local reactions following the immunisation. Local (pain, redness and swelling) and general (irritability, vomiting, fever, restlessness, change in sleeping patterns) reactions of children who received whole cell vaccines were significantly higher than those who received acellular vaccines. This Singaporean study confirmed studies done in non-Asian regions that the acellular pertussis vaccine is less reactogenic.(Shek et al., 2003)

Effectiveness of the acellular pertussis vaccine was tested in a matched case-control study in Japan.(Okada et al., 2009) This study was carried out over a non-epidemic period in contrast to other similar studies which are generally conducted during epidemics. The study involved administration of a questionnaire to parents of children who received a definitive diagnosis for pertussis (cases). Participating paediatricians provided diagnosis for pertussis. For each case, two or more controls were selected from the population for participation in the study. Results of the study showed that of the 15 cases that were reported to have pertussis, 12 had never been vaccinated. On the other hand, for the 59 controls, 20 had never been vaccinated against whooping cough. Cases were divided by duration of cough and number of vaccines administered for statistical analysis to determine vaccine effectiveness. It was found that the DTaP vaccine was 96% effective in preventing pertussis in children who had received three or four doses of the vaccine.(Okada et al., 2009) The study demonstrated the effectiveness of the DTaP vaccine in a non-epidemic period and the importance of completing primary series of immunisation in order to maximise protection received from the vaccine.(Okada et al., 2009)

Japanese vaccinations and practices were explored in a study with particular focus on polio and pertussis vaccines in 2010.(Nakano, 2011) The acellular pertussis vaccine is recommended for adult booster injections due to reduced likelihood of adverse events. However, DTaP is not in routine use in Japan as a result of the high cost associated with the vaccine. Therefore, the study investigated safety of an adjusted dose of DTP as a booster injection for adults. The adjusted booster dose was administered to 164 consenting adults and the participants were required to keep observation record for any reactions following the immunisation.(Nakano, 2011) Blood samples were also collected from participants before and after immunisation in order to test immunogenicity. Participants reported only mild, local reactions to the vaccination such as pain, redness and swelling.(Nakano, 2011) Two participants also reported mild fevers subsequent to the immunisation. All reported reactions were deemed to be minor by the researcher. Furthermore, evaluation of pertussis antibody titre from the blood samples showed that the vaccine was effective in increasing levels of immunity. In addition,

immunity was easier to enhance if the subject had received DTP vaccinations as a child.(Nakano, 2011) This suggests that completion of basic childhood immunisations can make booster injections more effective for adults.(Nakano, 2011) This study recommended use of booster injections on adults, adolescents and travellers. It also suggested ways in which resource prohibitive countries, which have difficulties implementing DTaP vaccines for adult boosters, can overcome this issue.

4.2.3 Strategies for Improving Immunisation Coverage and Reducing Pertussis Morbidity

As discussed previously, there has been a shift in pertussis epidemiology to adolescents and adults. Taking this into consideration, it is recommended that adults and adolescents are administered booster immunisations in order to maintain immunity against pertussis and prevent its spread to infants.(Singh and Lingappan, 2006) Due to adverse reactions associated with the whole cell pertussis vaccine, which are presented more potently when administered to adults, booster injections contain acellular pertussis toxoid.(Singh and Lingappan, 2006) However, acellular pertussis vaccine is more costly than the whole cell pertussis vaccine. It is this issue of cost which makes implementation of adult booster immunisation programmes rather challenging in developing nations such as those in South East Asian region.

A commonly discussed strategy regarding pertussis is cocooning.(Healy et al., 2011) Cocooning involves immunisation of adults and older children who are likely to be in close contact with new born children in order to prevent potential transmission of pertussis to young children (see 3.6). The cocooning strategy was implemented in a study carried out in USA.(Healy et al., 2011) The study was carried out in two phases. In the first phase DTaP immunisation was administered to postpartum women and in the second phase immunisation was offered to household contacts. The study was able to completely cocoon 26% of babies participating in the study. An interesting finding of the study was the fact that Asian women were least likely to decline DTaP immunisations compared to postpartum women of other ethnicities.(Healy et al., 2011) Only 9% of Asian women declined immunisation, showing that immunisation may be a priority and such strategies may easily be implemented in Asian countries if resources are available.

