

Practices to improve coverage of the *hepatitis B* birth dose vaccine

Immunization, Vaccines and Biologicals



World Health
Organization

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Abbreviations and acronyms

AAP	American Academy of Pediatrics
BCG	bacille Calmette-Guérin (vaccine)
CASP	Critical Appraisal Skills Programme
CI	95% confidence interval
CDC	US Centers for Disease Control and Prevention
CHIP	country health information programmes
CTC	controlled temperature chain
EPI	Expanded Programme on Immunization
GAVI	Global Alliance for Vaccines and Immunization
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBV	Hepatitis B virus
HBsAg	Hepatitis B surface antigen
HIS	health information systems
IEC	Information, Education and Communication
IMPAC	Integrated Management of Pregnancy and Childbirth
IPAC	Immunization Practices Advisory Committee
LMIC	low- and middle-income country
LSHTM	London School of Hygiene and Tropical Medicine
MCH	maternal and child health
MNH	maternal and neonatal health
MOH	Ministry of Health
MPS	Making Pregnancy Safer (WHO)
OCC	out-of-the-cold-chain (older terminology used by some studies)
OPV	oral polio vaccine
OR	odds ratio
PATH	Program for Appropriate Technology in Health

RCT	randomized control trial
TBA	traditional birth attendant
UNICEF	United Nations Children’s Fund
USA	United States of America
USPHS	United States Public Health Services
VHV	village health volunteer
VIDRL	Victorian Infectious Diseases Reference Laboratory
VVM	vaccine vial monitor
WHO	World Health Organization

Preface

This paper has been prepared for the World Health Organization (WHO), Immunization, Vaccines and Biologicals, Expanded Programme on Immunization (EPI) by Priya Mannava and Chris Morgan of the Burnet Institute. It is based on a background document prepared by Carville, Morgan, Cowie and Stewart for a Technical Consultation on hepatitis B birth dose held in Melbourne, Australia in December 2010, and includes re-examination of the evidence in the form of a scoping review conducted in March 2012. This document has been endorsed by the members of the Immunization Practices Advisory Committee of the WHO EPI.

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Executive summary

This scoping review summarizes and appraises the evidence from published and grey literature on improving coverage of the hepatitis B birth dose vaccine. The review looks at implementation evidence in relation to two main questions:

- What practices improve coverage of the hepatitis B birth dose?
- What are important facilitators and barriers to improving coverage of the birth dose?

The purpose of the review is to contribute to an evidence base on which to develop programmatic guidance for delivery of the birth dose, both in settings where this is being introduced for the first time, and in those requiring strengthening of services for birth dose vaccination.

A systematic search of published and grey literature, covering publications up until March 2012, was undertaken. This was supplemented, where necessary, by expert opinion and commentary, including the proceedings of a technical consultation convened in December 2010. Sixty-five studies were found that met the inclusion criteria. They covered 13 settings, with the broadest range of evidence coming from China, Indonesia, the United States of America (USA) and Viet Nam. No studies from Africa met the inclusion criteria.

Evidence exists to suggest that the following practices can be effective in improving coverage of timely birth dose vaccination. This list includes practices useful in all settings, as well as options to consider for special situations.

1) Service delivery arrangements

- Increasing access to skilled care at the time of childbirth.
- Integration of birth dose with maternal and newborn care in health facilities by:
 - a local health facility policy specifying birth dose vaccination;
 - standing orders for administration of birth dose in the delivery room or postnatal ward;
 - ensuring vaccine is available in the delivery room or postnatal ward;
 - clear delineation of who is responsible to vaccinate that includes maternal health-care providers;
 - appropriately positioning birth dose vaccination within essential newborn care in a way that does not interrupt urgent interventions;
 - coordinated planning between immunization and maternal health staff in health facilities and in districts, including supportive health-facility assessments.

-
- Linkages between immunization and private services providing childbirth care.
 - Where infants are born outside health facilities, considering options such as:
 - home visits to provide timely vaccination;
 - integration of birth dose with home visits for other postnatal care;
 - vaccine storage outside the standard cold chain in a controlled temperature chain;
 - careful pregnancy tracking.
- 2) Health workforce considerations
- Addressing health-care providers' lack of knowledge and particular attitudes and perceptions towards newborn vaccination.
 - Well-structured health-worker training, including education on perinatal transmission;
 - backed up by frequent follow-up and supportive supervision;
 - considering options for task-shifting to reach populations difficult to access.
- 3) Medical technologies relevant to birth dose
- Distribution and storage arrangements that utilize the potential for keeping vaccine outside the standard cold chain, and positioning it as close to the birth place as possible.
 - The potential use of Uniject by community-based health-care providers.
 - Ensuring supply of monovalent hepatitis B vaccine in single-dose or multi-dose presentations.
- 4) Health information system practices
- Birth registries and community birth notification, including tracking home births.
 - Incorporation of birth dose and its timing within vaccination records.
 - Accurate definition of timely birth dose in coverage reporting.
 - Consider options for the use of sero-surveys for establishment of need and for monitoring.
- 5) Financing arrangements influencing birth dose coverage
- Adequate funding for birth dose programmes, with consideration of transport efficiencies for distribution to the periphery.
 - Minimizing costs to families.
- 6) Addressing community concerns or lack of knowledge regarding birth dose
- Responding to low awareness of the birth dose vaccine and its importance.
 - Considering traditional practices of sequestering newborns.
 - Addressing fear of adverse events, including planning for the risk of coincidental newborn death or disease.
 - Responding to parental refusal of vaccination.

7) Leadership and governance practices include:

- consideration of a central policy that mandates universal newborn vaccination;
- clear national guidance defining timely birth dose as within 24 hours of birth;
- removing unnecessarily stringent restrictions contraindicating vaccination;
- considering options for vaccine use managed outside the standard cold chain in a controlled temperature chain (CTC), and accrediting new vaccinators;
- strong central communications to support public confidence in vaccines.

For certain important practices, guidance can rely on more general evidence for effective implementation of immunization programmes. These areas include:

- preparatory communication strategies that plan for likely public concerns;
- alignment with maternal, newborn and immunization care guidelines;
- costing of strategies to scale-up birth dose within and beyond health facilities.

Lastly, in countries without a universal birth dose, adding a birth dose is likely to require steps very similar to those for the introduction of a new vaccine, even if hepatitis B vaccination for older infants is already in place. For these settings, general resources from WHO and partners on the introduction of new vaccines will be useful to supplement guidance, specific to the birth dose, derived from the evidence base above.

1. Introduction

The World Health Organization (WHO) recommends that “all infants should receive their first dose of hepatitis B vaccine as soon as possible after birth, preferably within 24 hours” (1), even in countries where *Hepatitis B virus* (HBV) is of low endemicity. This scoping review compiles the evidence for practices that improve coverage of the hepatitis B ‘birth dose’¹, as well as barriers to, or facilitators of, improved coverage. The aim is to provide an evidence base for guidance documents, for regional and national managers working in immunization and maternal and newborn health-care programmes.

1.1 Birth dose vaccination is important to the control of HBV infection

As a leading cause of liver cancer and liver disease, HBV infection is an important threat to global health. Globally, over two billion people are estimated to be living with the virus, while around 360 million are chronically infected and at risk of developing life-threatening liver diseases. Many infections are acquired early in life; perinatally, or horizontally during early childhood, particularly in regions of high endemicity where these routes are the most common modes of HBV transmission (1). This has important implications for disease prevention and control as the likelihood of developing chronic infection is higher at younger ages: 90% if infected at birth; 25%–50% if infected between the ages of one to five years, and 5%–10% if infected over the age of five years (2,3).

Vaccination against HBV has proved to be an important tool in preventing transmission of the virus. Typically given in a series of three doses, the vaccine provides protection from infection in more than 95% of healthy infants, children and young adults. In infants born to infected mothers, vaccination reduces the likelihood of developing HBV infection by 3.5 times (1). The vaccine’s efficacy in preventing perinatal transmission however, decreases as the time period between birth and the first dose increases (3). The risk of HBV infection among infants born to hepatitis B surface antigen (HBsAg) positive mothers was found to be eight times higher when the birth dose was administered after seven days from birth, compared to when it was administered within the first three days after birth. In areas where chronic infection is endemic, it is especially critical that the first dose of the hepatitis B vaccine is administered with minimal delay after birth. In low endemicity countries as well, the birth dose remains important, to prevent early transmission (1). Resolution 63.18 of the World Health Assembly, which focused on viral hepatitis, urged the WHO to further support Member States in accelerating and strengthening prevention and control of viral hepatitis (4). In line with this mandate and the importance of the timing of hepatitis B vaccination, in 2009, WHO recommended that all infants worldwide receive a birth dose as soon as possible after birth, preferably within 24 hours (5).

1.2 The hepatitis B birth dose vaccination has unusual programmatic needs

The hepatitis B birth dose is different to other vaccinations administered under the Expanded Programme on Immunization (EPI) in that delivery of the vaccine is not schedulable. This places special demands on health systems to respond within 24 hours of childbirth, with different implications for where the vaccination should be provided, who should provide it and how it should be recorded. Attitudes and practices of families and providers at the time of childbirth are also often different to those relating to older infants. In many low- and middle-income countries (LMICs), health-system weaknesses limit access to skilled health-care providers at the time of childbirth, or in the early postnatal period (6) with many babies born outside health facilities (7). In early 2011, global coverage of the birth dose was still estimated to be very low, at 26% (8). Understanding how to increase delivery of birth dose in such settings is crucial; however there has been no review of the evidence for strategies pursued to increase and improve provision of timely (within 24 hours of birth) birth dose¹ of the hepatitis B vaccine, particularly made relevant to LMICs.

1.3 Objectives of this review

The review summarizes and appraises the evidence from published and grey literature on improving coverage of the hepatitis B birth dose. Specifically, the review looks at the evidence in relation to two main questions:

- what **practices** improve coverage of the hepatitis B birth dose? (the primary review question);
- what are important **facilitators** and **barriers** to improving coverage of the birth dose?

The purpose of this review is to provide an evidence base on which to develop programmatic guidance for delivery of the birth dose, both in settings where this is being introduced for the first time, and those requiring strengthening of services for birth dose vaccination. Users of such guidance are likely to be working in regional and national immunization and maternal and child health (MCH) programmes. The review elicits models on how to improve coverage of the birth dose from all settings, but seeks to make them especially applicable to LMICs. It also addresses the managerial issues around birth dose implementation, but does not address the health policy questions of whether or not a birth dose should be introduced — for this see the WHO hepatitis B Position Paper (1).

¹ From here on, timely birth dose refers to administration within 24 hours.

2. Methods

A review of published and grey literature was undertaken, covering publications up until March 2012. This was supplemented, where necessary, by expert opinion and commentary, including proceedings of a technical consultation convened in December 2010. Expert opinion, for this review, was defined as that expressed during the December 2010 Technical Consultation (Annex 2), or opinions published by the World Health Organization in the Weekly Epidemiological Record, their technical consultations, or the Western Pacific Regional Office's Operational Guidelines (3).