Combination vaccines are an effective way of administering multiple vaccines to children in one injection. This helps in improving immunisation uptake by being more time and cost efficient as well as being better accepted by parents due to fewer number of injections.(Poovorawan, 1997) A randomised controlled trial was conducted in Thailand to test the effectiveness of combining the Hepatitis B vaccine (HBV) with the diphtheria, tetanus and pertussis vaccine (DTP).(Poovorawan, 1997) The study also aimed for this to be a strategy in increasing DTP uptake. At the time the study was done, the two vaccines were administered separately. The study administered a combined vaccine to the first group, a combined vaccine with a different formulation to the second group and only DTP was administered to the third (control) group. Results from blood tests showed that the combined vaccines were just as effective as vaccines being administered separately. Furthermore, reactogenicity of both the combined and monovalent vaccines were similar. This indicated that it would be advantageous to use a combined vaccine in order to improve immunisation coverage rates.

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3 The strategy to use a combined vaccine of DTP, Hib and Hep B was also suggested in a review
4 carried out by Gentile et al., which highlighted the effectiveness and benefits of using combined
5 vaccines.(Gentile et al., 2010)
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8 One of the ways of improving immunisation coverage is through employment of health systems based
9 interventions.(Usman et al., 2011) A randomised controlled trial conducted in Pakistan used this
10 intervention to observe changes in DTP completion.(Usman et al., 2011) Mother-child pairs were
11 randomised into four groups. The first group was the control group, the second group received a
12 substantially re-designed immunisation card, the third group received centre-based education from
13 nurses, and the final group received a combination of centre-based education as well as a re-
14 designed immunisation card. The percentages of children who received all three doses of DTP were
15 39%, 66%, 61% and 67% for the control, re-designed immunisation card, centre based education and
16 combined intervention groups respectively.(Usman et al., 2011) Participants exposed to the
17 interventions had significantly higher rates of DTP completion than the control group. Simple
18 interventions such as these may be a viable option in countries in the Asian region as this study has
19 demonstrated that improvement in immunisation coverage is achievable through such measures.
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26 A crucial factor in obtaining and maintaining high immunisation coverage rates is health provider
27 knowledge, which is another form of health system intervention.(Robinson et al., 2001) An Indonesian
28 study investigated the impact of training nurses on immunisation coverage.(Robinson et al., 2001)
29 Experienced nurses were sent to 13 health practices to provide on the job training to less experienced
30 nurses on vaccination techniques, vaccine storage, cold chain maintenance and so forth. The training
31 was demonstrated to be successful in improving immunisation coverage rates. Comparison of
32 baseline coverage rates and rates after implementation of the training programme showed that DTP
33 coverage for the first dose had increased by 34% after training.(Robinson et al., 2001) Rates for other
34 vaccines such as polio and measles had also improved. The findings were statistically significant,
35 demonstrating that employing such training interventions can lead to improvements in immunisation
36 coverage. Such a programme may be useful in the Asian region as this is low cost and highly
37 effective.(Robinson et al., 2001)
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44 Another approach to increasing awareness is to educate patients on immunisation.(Andersson et al.,
45 2009) A randomised controlled trial conducted in one of the poorest districts in Pakistan demonstrated
46 that community-based education can have a positive impact on immunisation uptake. Thirty-two
47 enumeration areas in the province were divided into control (14 areas) and intervention (18 areas)
48 groups, in which the intervention was carried out in three phases. Trained facilitators were sent to
49 intervention areas and engaged in discussions with the communities. It was explained to the
50 communities that it is more costly to treat a vaccine preventable illness than to get a child immunised.
51 One of the measured outcomes was full DTP coverage before two years of age. Analysis showed
52 significant findings, that is, the intervention group were three times more likely to complete DTP
53 immunisation than the control cohort.(Andersson et al., 2009) The study successfully showed
54 evidence based discussions within community groups can help increase immunisation uptake without
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any reliance on health service improvements. This is another inexpensive yet effective strategy which can be utilised in developing nations to improve immunisation coverage.(Andersson et al., 2009)

A similar intervention was tested in a randomised controlled trial in India.(Pandey et al., 2007) A total of 105 village clusters were divided into intervention and control groups. This study was designed to create awareness among communities regarding services such as education and immunisation. Information campaigns were conducted in the intervention groups and participants received detailed information through meetings, posters and leaflets.(Pandey et al., 2007) A year later, it was observed that utilisation of health services was significantly higher in intervention groups than control groups.(Pandey et al., 2007) The study found that providing communities with a structured, informative programme helps improve utilisation of health and social services. However, the intervention required a rather long follow up and a large amount of time to be spent at the meeting by a facilitator.(Pandey et al., 2007) Although this intervention proved to be successful for the duration of the study, the feasibility to maintain such a rigorous programme may be doubtful in developing countries such as India.

Using incentives to improve immunisation coverage rates was tested in a study conducted in Pakistan.(Chandir et al., 2010) Families of the 2212 children in the incentive cohort received food coupons for getting their children immunised with three doses of DTP before the age of six months. By placing an age limit, the study was also able to test for timeliness of immunisations as well as coverage. As a result, coverage rate reported through this study was lower than those reported nationally, which uses 12 months as its milestone.(Chandir et al., 2010) The control group which had 847 children did not receive any incentive for immunisations.(Chandir et al., 2010) The study found that participants enrolled in the incentive cohort had a significantly higher rate of completion for three doses of DTP than participants in the control cohort. Participants receiving an incentive were two times more likely to complete all three doses of DTP.(Chandir et al., 2010) The study was able to demonstrate that the introduction of incentives may be successful in improving immunisation coverage rates. However, the sustainability of such programmes is vague in Asian countries where resources are limited.(Chandir et al., 2010) The researchers pointed out that such incentives may be helpful in the short term, but may not be sufficient on their own to improve general immunisation coverage and timeliness rates.(Chandir et al., 2010)

5. Discussion

This systematic review highlights the importance of immunising against pertussis, and the associated difficulties in doing so in the Asian region. A review carried out in 2010 highlighted geographical differences in regard to the burden of multiple childhood diseases.(Gentile et al., 2010) South East Asia was one of the geographical regions on which the review focussed. One of the issues raised through the review was the difficulty in estimating true disease burden as well as immunisation coverage rates in developing countries (most countries in the Asian region) due to lack of proper surveillance systems.(Gentile et al., 2010) This was issue was also mentioned by some studies