2.1 Search strategy

Five electronic databases were searched for relevant literature (published in English only), including dates up until March 2012. Inclusion criteria for this review were broad, recognizing that research related to implementation often lacks formal experimental studies. However, only literature that related practices, facilitators and/or barriers to an outcome of birth dose *coverage* or birth dose *uptake* was included. Publications were excluded that studied only selective testing and vaccination, plus those that only measured coverage, immunogenicity or vaccine efficacy, without providing analysis on underlying determinants of coverage. While the focus of this review is on birth dose delivered within 24 hours, literature that examined issues related to administration of the birth dose up to one week after birth was accepted. Papers that studied multiple vaccines were also accepted, provided that one of the vaccines was the hepatitis B birth dose.

A total of 3676 peer-review published titles were identified, yielding 2899 exclusive titles after removal of duplicates. Screening of titles resulted in 470 eligible abstracts, of which 334 were excluded. Two additional relevant articles were identified, from scanning of reference lists, giving 138 full-text articles for review. Twenty-six grey literature papers were also reviewed. Six older full-text articles were not accessible, so in total 158 full-text papers were assessed. A final number of 48 published articles and 17 grey literature papers were judged as meeting the inclusion criteria and were included in the review. Annex 1 provides additional detail on the search strategy, a figure describing the screening process, inclusion and exclusion criteria, and a table of excluded papers with reasons for exclusion.

2.2 Classification of practices, facilitators and barriers and data extraction

Practices, facilitators and barriers to improving coverage of the hepatitis B birth dose were classified into six groups, following a WHO framework for health systems: service delivery; health workforce; medical products, vaccines and technologies; health information systems; financing, and leadership and governance. Within these groups, there was further classification into sub-groups. Table 1 below provides an overview and description of the classification. Additional description of the data-extraction framework is provided in Annex 1.

Data from each of the 65 papers included in this review, were analysed and abstracted into a standard tool, developed by the authors and based around these health-system categories. These categories are also used to systematically summarize the findings, as shown in Annex 4.

Table 1: Classification of practices, facilitators and barriers studied in this review

Group classification	Description of the group*	Sub-group classification
Service delivery	"Management and organization of inputs and services to ensure access to safe and quality" hepatitis B birth dose vaccination "across different locations and over time" (9)	<ul style="list-style-type: none"> • Access to a trained health worker • Linkages between immunization and maternity and newborn care services • Integration with, and private health services • Linkages between immunization and community postnatal care services • Demand for vaccination: community characteristics; customs; knowledge; attitudes, and health-seeking behaviours • Quality improvement activities, local policies and guidelines
Health workforce	Actions taken to manage the health workforce involved in hepatitis B birth dose programmes, including "addressing entry into and exit from the workforce and improving the distribution and performance of the existent workforce" (9)	<ul style="list-style-type: none"> • Knowledge, attitudes and training • Delineation of responsibilities • Guidelines and protocols • Task-shifting • Payment and incentives
Medical products, vaccines and technologies	Actions to ensure equitable access to hepatitis B birth dose vaccines of "assured quality, safety, efficacy and cost-effectiveness" (9)	<ul style="list-style-type: none"> • Procurement, supply and distribution systems • Vaccine storage and access to the cold chain • Vaccine delivery technologies • Vaccine presentation
Health information systems (HIS)	The "production, analysis, dissemination and use of reliable and timely information" related to hepatitis B birth dose vaccination (9)	<ul style="list-style-type: none"> • Monitoring performance, equity and scale-up • Mother and child registries • Vaccination records • Estimation of coverage • Birth notification • Linkages with other health databases
Financing	Actions to "raise sufficient funds to ensure access to the hepatitis B birth dose vaccine, and that people do not incur financial catastrophe or impoverishment from payment" for the vaccine (9)	<ul style="list-style-type: none"> • Cost-effectiveness of vaccination strategies • Funding for birth dose programmes • Cost to recipient for vaccination
Leadership and governance	The government's role in guiding, overseeing and regulating hepatitis B birth dose programmes (9)	<ul style="list-style-type: none"> • Central policies and guidelines • Central communications and information • Political commitment

* Descriptions of the groups are based on the WHO building blocks framework for health systems.

2.3 Appraisal of the evidence

Each of the papers included in the review were independently appraised by both reviewers. The quality of evidence from randomized control trials (RCTs), observational and qualitative studies was assessed using quality-assessment tools developed by the Critical Appraisal Skills Programme (CASP)², and that from intervention studies assessed using a tool developed by the Centre for Evidence-Based Social Services.³ Grey literature was assessed based on criteria outlined in the box below (Box 1).

Following appraisal of each study, Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria (described elsewhere: (10)) were used to provide a final scoring on the body of evidence available for each type of practice.

Box 1: Appraisal criteria used to assess grey literature

- Type of resource
- Authors/institutions of standing in their field of expertise
- Clarity with which the methodology for the assessment is described
- Plausibility
- Potential for conflict of interest
- Description of study funding
- Involvement of the study sponsors in any aspect of the study
- Number of data sources used and use of data triangulation

Given that the primary focus of this review was on practices to improve birth dose coverage, evidence on barriers and facilitators was not formally assessed but was taken into account in formulating recommendations. In cases where evidence came from more than one type of study, only the highest level of evidence available was assessed in GRADE tables. Based on GRADE criteria, the order of levels of evidence from highest to lowest was RCTs and systematic reviews, followed by intervention studies, observational studies and, lastly, any other type of evidence (for example reviews). Grey literature was not assessed in GRADE tables.

Annex 3 provides an overview of the GRADE criteria and scoring methods used to appraise the evidence.

² Critical Appraisal Skills Programme (www.casp-uk.net).

³ Tool available at <http://libguides.mdx.ac.uk/content.php?pid=136038&sid=2095422>.

3. Overview of included studies

Annex 4 provides a listing of the characteristics and content of included studies.

3.1 Settings and focus of included studies

The broadest range of evidence comes from studies in China, Indonesia and the United States of America (USA). The table below summarizes the settings encompassed by this evidence base. No studies from Africa met the inclusion criteria. Although there is a large, long-running intervention trial for HBV control in the Gambia (11), no studies were found presenting experiences relating to strategies for increasing birth dose coverage.

Table 2: Settings of included studies

Setting	Number of publications included
United States of America	21
China	11
Indonesia	8
Viet Nam	4
Australia	3
Philippines (the)	2
Papua New Guinea	2
Columbia	1
Micronesia (Federated States of)	1
Micronesia (Federated States of) and Marshall Islands (the)	1
India	1
Israel	1
Thailand	1
Tonga	1
Western Pacific Region	6
Worldwide	1

Most papers provided evidence on practices, facilitators or barriers in the area of **service delivery** (n = 35) and **governance and leadership** (n = 22). Close to one third of the papers looked at issues related to **medical products, vaccines and technologies** (n = 19) and **human resources for health** (n = 19). The least examined components were **health information systems** (n = 14) and **financing** for the hepatitis B birth dose (n = 10). The majority of studies examined more than one type of practice/facilitator/barrier.

3.2 Varying definitions of birth dose

The definition of birth dose varied within the literature included in this review, although the majority of papers (n = 21) used the WHO definition, of vaccination administered within 24 hours of birth. A considerable number of papers did not specify the timing, and used a definition of “at birth” (n = 17). Other definitions used were: within 12 hours of birth (n = 2, set in the USA); before discharge from health facility (n = 9); within 48 hours of birth (n = 2); within 72 hours of birth (n = 4); within 7 days of birth (n = 8, studies set in Indonesia), and on the day of delivery (n = 2).

3.3 List of included studies

The table below lists the included studies and the health system sub-groups each addressed.

Table 3: List of included studies

	First author (Year)	Setting	Group	Health system sub-groups addressed
1	Aiken et al. (2002)	USA	HW	Knowledge, attitudes and training
			HIS	Vaccination records
			FN	Funding for birth dose programmes
2	Bascom et al. (2005)	USA	GL	Policies and guidelines
3	Bialek et al. (2010)	Marshall Islands (the) and Micronesia (Federated States of)	SD	Location of service delivery
4	Biroscak et al. (2003)	USA	GL	Polices and guidelines
5	Brayden et al. (2000)	USA	HIS	Vaccination records
6	Cabana, Aiken et al. (2002)	USA	GL	Policies and guidelines
7	Cabana, Aiken, Clark (2002)	USA	GL	Policies and guidelines
8	Chunsuttiwat (1997)	Thailand	SD	Integration within the EPI
9	Clark et al. (2001)	USA	HW	Knowledge, attitudes and training
			GL	Policies and guidelines
10	Clements (2006)	Western Pacific Region (WPR)	SD	Access to a trained health worker
			HW	Delineation of responsibilities
			T	Vaccine storage and access to the cold chain
11	Connors et al. (1998)	Australia	GL	Policies and guidelines
			GL	Standing orders

Abbreviations:

SD = service delivery; HW = health workforce; HIS = health information systems;
T = medical products, vaccines and technologies; FN = financing;
GL = governance and leadership.

	First author (Year)	Setting	Group	Health system sub-groups addressed
12	Cooper et al. (2001)	USA	SD	Location of service delivery
			HW	Knowledge, attitudes and training
			HIS	Vaccination records
			FN	Financing for birth dose
			GL	Policies and guidelines
13	Creati et al. (2007)	Indonesia	HW	Delineation of responsibilities
			HW	Knowledge, attitudes and training
			GL	Policies and guidelines
			T	Vaccine storage and cold chain
			T	Vaccine presentation
14	CDC. (2007)	China	SD	Demand for vaccination
			SD	Access to a trained health worker
			SD	Linkages with maternity services
			HW	Knowledge, attitudes and training
			T	Procurement, supply and distribution systems
15	Danielsson et al. (2009)	Tonga	HW	Task-shifting
16	de la Hoz et al. (2005)	Columbia	SD	Location of service delivery
			HW	Knowledge, attitudes and training
			T	Procurement, supply and distribution systems
17	Downing et al. (2008)	Papua New Guinea	HW	Knowledge, attitudes and training
			HW	Delineation of responsibilities
			T	Procurement, supply and distribution systems
18	Government of Indonesia (2008)	Indonesia	SD	Demand for vaccination
19	Government of the People's Republic of China (2006)	China	SD	Demand for vaccination
			HW	Knowledge, attitudes and training
			T	Procurement, supply and distribution systems
			HIS	Registries
			FN	Funding for birth dose programmes
20	Government of the People's Republic of China (2008)	China	SD	Access to a trained health worker
			T	Procurement, supply and distribution systems
			HIS	Registries
			FN	Funding for birth dose programmes
			GL	Policies and guidelines
21	Hu et al. (2001)	China	SD	Demand for vaccination
			HIS	Registries
22	Hurie et al. (2001)	USA	GL	Policies and guidelines
23	Jacques-Caroll et al. (2009)	USA	GL	Policies and guidelines
24	Kuruvilla et al. (2009)	India	SD	Location of service delivery
25	Levin et al. (2005)	Indonesia	T	Vaccine delivery technologies and disposal
26	Liang et al. (2009)	China	SD	Access to a trained health worker
			SD	Demand for vaccination
			FN	Cost to recipient
27	Luman et al. (2004)	USA	SD	Linkages with private health services
			SD	Location of service delivery
			GL	Policies and guidelines
			SD	Demand for vaccination
28	Maayan-Metzger et al (2005)	Israel	SD	Demand for vaccination

Abbreviations:

SD = service delivery; HW = health workforce; HIS = health information systems;
T = medical products, vaccines and technologies; FN = financing;
GL = governance and leadership.