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3 included in this review.(Singh and Lingappan, 2006, Bokhari et al., 2011) From some studies, it is also
4 observed that definition for timeliness of DTP immunisation is poor.(Nishi et al., 1990, Nakano, 2011,
5 Chandir et al., 2010) Immunisations were accepted as being timely and completed provided they were
6 administered before 24 or 12 months of age. This is of concern as pertussis is a disease which is
7 often most serious in young children, which means the vaccine should be administered and the
8 primary series should be completed as soon as possible.
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12 In terms of vaccine use, most countries in the Asian region seem to utilise whole cell pertussis
13 vaccines rather than acellular.(Singh and Lingappan, 2006, Shek et al., 2003, Poovorawan, 1997)
14 Using whole cell vaccines makes it harder to formulate booster doses for older children and adults,
15 meaning that this proportion of the population is vulnerable to pertussis infections and can pass it on
16 to younger, unimmunised infants. A major factor contributing to preference for whole cell vaccines in
17 this region may be the higher cost associated with acellular pertussis vaccine.(Gentile et al., 2010)
18 Since resources are limited in developing countries, that are most countries in the Asian region,
19 investment in acellular vaccines may not be practicable. On the other hand some of these studies are
20 more than five years old and the switch to acellular vaccines may have been made, but there are no
21 new studies suggesting this.
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27 Taking into account the low immunisation coverage rates in Asia, multiple studies(Usman et al., 2011,
28 Robinson et al., 2001, Andersson et al., 2009, Pandey et al., 2007, Chandir et al., 2010) have tested
29 interventions which may help improve these rates and reduce burden of disease. Most of the
30 interventions discussed in the study seemed to have helped in increasing immunisation uptake.
31 However, it is unclear whether or not these interventions have a long term effect on immunisation
32 rates or if the results are temporary. In addition, some results have been modest, which suggests
33 there may be a need to incorporate multiple strategies, such as educating patients as well as training
34 nurses for immunisation. A multi-faceted approach may prove more effective which was also
35 suggested in another review which focussed on interventions for improving immunisation
36 coverage.(Oyolta et al., 2011)
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42 The major issue with initiating and maintaining a surveillance system, switching to the less
43 reactogenic, acellular pertussis vaccine, and introducing interventions to improve immunisation
44 coverage is lack of resources. Developing countries are often resource deficient, which makes the
45 feasibility of maintaining immunisation programmes a complex task. It has been reported that uptake
46 of the third dose of DTP vaccine in the South-Asian region is poor, and the estimated overall
47 coverage is less than 75%.(Gentile et al., 2010) Poor immunisation coverage is directly correlated to
48 high disease morbidity, and South-East Asia was found to have the greatest number of pertussis
49 cases.
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55 **6. Limitations**

56 Despite following the scoring criteria regarding for generalisability, reliability and validity, some articles
57 were difficult to evaluate accurately. The precondition of including only full text articles and articles
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published in the English language in the review are further limitations. Furthermore, the screening and inclusion of articles was decided on by a single investigator. Although PRISMA guidelines were followed to minimise the risk of selection bias, these limitations were present in the review.

7. Future Research

There were a number of gaps found through this systematic review which can be addressed by future research. Firstly, there were no research studies found through the search which related to pertussis and immunisation among immigrant Asians. Most studies were conducted in an Asian country and focussed on a single Asian ethnicity. This creates complex issues in regard to the usage of the term Asian in a setting such as NZ, where all the Asian sub-groups are classified under one category. An issue which faces one Asian sub-group may not be homogenous to other sub-groups. There is also a lack of studies in NZ on this topic. It was interesting to see some studies report a lack of awareness among Asian people regarding immunisation, yet rates of immunisation coverage are highest among this ethnicity in NZ.(Ministry of Health, 2012) This shows a need to investigate this in NZ to understand the health behaviours of this group. Finally, there is a lack of qualitative studies on this particular topic, and more research needs to be done to further understand this area of research.

8. Conclusion

This chapter summarised all available and relevant studies conducted thus far on the topic of pertussis and DTaP/DTP vaccines among Asian populations. The review helped in highlighting gaps in the literature and the scope and relevance of the topic.