	First author (Year)	Setting	Group	Health system sub-groups addressed
29	Madlon-Kay et al. (2011)	USA	GL	Standing orders
			HIS	Vaccination records
30	Manea et al	Micronesia (Federated States of)	HW	Delineation of responsibilities
			HIS	Vaccination records
31	Mercier et al. (2007)	USA	SD	Quality improvement
32	Morgan et al. (2010)	Papua New Guinea	SD	Linkages with early newborn care services
			HW	Task-shifting
			T	Vaccine delivery technologies
			T	Storage and access to the cold chain
			HIS	Birth notification
33	Murakami et al. (2008)	Viet Nam	SD	Linkages with private health-care services
			HIS	Registries
			GL	Policies and guidelines
			SD	Demand for vaccination
34	O'Leary et al. (2012)	USA	SD	Demand for vaccination
			GL	Policies and guidelines
35	Oram et al. (2001)	USA	GL	Policies and guidelines
36	PATH (1998)	Indonesia	SD	Linkages with postnatal care services
37	PATH (2003)	Indonesia	HW	Knowledge, attitudes and training
			SD	Demand for vaccination
			HIS	Birth notification
38	PATH (2003)	Indonesia	HIS	Birth notification
39	PATH (2005)	China	T	Storage and access to the cold chain
40	PATH et al. (2006)	Viet Nam	T	Storage and access to the cold chain
41	PATH (2007)	Viet Nam	T	Storage and access to the cold chain
42	PATH (2008)	Indonesia	SD	Linkages with postnatal care services
43	PATH (2010)	Viet Nam	SD	Demand for vaccination
			GL	Political commitment
44	Pearce et al. (2008)	Australia	HW	Knowledge, attitudes and training
45	Ruff et al. (1995)	Indonesia	HIS	Birth notification
46	Ruff et al. (2009)	Philippines (the)	SD	Access to a trained health worker
			T	Vaccine procurement, supply and distribution
47	Sobel et al. (2010)	Philippines (the)	GL	Policies and guidelines
			GL	Standing orders
			HW	Knowledge, attitudes and training
48	Sun et al. (2002)	China	SD	Location of service delivery
49	Thomas et al. (2004)	USA	GL	Policies and guidelines
50	Wang et al. (2007)	China	HW	Training
			T	Storage and access to the cold chain
			T	Vaccines delivery technologies and disposal
51	White et al. (2009)	USA	GL	Policies and guidelines
			HIS	Vaccination records
52	WHO (2002)	China	FN	Cost to recipient
53	WHO (2006)	Mongolia	HW	Knowledge, attitudes and training

Abbreviations:

SD = service delivery; HW = health workforce; HIS = health information systems;
T = medical products, vaccines and technologies; FN = financing;
GL = governance and leadership.

	First author (Year)	Setting	Group	Health system sub-groups addressed
54	WHO (2007)	Western Pacific Region	SD	Access to a trained health worker
			T	Storage and access to the cold chain
			T	Vaccine presentation
			FN	Cost to the recipient
			GL	Policies and guidelines
55	WHO (2008)	Viet Nam	SD	Demand for vaccination
56	WHO (2008)	Worldwide	SD	Access to a trained health worker
			SD	Linkages with maternity and private services
			T	Procurement, supply and distribution systems
57	WHO (2011)	Western Pacific Region	SD	Access to a trained health worker
			SD	Demand for vaccination
			HIS	Procurement, supply and distribution systems
			FN	Funding for birth dose programmes
58	Willis et al. (2010)	USA	SD	Location of service delivery
			GL	Polices and guidelines
59	Wood et al. (2008)	Australia	HIS	Monitoring performance, equity and scale-up
60	Yusuf et al. (1999)	USA	GL	Policies and guidelines
			SD	Demand for vaccination
61	Zeng et al. (1999)	China	SD	Location of service delivery
62	Zhao et al. (2011)	USA	GL	Policies and guidelines
63	Zhou et al. (2008)	China	FN	Cost to recipient
64	Zhou et al. (2009)	China	SD	Demand for vaccination
			SD	Access to a trained health worker
			HIS	Vaccination records
65	Zola et al. (1997)	USA	HW	Knowledge, attitudes and training

Abbreviations:

SD = service delivery; HW = health workforce; HIS = health information systems;
T = medical products, vaccines and technologies; FN = financing;
GL = governance and leadership.

3.4 Types of studies found and notes on evidence quality

The 65 papers included in this review were of different types. Of the 48 published articles, the most common study types were surveys (n = 24), and reviews (n = 7). There were also six cohort and five qualitative studies, three intervention studies, one cost-effective analysis, one RCT and one epidemiological report. Within the grey literature (n = 17), papers were mainly reports (n = 11) and workshop/ conference proceedings (n = 4). There was also one evaluation and one operational field manual.

Quality appraisals showed wide variation, as is common for studies of health-service implementation. Most limitations related to study design and data analysis. Of the 24 surveys included in this review, eight collected data through self-administered questionnaires, with the potential for recall or self-reporting biases. In the only RCT, the method of randomization of villages and allocation concealment was not described. Several quantitative studies (n = 6) did not adjust for confounding factors in data analysis, with potential under- or over-estimation of the practice, facilitator or barrier discussed. Most of the evidence comes from studies undertaken in specific settings, which need to be noted when considering generalizability of their findings. For qualitative studies, there was rarely discussion of how variability within the studied sample may have influenced findings.

In the grey literature, three studies did not describe data analysis, two did not detail how participants were recruited and, in most, there was inadequate evidence to support the arguments or conclusions made. The biggest limitation identified across the several studies that reported on a range of practices, was their inability to attribute the relative contribution of each practice to improving coverage.

We examined the applicability of combining studies and applying GRADE criteria to display recommendations in the form commonly used for guidelines on specific interventions. We also examined the use of Cochrane methods to combine qualitative data from systematic reviews (12). However, these techniques could only apply to a small subset of our review, displayed in Annex 5, for important practices. The large variability in the implementation descriptions we found meant that such approaches to evidence would unhelpfully limit our ability to derive meaningful recommendations, based on practices that expert opinion deemed likely to be effective.

When considering the range of studies found, it is also important to note some limitations; our review was restricted to publications in English and our search of the grey literature was conducted by online searching and through author contacts. With this caveat, however, discussion with expert opinion (as defined in the 'Methods' section) does suggest that we have covered the most important likely sources of implementation evidence, including Chinese studies, most suited to inform the evidence base.

4. Practices that improve birth dose coverage

Findings are presented aligned with the WHO's health-system categories used in data analysis (see Section 2), with practices addressing community knowledge and attitudes treated separately from other service-delivery issues. Under each category, findings on *barriers or facilitators* are presented if relevant, with the main emphasis placed on those *practices* found to improve coverage of the birth dose. Odds ratios or measured changes in birth dose coverage are included, where these were available, but only to provide a general indication of the relative importance of any particular practice. Many effect estimates must be treated with caution as noted here, and in the Annexes. Where judgments are derived from expert opinion, this is indicated through referencing. These findings list practices beneficial for all settings, as well as options to consider for special situations (where practices are not universally beneficial, this is indicated in the description of the practice).

As mentioned in the 'Methods' section, not all studies were graded for quality of evidence. Of those that were graded, all but one study (46) were of low or very low quality (see Annex 5). Despite the limitations of the available evidence, there is still sufficient information to recommend certain practices important to improved coverage of timely hepatitis B birth dose vaccination: these are highlighted in **bold** in the narrative below.

4.1 Service delivery arrangements

4.1.1 *Increasing access to skilled care at the time of childbirth*

Births outside health facilities (home births) were associated with lower coverage of birth dose in seven studies, with lack of access to trained health staff as the critical barrier (13–18). In China, one survey found coverage of timely birth dose was only 13% for home births compared to 49% for births in township hospitals, 54% in higher-level hospitals and 59% in private clinics (14); another large survey across 31 provinces found 31% timely birth dose coverage among home births compared to 78% and 85% for births in township hospitals and county hospitals respectively (15). Access difficulties were highlighted by variable coverage in Tamil Nadu, India, with rural coverage measured at 3.5% compared to urban at 11% (19). Home births were cited as an important reason for low coverage (52%) for hepatitis B birth dose administered within seven days of birth in Cambodia (20). In Lombok, Indonesia, where over 90% of births were at home, only 5% of births were attended by nurses or midwives who could vaccinate (21).

Increasing skilled attendance at birth, preferably in well-supported health facilities, is a critical part of improving birth dose coverage (22,23), requiring broader initiatives for maternal and newborn survival (24) and integration of birth dose vaccination into maternal and newborn care, as discussed below.

4.1.2 Integration of birth dose with maternal and newborn care in health facilities

Provision of birth dose as part of the management of childbirth in health facilities has proved to be feasible in settings as varied as China (Province of Taiwan) (26), the United States (27), Oman (28), the Republic of the Marshall Islands and the Federated States of Micronesia (29). A number of specific practices that support this are documented in the evidence base and are discussed below.

A local health-facility policy specifying birth dose vaccination was found to improve coverage in four studies. In a focused effort to improve birth dose in the Republic of the Philippines, hospitals with a copy of the hepatitis B vaccine vaccination policy were 4.7 (CI 1.2 – 18) times more likely to have more than 50% coverage with birth dose (30). This study did not control for confounding factors, implying that the size of the effect may have been over- or under-estimated. Recent studies in the United States also found local policies significantly associated with higher coverage; 87% compared to 38% without a policy ($p < 0.001$) in one site (31), and 41% compared with 15% for another (32), while an earlier study in Australia found comparable associations with hospital recommendations, 93% compared with 77% (33). The Australian study, however, was only undertaken in two urban hospitals and did not test for statistical significance in differences in coverage between the hospitals.

Standing orders for administration of birth dose in the delivery room or postnatal ward are effective in improving coverage. In the Philippines study described above, hospitals with standing orders were 4.8 (CI 1.3 – 18.1) times more likely to have greater than 50% coverage, noting that this effect size is to be interpreted with caution, given the limitations noted above. In a quality improvement intervention in the USA, coverage of birth dose increased from 73% to 84% following implementation of a nursery order requiring physicians to provide birth dose vaccination, unless they actively ‘opted out’ (34). Similar gains were seen in Australia (33). Health-facility guidelines that prescribe the birth dose to “follow birth within 24 hours” rather than as “prior to discharge”, helped improve timely vaccination in one hospital in Papua New Guinea (35). Interpretation of these effect sizes should be done with caution, as these studies did not fully control for confounding factors.

Ensuring vaccine is available in the delivery room or postnatal ward is important to timely vaccination. In Tonga, this was one element seen as contributing to increased birth dose coverage (36) and, in a review of hospitals in Papua New Guinea, non-availability of birth dose vaccines in the delivery room was reported as the most common barrier to vaccination (35). Expert opinion noted the lack of cold-storage facilities as a contributor to low coverage in the Western Pacific Region (13,37), reported the effectiveness of storing vaccines in delivery rooms of public hospitals in Viet Nam (20), and supported the use of vaccine carriers to aid in this (3,35). Since the hepatitis B vaccine can be stored outside standard cold-chain arrangements (OCC) (38,39) there is potential for managed usage without refrigeration, now known as a controlled temperature chain (CTC), in peripheral health facilities.

Studies in Viet Nam confirm this; a four district study saw an increase in coverage (from 45% to 73%) in health centres where the birth dose was stored OCC, equivalent to gains seen in hospitals (40), and single-dose vials stored OCC in community health centres for up to four weeks (41) were associated with increased coverage (45% to 89%) of birth dose administered within 72 hours (37,41). It should, however, be noted that two of these studies did not provide sufficient details on methods to fully support these estimates of effect (37,40). Another analysis in Viet Nam (42) confirmed the feasibility of OCC storage at peripheral health facilities, but found that this was not associated with higher coverage unless other arrangements (for example, to increase vaccinator numbers) were also in place. These factors, and the potential of CTC storage to reach home births, are discussed further in the sections below.

Clear delineation of who is responsible to vaccinate that includes maternal health-care providers is discussed as a contributor in some of the literature. Expert opinion noted failure to give birth attendants responsibility for vaccination as a barrier (13), confirming findings from demonstration sites in Indonesia (21) and from Viet Nam, where restricting vaccination to public-health nurses was associated with limitation of coverage (42). In Tonga, timely vaccination with hepatitis B vaccine significantly outstripped bacille Calmette-Guérin (BCG) vaccination (also timed for birth) when delivery-room staff were delegated authority to give the hepatitis B vaccine (36). While having a birth attendant able to vaccinate is clearly important, assigning a public-health staff with coordination and facilitation roles is also worthwhile; having an assigned immunization nurse helped to increase coverage of timely birth dose from under 40% to over 80% in one hospital in Papua New Guinea (35), public-health nurses visit postnatal wards daily to vaccinate in Oman (28), and having a dedicated nurse to coordinate the birth dose vaccination campaign helped to increase coverage in the Federated States of Micronesia (43). In all these studies, confounding factors were not tightly controlled, and staff assignment is likely to be just one of a number of contributors to improving coverage.

Positioning birth dose vaccination as part of essential newborn care and ensuring it does not interrupt urgent interventions is important to ensure the birth dose is provided appropriately (3); noting that vaccination should not precede other early care, such as resuscitation, keeping the newborn warm and establishment of breastfeeding. In the Philippines' successful hospital- and health-centre interventions for improving birth dose coverage (30), one facility developed an essential newborn care protocol which timed birth dose vaccination to take place after the first full breastfeed (44).

Coordinated planning between immunization and maternal health staff in health facilities and in districts is critical to birth dose vaccination, as noted by expert opinion (22), with supporting descriptions of collaborations between immunization programmes and the maternal health department in Viet Nam (20,42), although no studies measured the impact of this. Experiences of improved coverage in Papua New Guinea and the Philippines clearly demonstrated the important role in sustaining coverage of **structured health-facility assessments** and local problem-solving and education, as well as repeated follow-up (30,35).

4.1.3 Linkages between immunization and private health services

Two studies reported on barriers related to birth dose delivered within private health services. In Viet Nam, coverage of birth dose delivered within 72 hours was lowest, at 47% (statistical testing not reported), in the province with the highest percentage of deliveries in private facilities. This was attributed to weak linkages between private health facilities and the national EPI (42), although rigorous evidence was not provided to support this conclusion. In multivariate analyses of findings from a survey undertaken among 41 589 children in the United States, infants with a public provider were 1.3 (CI 1.2 – 1.5) times more likely to receive the birth dose compared to infants with private providers (45).

4.1.4 Reaching infants born outside health facilities

Intervention trials and observational studies in China, Indonesia, Papua New Guinea, the Philippines and Viet Nam, have demonstrated that, while difficult, it is possible to reach infants born outside health facilities with birth dose vaccination (noting that the definitions of timeliness varied in these studies). Effective practices to achieve this are presented below.

Home visits to provide timely vaccination after home birth were found to be more effective than requiring families to bring newborns to health facilities in all studies that compared these modes. In a RCT in China, the two study arms with village health workers visiting homes saw a significantly greater increase in birth dose coverage, from 11.3% (CI 7.3% – 15.2%) to 67.8% (CI 61.5% – 74.2%) and from 6.8% (CI 4.1% – 5.9%) to 77.3% (CI 71.5% – 83%) respectively, than did the group relying on vaccination in township clinics, which saw a lower coverage increase from 8% (CI 4.7% – 11.2%) to 57.9% (CI 50.3% – 65.4%) (46,47). In urban Manila, home visits by community staff were part of an intensive programme that saw timely birth dose coverage increase from 17% to 86% for infants born at home (30,48). A number of analyses in Viet Nam, that included home visits for vaccination, all saw significant increases in birth dose coverage to above 80% where this was included in the strategy (37,39,40,42). Apart from the China RCT, confounding factors were not tightly controlled in these studies, and other factors, in addition to home visits, may have contributed to improving coverage.

Integration of birth dose with home visits for other postnatal care is an alternative to the vaccination-specific home visits discussed above. This option for service delivery has been examined in three studies in Indonesia and Papua New Guinea. Creati and colleagues' review described various projects integrating birth dose administration within larger packages of postnatal care services delivered by village midwives. In one project, after five years of implementation (no baseline provided), coverage of birth dose for infants born at home was at 39% for within seven days of birth (noting Indonesian policy allowed timely birth dose up to seven days) (21); in an earlier initiative, in three provinces, coverage increases varied — in Lombok from 33% to 83%, in Mataram from 24% to 51% and in Sumbawa from 3% to 90% (49). In Papua New Guinea, a similar district feasibility trial in East Sepik Province estimated local coverage increase at 74% coverage for home births compared with 93% coverage for health-centre births (50). A WHO/UNICEF guideline on general community-based postnatal care recommends that a home visit should take place within 24 hours of a home birth (51).

Vaccine storage OCC, careful pregnancy tracking and the use of Uniject™ were also key contributors to reaching infants born at home. OCC usage, including the provision to maintain the vaccine for up to 30 days outside of standard cold-chain arrangements (3) and Uniject, are discussed further under ‘Medical Technologies’, and pregnancy tracking is discussed under ‘Health Information Systems’.

4.2 Health workforce considerations

4.2.1 Health-care provider knowledge and attitudes

Five studies and a WHO operational manual provided evidence that health workers’ knowledge and attitudes are barriers or facilitators to improving coverage of the birth dose. In hospital assessments in Papua New Guinea (3,35) and in peripheral health facilities in China (52) **inadequate knowledge among staff** was reported as a barrier to achieving higher coverage of timely birth dose vaccination. Health staff **perceptions and attitudes** were found to be important determinants of willingness to vaccinate newborns. In the United States, health provider resistance to vaccination, including perceptions that population health risks were low, were barriers to timely birth dose in surveys of 296 hospital nurseries (53) and of a random sample of 773 hospitals. In the latter survey, coverage with birth dose vaccination prior to discharge was at 38% for hospitals that reported physician resistance, compared to 62% of hospitals where there was no physician resistance ($p < 0.05$) (54). The findings from this study were based on self-reported data, and thus subject to bias. Also in the USA, physician’s belief in the importance of birth dose was a statistically significant determinant of higher coverage (55). Midwife concern for the autonomy of their clients in vaccination choices, when accompanied by lack of awareness of the rationale for vaccine timing in preventing perinatal transmission, was seen as a barrier to birth dose in a qualitative study in Australia (56). **Unspecified newborn safety concerns** among village midwives in rural Indonesia (Lombok), who feared blame for perceived adverse events, was reported to impede administration of the birth dose (21).

4.2.2 Health-care worker education and training practices and their impact

Five studies reported evidence on effective training practices. Education on the epidemiological rationale for birth dose is associated with higher coverage. The RCT in China that explored the feasibility and effectiveness of OCC strategies found an association between education of township health workers, village doctors and midwives, with a significantly decreased risk that parents would report not being informed about the importance of timely birth dose. This was seen most strongly for those whose infant was delivered in the hospital (46).

In an evaluation of the impact of training for urban health facility and outreach staff in the Philippines, coverage of timely birth dose increased from 19% before the training intervention to 74% during the two months after the training. For infants born at home, coverage increased from 17% to 86%, and for infants born in lie-in clinics, from 26% to 75%. Hospitals with neonatal practitioners who had undergone training were 14.4 (CI 3.1 – 87.9) times more likely to have over 50% coverage of birth dose administered before. The training impact is striking, although it is noted that this study did not have a control group and not all confounding factors could be controlled (30). Papua New Guinea researchers noted the importance of including a staff education

component as part of hospital assessments, qualitatively linking this to better coverage (35). In both these situations, the documented training content covered: diseases caused by HBV and the importance of early vaccination; vaccine and cold-chain management; giving the vaccination safely, and common misconceptions regarding birth dose administration, including false contraindications.

Within the grey literature, supervision and training of health workers, including village doctors and birth attendants, in the province of Qinghai, China was given as a reason for improved coverage of timely birth dose from 40% in 2004 to 70% at the end of 2005 (52,57). The experience of the Philippines emphasized the critical contribution of supportive supervision and follow-up to any training outcomes (48). The role of supervision in improving primary health-care services has been the subject of a recent Cochrane systematic review (58), finding a modest effect on health-worker practices and knowledge, albeit based on studies rated as low, to very low, for quality of evidence.

4.2.3 Task-shifting

As noted above, the service delivery evidence for increasing coverage in health facilities includes tasking of delivery room or postnatal care staff with vaccination responsibilities. Expert opinion notes, that such staff usually provide other injections at birth, such that formal task-shifting (defined as the shifting of health-care tasks from more specialized to less specialized health-care providers) is not required.

Task-shifting may be considered as an option for reaching infants born at home. Studies in Indonesia (21), China (46) and Viet Nam (59) involved training some peripheral health staff who had not previously provided vaccination injections. One study, in order to reach home births in remote villages, trained lay health workers (known as village health volunteers) to provide birth dose vaccination, attributing much of the gains in coverage in that difficult environment to this cadre (50). Presentation of the vaccine in Uniject (discussed below) was an important facilitator, and expert consensus suggests that this is the only form of vaccination device suitable for use by trained lay health workers (39,60). A Cochrane systematic review of 82 studies on the effect of lay health workers (61) demonstrates their benefit in promoting immunization uptake and postnatal care, such as breastfeeding, in addition to other community health activities.