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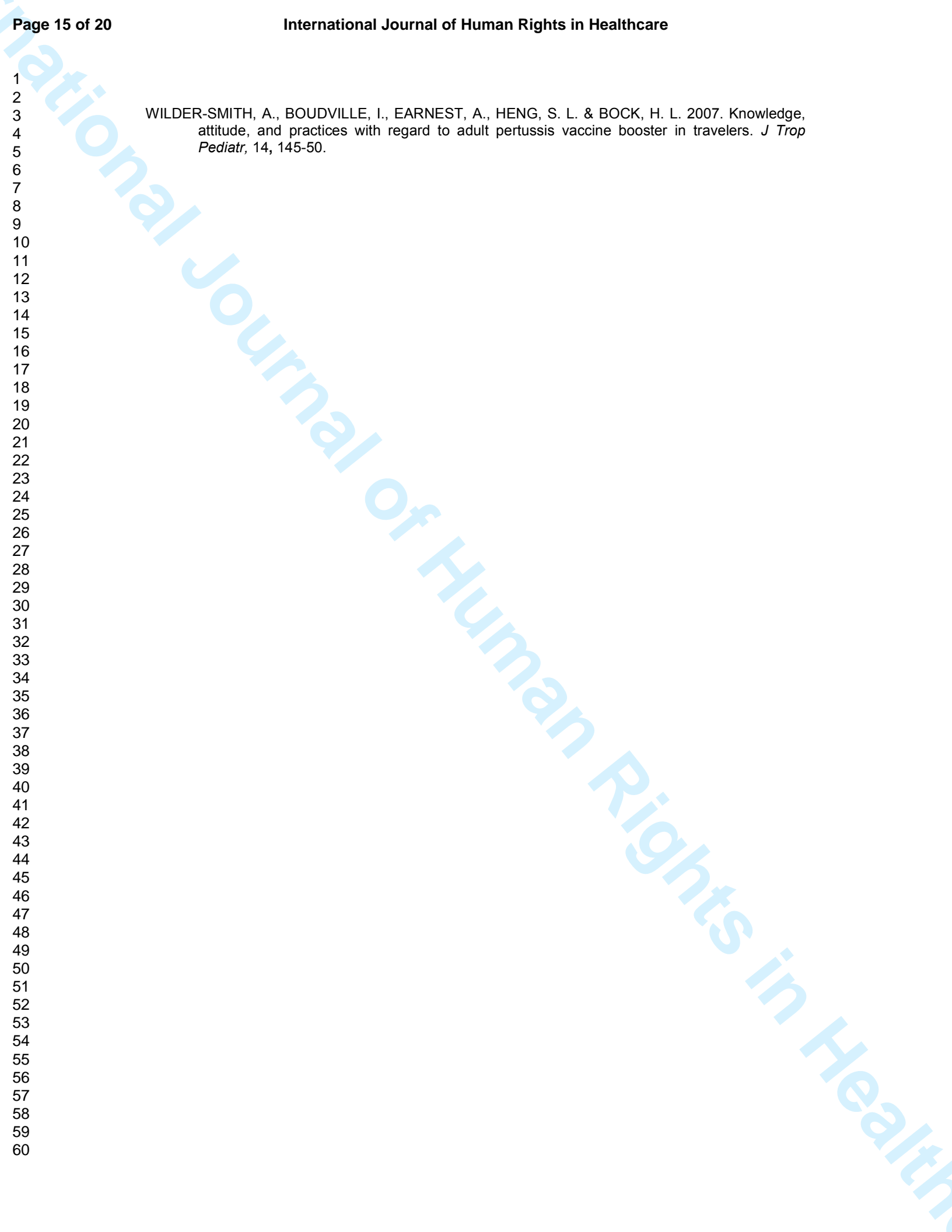


Table Error! No text of specified style in document..1: Checklist for full text screening

Checklist
Pertussis and immunisation among Asians as main topics
Epidemiology of pertussis and pertussis control
Human participants
Non-biomedical
Non-religious
Non-philosophical
Full text

Table Error! No text of specified style in document..2: Measure for quality rating of selected articles

Scoring criteria	Definition
Reliability	Whether an instrument/s is able to yield consistent results when repeated under the same conditions across different situations ³
Validity	The ability of an instrument/s to measure what it was designed to measure ³
Generalisability	The ability to generalise the results of a specific study to other subjects, groups, or conditions ⁴

Table Error! No text of specified style in document..3: Reason for exclusion of articles after full text screening

Reason for exclusion	Number of records
Irrelevant	5
Not meeting criteria	28
Opinion piece/commentary/religious/philosophical	3
Unavailable	-

Table Error! No text of specified style in document..4: Types of studies included in systematic review