4.3 Medical products and technologies relevant to birth dose

4.3.1 Vaccine distribution and storage systems

Three studies (16,35,62) and two reports (18,63) described unavailability of the birth dose vaccine as a barrier to improving coverage, while two reports stated that poor management of vaccine supplies and auto-disposal syringes in China was a reason for low coverage of timely birth dose (18,52). As noted under 'Service Delivery', birth dose is improved by making appropriate vaccine storage as close to the location of birth as possible, both in the cold chain using refrigerators, or vaccine carriers and OCC. This was well demonstrated by the coverage gains in studies in Viet Nam (40,42) and the RCT in China (additional detail below) (46,47), and noted as an essential facilitator for home-based vaccination in Papua New Guinea (50). In all these settings, storage of the vaccine under managed OCC conditions was associated with the

best coverage gains for settings where home births remain common. Other work, beyond the scope of this review, has demonstrated the safety and efficacy of hepatitis B vaccine storage outside the standard cold chain, as part of a CTC (39). Expert opinion on effective CTC practices requires vaccines to have a vaccine vial monitor (VVM) attached to detect heat exposure, and that vaccines remain outside of standard cold-chain arrangements for no more than 30 days (3). Experimental work is currently underway to validate and extend the flexibility of deployment of hepatitis B vaccine in a CTC (64).

4.3.2 Vaccine presentations

Uniject is a compact pre-filled auto-disable injection device that is simpler to use than standard needles and syringes (65). WHO and other international organizations support its use (66,67) for vaccines and medicines, including hepatitis B vaccine. The Indonesian Government offers birth dose nationally in the Uniject presentation. Studies described above have explored its use when combined with storage OCC in delivering the birth dose vaccine, as noted above, in China, Indonesia, Papua New Guinea and Viet Nam. Two studies in particular attest to the presentation in Uniject as an option worth considering, given its clear association with improved birth dose coverage in situations where home births are common.

The China RCT compared, in rural counties of Hunan Province, single-dose vial vaccines stored within the cold chain and administered in township hospitals (Group 1), with single-dose vial vaccines stored OCC in villages and administered by village health workers in homes (Group 2) and with Uniject vaccines stored OCC and administered by village health workers in homes (Group 3). Compared to coverage levels at the start of the study, coverage of timely birth dose increased from 8% (CI 4.7% – 11.2%) to 57.9% (CI 50.3%–65.4%) in Group 1, from 11.3% (CI 7.3% – 15.2%) to 67.8% (CI 61.5% – 74.2%) in Group 2 and from 6.8% (CI 4.1% – 5.9%) to 77.3% (CI 71.5% – 83%) in Group 3 ($p < 0.05$ for differences in coverage between groups). **These data indicate that the highest increase in coverage was experienced with birth dose delivered in Uniject devices OCC (46,47).** One study provides additional evidence relating solely to the use of Uniject in the delivery of the birth dose vaccine in Indonesia. After two years of using Uniject devices to deliver the birth dose vaccine, coverage of birth dose within seven days of birth increased from 68% to 80% in the province of West Nusa Tenggara, from 0% to 86% in Yogyakarta and from 0% to 38% in East Java (68). This study did not differentiate the Uniject effect from the contribution of other hepatitis B birth dose vaccination practices which were simultaneously implemented in improving coverage.

Monovalent hepatitis B vaccine in single-dose or multi-dose presentations is a requirement for birth dose, as combination vaccines should not be given at birth (1). Barriers and practices related to presentation of the birth dose vaccine were described in one study and one report of proceedings from a WHO Western Pacific Regional Office meeting held in 2007. In Indonesia, reluctance to open 10-dose vials of birth dose vaccines to vaccinate a few infants, due to concerns about wastage, was reported as a barrier to administering the birth dose (21). To overcome such challenges, single-dose vials for the birth dose vaccine were used in public hospitals in Viet Nam — a practice which was reported to help increase timely birth dose coverage in the hospitals (20). Expert consensus suggests that single-dose vials are more suitable for outreach for home-based vaccination (as usually only one birth can be accessed per visit), or settings with low volumes of births (3,48,69).

4.4 Health-information system considerations for birth dose

4.4.1 *Birth registries*

Four papers, one survey, one qualitative and survey study and two reports, suggested that registration in various population registries was important to estimate the target population for birth dose, and therefore also important for improved coverage. Expert consensus generally, and a report from China specifically, identified mobile and migrant populations, who may not be well tracked by local information systems, as challenging to vaccinate with the birth dose (18). In a study in Zhejiang province, China, infants from households that were registered with the local authorities were 2.7 (CI 1.8 – 4.1) times more likely to be vaccinated than infants from migrant families who were not registered (70). Registration of pregnant women was listed as a contributor to increased overall coverage (40% to 70%) and home birth coverage (20% to 60%) between 2004 and 2005 in Qinghai Province of China (52).

4.4.2 *Birth notification and pregnancy tracking*

In Viet Nam, a study found that **meticulous tracking of pregnancies and births by village and community health workers helped to improve coverage of the birth dose**. In two districts where pregnancies were tracked, coverage of birth dose administered within 72 hours was 97% and 90%, compared to 87%, 52% and 45% in districts where there was no tracking (42). Differences in coverage were not tested for statistical significance, nor were confounding factors controlled. Three papers in Indonesia mentioned **the role of birth notification in improving coverage for home births**. In the hepatitis B birth dose immunization project carried out in Lombok between 1987 and 1991, written and verbal birth notification systems were used to ensure that health workers visited homes of newborns soon after birth to administer the vaccine (21,71). Cadres of the Indonesian village women's movement (PKK) and traditional birth attendants relayed information about births, and information was then given to vaccinators during their weekly visits to the village. Other mechanisms also evolved, such as vaccinators actively seeking newborns, and direct notifications of births to vaccinators by traditional birth attendants (TBAs), midwives and local community members. Although no data on baseline or endline coverage of birth dose was provided, coverage of birth dose in the study population (administered within seven days of birth) was reported at 95% in 1989 and 1991 (71). In the Healthy Start programme that followed (1990–1997) in Lombok, TBAs used colour-coded cards to notify midwives about births, which then prompted them to visit homes and administer the birth dose (72).

4.4.3 *Vaccination records, monitoring and reporting of vaccine coverage*

Three studies provide evidence on the **importance of incorporation of birth dose within vaccination records** to improving birth dose coverage. In the United States, difficulties in transferring vaccination records to primary physicians created a barrier to birth dose (53) and, in another survey, clinicians who perceived difficulties in tracking vaccinations were less likely to administer birth dose vaccination (55). In China, children who lacked an immunization registration book or card were 0.6 times less likely to be vaccinated with timely birth dose ($p < 0.0001$) (14). In the Federated States of Micronesia, use of existing vaccination records and forms to report on hepatitis B vaccination was noted as a factor contributing to increased coverage of hepatitis B vaccination (43).

Expert consensus provides guidance on **coverage reporting**. The WHO Western Pacific Region has worked to improve country monitoring of birth dose through national systems and improvements in the Joint Reporting Form. It is important that these clearly identify time of vaccination in relation to birth by defining a birth dose as within 24 hours, and/or noting the date of vaccination in relation to date of birth. WHO also recommends **serological surveys of HBV prevalence** as useful options for establishing baselines and monitoring of programmes, and these have been an important component of Western Pacific Region regional strategies to control HBV (1,23).

4.5 Influence of vaccine financing on birth dose coverage

The cost-effectiveness of birth dose vaccination or hepatitis B vaccination in general is well documented (1); hence here we present only those studies which show a link between financing arrangements and improved coverage.

4.5.1 *Funding for birth dose programmes*

Three papers, one study set in the USA and two reports on Chinese immunization programmes, mentioned that funding-related issues were barriers to improving coverage of the birth dose. In China, the barrier was simply due to insufficient funding, particularly for operational activities (18,52). In the USA, a sample of hospital nurseries reported not offering the birth dose to newborns because of difficulties in obtaining reimbursement for it from public programmes (53). A multi-site study in Indonesia assessed incremental costs of various strategies aiming to provide birth dose in peripheral facilities and the home. It found that service delivery costs were higher where community staff needed to travel to collect vaccines, and lower when vaccines were stored at the most peripheral point possible (42). Uniject is more expensive than other presentations; however one study in Indonesia suggested that it is cost-effective when the alternative is multi-dose vials with a wastage rate of 33% (68). At present, there is little evidence providing detail on the financial implications of maximising coverage, in either our systematic review or in expert consensus.

4.5.2 *Minimizing costs to families*

User fees for birth dose were reported as a reason for low coverage in China in a study conducted before user fees were removed (62). Paediatrician perceptions of increased cost, including reduced options for insurance reimbursement, were significantly associated with reduced birth dose vaccination in the USA (55). The response rate in this study, however, was low, and association was only tested in bivariate and not multivariate analyses. Four papers stated that removal or reduction of user fees for birth dose vaccination helped to improve coverage of the birth dose. In China, coverage of timely birth dose increased to 76% in 2002, with the halving of user fees for vaccination cited as a contributing factor (57). When vaccination was provided free-of-charge to all newborns in select provinces, average coverage of timely birth dose also increased (from 47% to 89% in township hospitals and from 61% to between 90% and 97% in city province hospitals) between 1998/1999 and 2005 (14). When birth dose administration was subsequently made free for all infants across China, coverage was found to have increased in rural areas — from within a range of 18% to 50% in 1993–1994 to 84% to 97% after 2005 (exact year not provided) (73). In the Republic of Korea, a high coverage of the birth dose in 2007, at 95% of newborns vaccinated before discharge, was partly attributed to the fact that vaccination had been covered under the National Insurance Act since 2002 (20).

4.6 Addressing community concerns or lack of knowledge regarding birth dose

4.6.1 *Family knowledge and practices influence birth dose coverage*

Five studies in our review highlight important family knowledge, customs and attitudes that can determine birth dose coverage. A report from Indonesia, and a survey undertaken among 3390 parents or guardians in four provinces in China, stated that parents' **low awareness of the birth dose vaccine and its importance were reasons for low coverage and uptake of the vaccine** (14). In multivariate analysis of findings from the survey, children whose parents did not know that the birth dose should be given within 24 hours of birth were 0.62 times less likely to be vaccinated compared to children whose parents did know ($p < 0.01$). **Parents' perception that the birth dose was not required was also reported as a barrier to receipt of the birth dose** in three papers (42,74,75). Higher incomes and education predisposes families to birth dose in China, where in Zhejiang Province infants from high-income families were 2.3 (CI 1.3 – 2.9, $p < 0.05$) times more likely to be vaccinated compared to infants from low-income families. Similarly, infants whose mothers had college or higher-level education were 2.8 (1.1 – 7.3, $p < 0.05$) times more likely to be vaccinated compared to infants whose mothers had middle-school education (70). The opposite trend is found in Israel and the USA, possibly for different reasons, as discussed in section 4.6.2 below.

In a qualitative study among 48 mothers in four provinces of Viet Nam, **traditional practices of sequestering newborns** at home during the first month of delivery was reported as a reason for infants not being vaccinated with the birth dose (42) and this was also reported for Indonesia (21). The impact of this barrier has not been quantified, although the practice is noted as adding weight to the potential value of home visits for postnatal care (51).

4.6.2 *Fear of adverse events or harm and parental refusal of vaccination*

Fear of adverse events or harm was a barrier documented in several papers (14,74,75). Among the parents of 1075 children who did not receive timely birth dose in a Chinese survey, 16% stated this was because of fear of an adverse event (14). In two reports from Viet Nam, **public anxiety due to deaths of newborns** following vaccination with the birth dose was stated as the reason for a decrease in coverage of timely birth dose from 64.3% in 2006 to 29% by the end of 2007 (63) and to 20% by the end of 2008 (59). Coincidental death is likely to be a higher risk with birth dose than other vaccines due to the higher risk of death in the first few days of life (76).

Eight studies from the USA examined the impact of changes in national recommendations in 1999 in response to **concerns regarding hypothetical and subsequently disproven adverse effects of thiomersal⁴** content in the vaccine, particularly for a newborn. Recommendations were changed so that 'low-risk infants' would not receive the birth dose. Two months later, a thiomersal-free vaccine was made available. All studies,

⁴ It is important to note that continued worldwide study and scrutiny has failed to document actual safety concerns with thiomersal. Thiomersal-containing vaccines remain prequalified by WHO as they continue to satisfy all reviews of safety and quality, as documented by the WHO Global Advisory Committee on Vaccine Safety.

some which looked at state-wide and others at nationwide samples of newborns, found that birth dose coverage decreased for all infants during the policy change and remained lower than pre-July 1999 levels, even after recommendations were reinstated, not returning to previous levels until after approximately one year (27,45,54,77–80).

We failed, however, to find additional evidence that parental fears are particularly linked to the fact that it is a newborn who is being vaccinated, as opposed to an older infant. Large multivariate analyses from the USA, regarding families with lower birth dose coverage despite good access, suggest that they are of higher socio-economic status, higher income, higher education and, more likely to be urban (32,31,45). In all cases, the effect sizes, though statistically significant, were relatively small and it seems likely that this represents the **small sub-set of parents who refuse vaccination in general**, rather than birth dose specifically. Similar findings were reported in an Israeli study, where mothers who did not give consent for vaccination were of a higher income or education level than mothers who did give consent, and this group were also less likely to intend to comply with the full series of hepatitis B vaccination (74).

The review of Indonesian projects by Creati and colleagues reviewed qualitative evidence for this and concluded that, in that setting characterized by high home-birth rates, parental refusal or distrust was a minor barrier, especially when compared with health-system barriers (21). In multivariate analyses of findings from a survey of 2632 children in Zhejiang Province in China, **parents' satisfaction with immunization services** was a factor in improving uptake of the birth dose; infants whose families were satisfied with services were two times (CI: 1.5 – 4.3, $p < 0.05$) more likely to be vaccinated compared to infants whose families were not satisfied (70). This study looked at multiple vaccines, including the birth dose vaccine, and so it is possible that findings may have been different had results from birth dose vaccination only been analysed.

4.6.3 Communication practices for improved birth dose coverage

Successful national commitments to HBV control (discussed below) have noted the importance of community education efforts in various settings, including China (17), Taiwan, China (26), the Federated States of Micronesia (43) and the Philippines (25), but these descriptions do not address the specifics of communications for newborn vaccination. One report does provide evidence of a public education programme aimed at increasing awareness about the hepatitis B birth dose; in Qinghai Province in China, communication activities were reported to have contributed to an increase in timely birth dose coverage from 40% in 2004 to 70% in 2005 (52).

The possibility of coincidental newborn death, and other examples in Europe where unvalidated and broader community concerns in relation to hepatitis B vaccine have been raised (81,82), demonstrate the need for birth dose programmes to prepare communications for rapid responses to adverse perceptions. Expert opinion has suggested the use of trustworthy modelling to estimate the expected number of newborn deaths, such as that by Black and colleagues (83), as a basis for pre-emptive communication strategies.

The Viet Nam experience (59) can help inform these, as can more general guides to immunization communication (84), UNICEF's communications framework guides⁵ and broader work to improve public confidence in vaccines (85), which is also discussed below.

4.7 Leadership and governance

Of the 21 studies that provided evidence about leadership and governance issues, the majority focused on policies and guidelines related to the birth dose. Those at national or state level are discussed here and those at health-facility level under 'Service Delivery'.

A central policy which mandates that all newborns be vaccinated with the birth dose is associated with high coverage and is an option for consideration. In the Republic of the Marshall Islands, coverage of birth dose among children born before implementation of a universal policy on birth dose vaccination was 29%, compared to 79% for children born after the policy was implemented ($p < 0.001$) (29). In a nationwide survey in the United States, 84% of infants in states with a universal policy were vaccinated with the hepatitis B birth dose compared to 58% of infants born in states without a universal policy ($p < 0.001$) (31). In a survey of American paediatricians, 80% of paediatricians based in a state with a universal vaccination policy administered the birth dose as opposed to less than 50% of paediatricians in states with no universal policy ($p < 0.001$) (55). In a third American survey, median coverage of the birth dose was 65% (CI: 21% – 83%) in vaccination programmes that had a universal policy for birth dose vaccination compared to 43% (CI: 10% – 65%) for programmes that did not have a policy ($p < 0.05$) (86). Three of these studies, however, did not control for confounding factors (29,55,86) and one was based on self-reported data (31).

Clear national guidance defining timely birth dose as within 24 hours of birth is important. In Indonesia, the national policy statement that allowed 'birth dose' within seven days of birth was felt to contribute to the fact that only 16% home births in one project were covered within 24 hours, although more than double that many were vaccinated by day seven (21). By 2009, in response to the Western Pacific Region's regional strategy, a number of countries were recorded as having changed guidance so as to conform to the 24-hour definition of a birth dose, including Mongolia (previously defined as within 24–48 hours), the Philippines (previously first dose was at six weeks) and Viet Nam (previously had been within seven days) (25).

Unnecessarily stringent restrictions contraindicating vaccination can form a barrier. In Viet Nam, out-dated policies on vaccination of underweight or sick neonates was a reason for delayed vaccination (42), while in China, strict standards on vaccine contraindications meant that premature or low-birth-weight infants were not receiving timely birth dose (18).

⁵ For example, at <https://sites.google.com/site/commframe/annexes/annex-2>.

Endorsing vaccine use beyond the standard cold chain (using a CTC) and accrediting new vaccinators can help extend programme reach. In countries across the Western Pacific Region, a lack of guidelines on storing vaccines beyond the standard cold chain, and on explicit vaccine labelling, was another reported barrier to improving coverage of timely birth dose vaccination (20). Examples from Viet Nam and Indonesia cited above represent settings where government policy attempts to overcome this to reach newborns in difficult settings (23,25).

Strong central communications to support public confidence in vaccines is essential. The restoration of birth dose coverage in the USA, following the thiomersal-related pause in 1999, required clear national guidance (27). A critical role for specialist societies, particularly paediatric societies, was noted in this process (87). The importance of preparatory communication strategies that anticipate public concerns was discussed in the section above, although at present there are no practice examples specific to birth dose.

In countries without a universal birth dose, adding a birth dose is likely to require steps very similar to those for the introduction of a new vaccine, especially if (as is common) existing older infant hepatitis B vaccine is provided as part of a combination vaccine presentation. In these situations, generic WHO guidance on new vaccine introduction (88) and practices is documented at the WHO new and underutilized vaccines implementation website.⁶

⁶ At <http://www.who.int/nuvi/en/>

5. Conclusion

although the evidence base is not large, as is common in questions relating to implementation of health services in low- and middle-income countries (LMICs), there is sufficient evidence to support the production of guidance documents on improving birth dose coverage at global, regional and national levels. Box 2 below provides a summary of the practices deemed to be effective in improving coverage of birth dose vaccination, based on this review of the evidence.

The evidence for effective practices has been broadened considerably through publications in recent years and now extends beyond the earlier demonstration sites in China, Indonesia and Viet Nam. There are studies specific to the implementation of hepatitis B birth dose vaccination across a range of LMIC and higher-income settings that demonstrate the effectiveness of practices within national planning and policy, district planning, implementation within childbirth care in health facilities, reaching newborns born at home, health-worker training and improved health information systems.

Improving birth dose coverage requires intervention across all areas of the health system and, for certain important practices, guidance will need to rely on more general evidence for effective implementation of immunization programmes. As noted in this review, such areas include preparatory communication strategies that plan for public concerns and the local costing of strategies to scale-up birth dose within and beyond health facilities.

One important step is the alignment, at international and national levels, of birth dose vaccination advice within general guidance documents for maternal and newborn health care, including those that provide support on community-based postnatal care. Continued implementation research, particularly to document country experiences of effective practices to increase routine coverage and integration of services, will help further build the evidence base in the future.

Lastly, in countries without a universal hepatitis B birth dose, adding a birth dose is likely to require steps very similar to those for the introduction of a new vaccine, even if hepatitis B for older infants is already in use. For these settings, general resources from WHO and its partners on the introduction of new vaccines will be useful to supplement guidance specific to the birth dose derived from the evidence base above.

Box 2: Effective practices for improving coverage with hepatitis B birth dose vaccine

Service delivery arrangements

- Increasing access to skilled care at the time of childbirth.
- Integration of birth dose with maternal and newborn care in health facilities by:
 - a local health-facility policy specifying birth dose vaccination;
 - standing orders for administration of birth dose in delivery room or postnatal ward;
 - ensuring vaccine is available in the delivery room or postnatal ward;
 - clear delineation of who is to vaccinate that includes maternal health providers;
 - positioning birth dose vaccination as part of essential newborn care in a way that does not interrupt urgent interventions;
 - coordinated planning between immunization and maternal health staff in health facilities and in districts, including supportive health-facility assessments.
- Linkages between immunization and private services providing childbirth care.
- Where infants are born outside health facilities, considering options such as:
 - home visits to provide timely vaccination;
 - integration of birth dose with home visits for other postnatal care;
 - vaccine storage outside the standard cold chain in a CTC;
 - careful community-based pregnancy tracking.

Health workforce considerations

- Addressing health-care providers' lack of knowledge and particular attitudes and perceptions towards newborn vaccination.
- Well-structured health-worker training, including education on perinatal transmission, backed up by frequent follow-up and supportive supervision.
- Consideration options for task-shifting to reach populations difficult to access.