Type	Number
Journal Articles	13
Reports	1
Whole Books	-
Theses	-

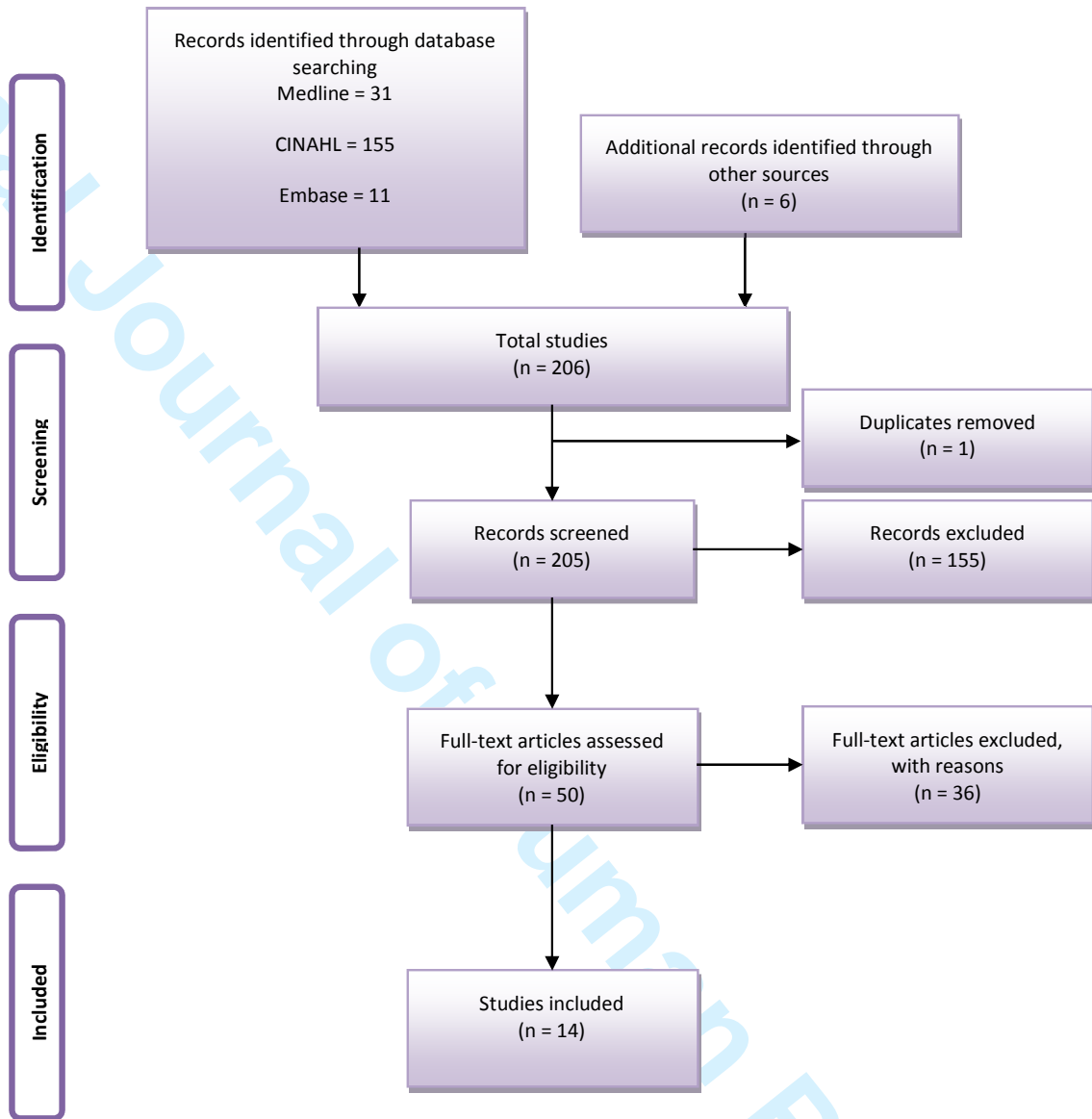
Table Error! No text of specified style in document..5: Table of studies included in review