Medical technologies relevant to birth dose

- Distribution and storage arrangements that utilize the potential for keeping vaccine outside the standard cold chain, positioning it as close to the birth place as possible.
- The potential use of Uniject by community-based health-care providers.
- Ensuring monovalent hepatitis B vaccine in single-dose or multi-dose presentations.

Health information system strengthening practices

- Birth registries and community birth notification, including tracking home births.
- Incorporation of birth dose and its timing within vaccination records.
- Accurate definition of timely birth dose in coverage reporting.
- Considering options for sero-surveys for establishment of need and for monitoring.

Financing arrangements influencing birth dose coverage

- Adequate funding for birth dose programmes, with consideration of transport efficiencies for distribution to the periphery.
- Minimizing costs to families.

Addressing community concerns or lack of knowledge regarding birth dose

- Responding to low awareness of the birth dose vaccine and its importance.
- Considering traditional practices of sequestering newborns.
- Addressing fear of adverse events, including planning for the risk of coincidental newborn death or disease.
- Responding to parental refusal of vaccination.

Leadership and governance practices

- A national policy for universal newborn vaccination.
- Clear national guidance defining timely birth dose as within 24 hours of birth.
- Removing unnecessarily stringent restrictions contraindicating vaccination.
- Considering options for vaccine use in CTC and accrediting new vaccinators.
- Strong central communications to support public confidence in vaccines.

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Annex 1:

Detailed Methodology

A1.1 Search strategy

Four electronic databases, CINAHL+, Embase, Pubmed and Web of Science, were searched for relevant literature, published in English only. No time restrictions were placed on the date of publication; literature published up to March 2012 (in line with the timing of the review) was accepted for inclusion. Search strings comprised MESH terms and keywords, such as “newborn”, “infant”, “hepatitis B”, “birth dose”, “vaccination” and “coverage”, combined with terms related to practices which increase, as well as facilitators and barriers to birth dose vaccination. Based on the premise that these practices, facilitators and barriers would revolve around health systems components, such as human resources or financing, the WHO Health Systems Building Blocks Framework (9) was used as a guide to identify relevant search terms.

Additional published literature was identified by scanning the reference lists of included articles, and using the citation tracking functions of PubMed. To take into account delays between publication of articles and appearance in electronic databases, the online medical research guide, Amedeo, was searched for articles published in the months of December 2011 and January and February 2012, under the search category of “vaccines”.

Grey literature was identified by searching the websites of key organizations working in the area of hepatitis B vaccination, including: WHO, the United Nations Children’s Fund (UNICEF), GAVI Alliance, Program for Appropriate Technology in Health (PATH) and Technet 21. Search terms used comprised “hepatitis B”, “birth dose”, “vaccine”, “vaccination” and “immunisation/immunization”. The same terms were used to carry out a search in the Google search engine to identify additional grey literature.

Expert opinions included in our findings were: professional contacts; authors of relevant publications, and discussions during the “Technical Consultation on Birth Dose Vaccination for Prevention of Perinatal Transmission of Hepatitis B”, held 7–8 December 2010 and jointly convened by WHO, the Burnet Institute, Compass: the Women’s and Children’s Knowledge Hub for Health and the Victorian Infectious Diseases Reference Laboratory. Details of the participants and the agenda for this consultation are provided in Annex 2.

A1.2 Search strategy used in Embase, Pubmed and Web of Knowledge

Step 1

Child OR children OR infant* OR baby OR newborn OR neonat*

Step 2

(Hepatitis B vaccines/administration and dosage*) OR (Immunization program*) OR (Training OR skills building OR staff responsibilities OR standards OR staffing OR human resource* OR health worker OR community health worker OR voluntary worker OR traditional birth attendant) OR (Home care service OR community care OR outreach OR home visit) OR (Cold chain OR cold temperature OR supply chain OR distribution) OR (Drug storage OR medicine storage OR vaccine storage OR Uniject) OR (Birth delivery AND health facility OR health centre OR health center) OR (Monitor* OR Regist* OR record OR data collection) OR (Organization OR organisation OR management OR integrated OR administration) OR (Immunization program* AND /economics OR costs OR cost analysis OR funds OR funding OR finance* OR financial resource*) OR (Immunization programmes* AND /standards OR immunization schedule) OR (knowledge OR attitudes OR practice* OR barriers OR obstacles OR determinants OR facilitators OR enablers OR policy)

Step 3

Coverage OR birth dose OR hepatitis B vaccination OR hepatitis B immunization or hepatitis B immunization

Step 4

#1 AND #2 AND #3

Limit: English language

1. Search strategy used in CINAHL+

Step 1

Searched: Hepatitis B vaccine birth dose

Step 2

Major concept selected: Hepatitis B vaccine

Step 3

Subheadings selected: administration and dosage, adverse effects, analysis, classification, contraindications, economics, legislation and jurisprudence, standards, supply & distribution

Limits: English language

Age restrictions: Infant newborn, newborn, child preschool

A1.3 Inclusion and exclusion criteria

Inclusion criteria for this review were broad. Given that the review questions revolved around issues related to implementation, and the lack of experimental studies in this field of research, no restrictions were placed on study design. However, only literature which related practices, facilitators and/or barriers to an outcome of birth dose coverage or birth dose uptake were included. Although the focus of this review is on birth dose delivered within 24 hours, literature that examined issues related to administration of the birth dose up to one week after birth was accepted to ensure that all relevant evidence was captured. Papers that studied multiple vaccines were also accepted, provided that one of the vaccines was the hepatitis B birth dose.

Literature was excluded if:

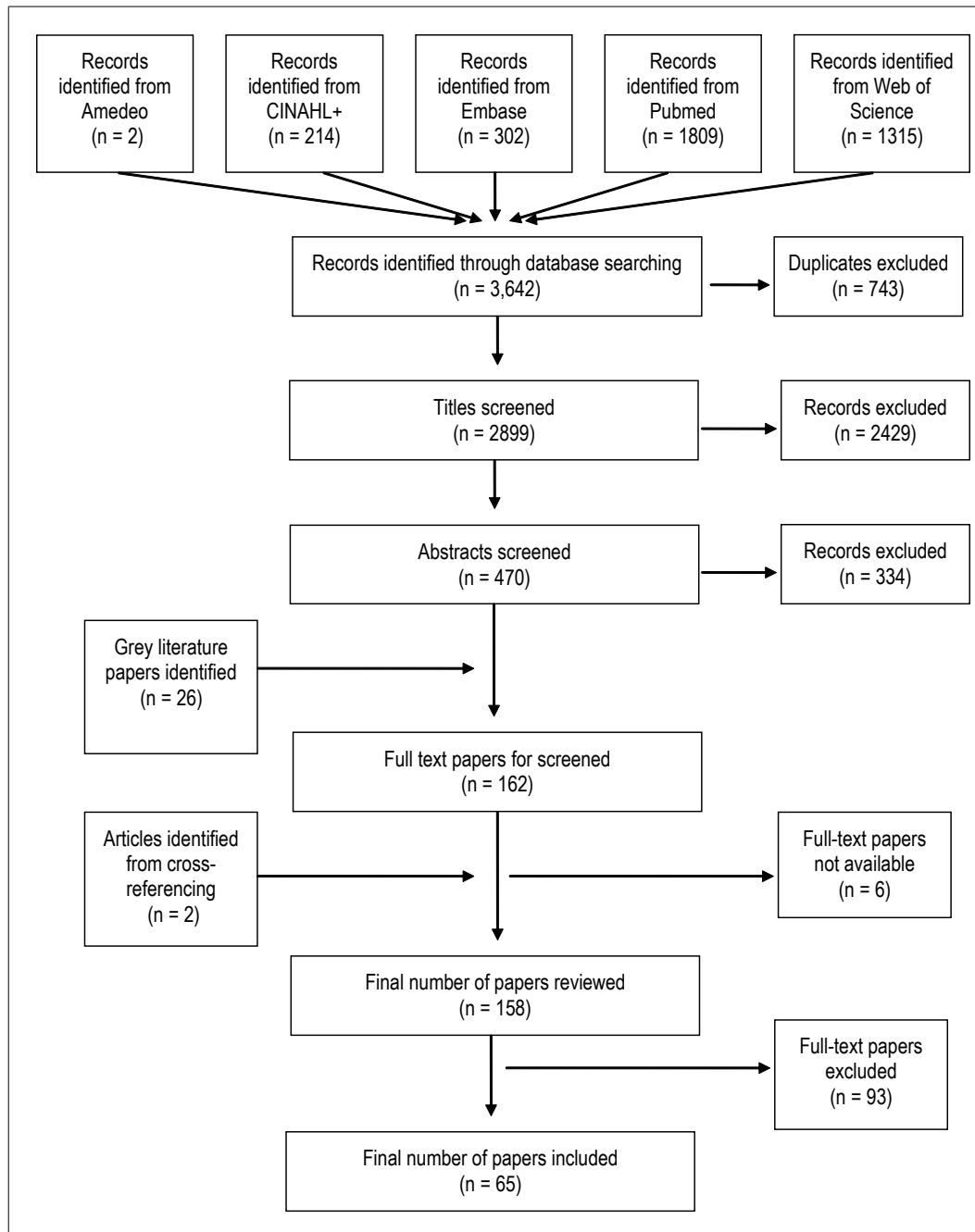
- the focus was not on *universal* administration of the hepatitis B birth dose (we excluded studies of prenatal screening and targeted vaccination);
- the study was restricted to measurement of coverage, immunogenicity or efficacy of the vaccine, without data on determinants of vaccine coverage;
- there was no clear source(s) of evidence or a research method (for published studies);
- not in English;
- full-text version was not accessible.

A1.4 Selection of the literature

Two reviewers independently screened the titles identified from the searches of published literature. In this first stage, titles that were deemed as relevant by either reviewer were retained. Both reviewers then read the abstracts of the remaining titles. In this round, only abstracts judged as meeting the inclusion criteria by both reviewers were retained. In the final round of the selection process, full-text articles of the remaining titles, as well as of the titles deemed relevant but for which no abstract was available, were assessed by both reviewers. Full-text versions of grey literature titles that were found to be relevant from the searches were also assessed at this stage. Only published and grey literature that was judged as fulfilling the inclusion criteria by both reviewers were finally included in the review. Any disagreement between the reviewers was resolved through discussion.

Figure A1 provides a summary of the results from the literature search and selection process. A total of 3676 titles were identified from the five databases. Export to Endnote X4 and removal of duplicates yielded a final total of 2899 exclusive titles. Screening of titles resulted in 470 abstracts eligible for review, of which 334 were excluded. Two relevant articles were identified from scanning references lists, giving 138 full-text articles for review, in addition to 26 grey literature papers. Of the 138 articles, six full-texts were not accessible so, in total, 158 full text papers were assessed. A final number of 48 published articles and 17 grey literature papers were judged as meeting the inclusion criteria and included in the review.