Studies	Year	Participants (n)	Setting	Methods	Measure	Outcome	Category	Reliability	Validity	Generalisability	Quality (H=high, M=moderate, L= low)
Andersson et al ⁵	2009	5641 children	2005, Lasbela, Pakistan	Randomised cluster controlled trial	Uptake of measles and full DTP immunisation	Higher immunisation uptake in intervention group	Vaccine Use	Moderate	Moderate	High	M
Bokhari et al ⁶	2011	802 children	2005-2009, Pakistan	Observational study for infection with pertussis by using nasopharyngeal swabs and cough plate method	Methods to identify pertussis strain from suspected whooping cough cases	B. paraperussis was the more common strain found among the samples	Epidemiology	Moderate	High	Moderate	M
Chandir ⁷	2010	3059 children	2006-2007, Pakistan	Cohort study	Difference in timely DTP uptake between control and intervention groups	A two-fold increase in timely DTP uptake was observed in the intervention group	Vaccine Use	Moderate	Moderate	High	M
Healy et al ⁸	2010	Phase 1- 8334 postpartum women Phase 2 – 2969 postpartum women & 1860 household contacts	2008-2010, Houston	2 Phase intervention study to encourage cocooning	Tdap uptake by mothers in a high risk area.	75% of women in phase 1 and 86% in phase 2 accepted the immunisation showing the strategy was successful.	Strategy	High	High	High	H
Nakano ⁹	2010	164 adults	Japan	Intervention study.	Cases of AEFI following immunisation with Tdap	No serious AEFIs were reported and the vaccine was deemed safe for adults.	Vaccine Use	Moderate	Moderate	Moderate	M
Nishi et al ¹⁰	1990	Mothers of 1680 school children.	1989, Sapporo City, Japan	Questionnaire based study	Rates and timeliness of immunisation from health cards	Timeliness was extremely poor for DTP immunisation.	Epidemiology	Moderate	Moderate	Moderate	M
Okada et al ¹¹	2009	Parents of 74 infants.	1999-2001, Japan	Matched case control study.	Vaccine effectiveness of DTaP	The effectiveness was 96% for children who received 3-4 immunisations	Vaccine Use	Low	Low	Low	L
Pandey et al ¹²	2007	105 village clusters	2004-2005, India	Cluster randomised controlled trial	Levels of entitled health and social services	Intervention group reported high levels of service usage than control.	Strategy	Moderate	Moderate	Moderate	M

Studies	Year	Participants (n)	Setting	Methods	Measure	Outcome	Category	Reliability	Validity	Generalisability	Quality (H=high, M=moderate, L= low)
Poovorawan ¹³	1997	160 infants	1991, Thailand	Randomised controlled trial and follow up study.	Levels of induced immunity of DTP-HB vaccine and separately administered vaccine	Levels of immunity were similar for the vaccines so the combined vaccine was recommended	Epidemiology	High	High	Moderate	H
Robinson et al ¹⁴	2001	13 health centres	1993-1994, Maluku, Indonesia	Intervention study of educating nurses on immunisation	Immunisation performance of nurses	Immunisation increased by 39% in intervention centres.	Strategy	High	High	Moderate	H
Shek et al ¹⁵	2003	180 infants aged 12-16 weeks	Singapore	Single blinded randomised controlled trial	Reactogenicity of DTaP and DTwP	Whole cell vaccines were more reactogenic	Vaccine Use	High	High	High	H
Usman et al ¹⁶	2011	1506 mother-child pairs	2003-2004, Pakistan	Randomised controlled trial	Rate of third DTP immunisation	Immunisation rate of third DTP increased significantly in the intervention groups	Strategy	High	High	High	H
Wilder-Smith ¹⁷	2007	184 Adult travellers	2006, Singapore	Questionnaire survey	Awareness level of pertussis	Knowledge of pertussis adult boosters as extremely poor among travellers.	Strategy	Moderate	Moderate	High	M

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