Figure A1: Results from the literature search and selection process



A1.5: Reasons for exclusion of full-text papers reviewed

In this review, literature was excluded from the systematic review of practices, barriers and facilitators, if:

- 1) the focus was not on *universal* administration of the hepatitis B birth dose given within seven days or less;
- 2) outcome measured was not coverage of birth dose;
- 3) it did not report on practices, barriers or facilitators to improving coverage;
- 4) studies were epidemiological or focusing on the immunogenicity or efficacy of the vaccine;
- 5) there was no clear source(s) of evidence or a research method (for published studies);
- 6) not in English;
- 7) full-text version was not accessible.

Table A1: List of excluded studies and reasons determined

First author (Year)	Title	Reason for exclusion
Published articles		
Adamo et al. (1998)	Ad hoc survey of hepatitis B virus (HBV) vaccination campaign in newborns of HBsAg positive mothers and in 12-year-old subjects in southern Italy	1, 2
Angelilo et al. (1999)	Mothers and vaccination knowledge, attitudes and behaviour in Italy	1
Ashworth (1988)	HBV immunization in Tauranga	1, 2
Balinska (2009)	HBV vaccination and French society ten years after the suspension of the vaccination campaign: how should we raise infant immunization coverage rates?	1
Basaleem et al. (2010)	Immunization coverage and its determinants among children 12 to 23 months-of-age in Aden, Yemen	1 Focuses on the three dose series, does not specify if birth dose was included
Berlioz-Arthaud et al. (2003)	10-year assessment of infant HBV vaccination programme, in the Loyalty Islands (New Caledonia)	1, 2
Bertolino (1996)	Newborn HBV immunization rates in primary care practices	1
Bonani (1995)	Implementation in Italy of a universal vaccination programme against HBV	1
Bonani et al. (2003)	Impact of universal vaccination programmes on the epidemiology of HBV: 10 years of experience in Italy	1
Chang et al. (2007)	Perinatal HBV transmission and vaccination timing in a managed care cohort: assessment of the temporary delay in newborn HBV vaccination due to thimerosal content	1 Birth dose defined as within 90 days
Chen et al. (2001)	Developing partnerships in Washington State to prevent HBV infection in Asian Americans and Pacific Islanders	7

First author (Year)	Title	Reason for exclusion
Chien et al. (2006)	Nationwide HBV vaccination programme in Taiwan, China: effectiveness in the 20 years after it was launched	3
Clark et al. (2011)	Private-sector vaccine purchase costs and insurer payments: a disincentive for using combination vaccines?	1
Clayton et al. (1993)	HBV control in China: knowledge and practices among village doctors	1 Not clear if birth dose was included
Cui et al. (2010)	Factors associated with effectiveness of the first dose of hepatitis B vaccine in China: 1992–2005	4
Da Vila et al. (1992)	A pilot model of vaccination against HBV suitable for mass vaccination campaigns in hyperendemic areas	1
Dawar et al. (2002)	Measuring hepatitis B uptake in a new universal infant programme	1
De Wals (2011)	Optimizing the acceptability, effectiveness and costs of immunization programmes: the Quebec experience	1
Denis et al. (2006)	Mass vaccination against hepatitis B: the French example	1, 2
Euler et al. (2003)	Impact of four urban perinatal hepatitis B prevention programmes on screening and vaccination of infants and household members	4
Faustini et al. (2001)	Factors associated with HBV immunization coverage at the beginning of a population campaign in the Lazio region, Italy	1
Ferson et al. (1997)	Fragmentation of scheduled visits and missed doses among infants receiving multiple injected vaccines	2
Fong et al. (1990)	Awareness and acceptance of hepatitis B vaccination in Clementi, Singapore	1
Froehlich et al. (2001)	Compliance with hepatitis B vaccination in a high-risk population	1
Gilca et al. (2009)	Attitudes of nurses toward current and proposed vaccines for public programs: a questionnaire survey	2
Giraudon et al. (2009)	Factors associated with incomplete vaccination of babies at risk of perinatal hepatitis B transmission: a London study in 2006	1
Glauber et al. (2003)	The immunization delivery effectiveness assessment score: a better immunization measure?	1
Harpaz et al. (2000)	Elimination of new chronic HBV infections: results of the Alaska immunization program	4
Henning et al. (1992)	A neonatal hepatitis B surveillance and vaccination program in New York city, 1987 to 1988	3
Hipgrave et al. (2003)	Hepatitis B infection in rural Viet Nam and the implications for a national program of infant immunization	4
Hipgrave et al. (2006)	Immunogenicity of a locally produced hepatitis B vaccine with the birth dose stored outside-the-cold-chain in rural Viet Nam	4
Hipgrave et al. (2006)	Improving birth dose coverage of hepatitis B vaccine	2
Hontelez et al. (2010)	Parental attitude towards childhood HBV vaccination in the Netherlands	1, 2

First author (Year)	Title	Reason for exclusion
Hughart et al. (1999)	The relation of parent and provider characteristics to vaccination status of children in private practices and managed care organizations in Maryland	1
Hutton et al. (2010)	Cost-effectiveness of nationwide hepatitis B catch-up vaccination among children and adolescents in China	1
Ikeda et al. (1995)	Use of multiple reporting sources for perinatal hepatitis B surveillance and follow-up	3
Jiles et al. (2001)	Undervaccination with hepatitis B vaccine: missed opportunities or choice?	1
Joyce et al. (2005)	CHIP shots: association between the state children's health insurance programs and immunization rates	1
Kramvis et al. (2010)	Implementing a birth dose of hepatitis B vaccine for home deliveries too soon in Africa	2
Larcher et al. (2001)	Overcoming barriers to hepatitis B immunisation by a dedicated hepatitis B immunisation service	1
Lauderdale et al. (1999)	Hepatitis B vaccination among children in inner-city public housing 1991–1997	1 Birth dose not within seven days
Levin et al. (2007)	An economic evaluation of thermostable vaccines in Cambodia, Ghana and Bangladesh	1
Libbus et al. (2009)	Public health management of perinatal HBV	1, 2 Refers to other studies which are not eligible
Lin et al. (2006)	Variation in hepatitis B immunization coverage rates associated with provider practices after the temporary suspension of the birth dose	2
Lu et al. (2010)	Epidemiology and prevention of HBV infection in China	4
Luna et al. (2009)	Household survey of hepatitis B vaccine coverage among Brazilian children	4
Manikkavasagan et al. (2009)	Hepatitis B vaccine uptake among at-risk infants: experience from a dedicated inner-city clinic	1
McElligott et al. (2010)	Are patient-held vaccination records associated with improved vaccination coverage rates?	1
McIntyre et al. (2004)	Does universal hepatitis B vaccination at birth have a negative impact on breastfeeding?	3
Mennito et al. (2010)	Impact of practice policies on paediatric immunization rates	1
Moisi et al. (2010)	Spatial and socio-demographic predictors of time-to-immunization in a rural area in Kenya: is equity attainable?	1
Naeem et al. (2011)	Factors associated with low hepatitis B vaccination: a user and provider perspective study in Peshawar	1
Odusanya et al. (2008)	Determinants of vaccination coverage in rural Nigeria	2
Odusanya et al. (2003)	Short-term evaluation of a rural immunization programme in Nigeria	2

First author (Year)	Title	Reason for exclusion
Owais et al. (2011)	Does improving maternal knowledge of vaccines impact infant immunization rates? A community-based randomized-controlled trial in Karachi, Pakistan	2, 3
Pathman et al. (1996)	The awareness-to-adherence model of the steps to clinical guideline compliance: the case of paediatric vaccine recommendations	1
Qiu et al. (2010)	Hepatitis B and breastfeeding in Hangzhou, Zhejiang Province, the People's Republic of China	7
Rani et al. (2009)	Hepatitis B control by 2012 in the WHO Western Pacific Region: rationale and implications	2
Reilly (2001)	The national Task Force on Hepatitis B Immunization, focus on Asians and Pacific Islanders: a chronicle of achievement	7
Ren et al. (2009)	Evaluation of an outside-the-cold-chain vaccine delivery strategy in remote regions of western China	4
Reznik (1991)	A hepatitis B vaccination programme for inner metropolitan Sydney neonates	2
Rhiner et al. (2007)	Selective immunisation strategy to protect newborns at risk for transmission of hepatitis B: retrospective audit of vaccine uptake	3
Robotin (2011)	Hepatitis B prevention and control: lessons from the east and the west	1
Ropero et al. (2005)	Progress in vaccination against hepatitis B in the Americas	3
Rubin et al. (2007)	An evaluation of the efficacy of the national immunization programme for hepatitis B	4
Santoli et al. (2004)	Insurance status and vaccination coverage among US preschool children	1
Schwarz (2012)	More lessons from the taiwanese hepatitis B virus vaccine program	3
Shen et al. (2011)	Epidemiological changes in hepatitis B prevalence in an entire population after 20 years of the universal HBV vaccination programme	4
Sloan et al. (2005)	Prevention of perinatal transmission of hepatitis B to babies at high risk: an evaluation	1
Smith et al. (1994)	Implementation of government recommendations for immunising infants at risk of hepatitis B	3
Sun et al. (2010)	Immunization status and risk factors of migrant children in densely populated areas of Beijing, China	2
Sutanto et al. (1999)	Home delivery of heat-stable vaccines in Indonesia: outreach immunization with a prefilled, single-use injection device	2
Van Damme et al. (2010)	Strategies for global prevention of HBV infection	3
Voigt et al. (1995)	Universal infant immunization for hepatitis B - from dream to reality	2
Walter et al. (1994)	A major barrier to universal hepatitis B immunization of infants	1
Wang et al. (2011)	Control of hepatitis B in China: prevention and treatment	3

First author (Year)	Title	Reason for exclusion
White et al. (1995)	Compliance with neonatal hepatitis B vaccination	3
White et al. (2009)	Evaluating hepatitis B universal birth dose vaccination at Minnesota birthing hospitals by utilizing immunization information systems, birth certificates and chart reviews 2007–2008	7
Wilson et al. (2000)	The effectiveness of the infant hepatitis B immunisation program in Fiji, Kiribati, Tonga and Vanuatu	4
Wood et al. (1995)	California paediatricians' knowledge of and response to recommendations for universal infant hepatitis B immunization	1
Woodruff et al. (1996)	Progress towards integrating hepatitis B vaccine into routine infant immunization schedules in the United States, 1991 through 1994	7
Wong et al. (1994)	A mass hepatitis B vaccination programme in Taiwan, China: its preparation, results and reasons for uncompleted vaccinations	7
Yusuf et al. (2000)	Association between administration of hepatitis B vaccine at birth and completion of the hepatitis B and 4:3:1:3 vaccine series	1
Zeng et al. (1999)	Survey of coverage, strategy and cost of hepatitis B vaccination in rural and urban areas of China	3
Zhang et al. (2010)	Perinatal transmission of HBV: could hospitals be doing more?	3
Grey literature		
Government of Cambodia (2005)	2005 Progress Report to the Global Alliance for Vaccines and Immunization (GAVI)	2, 3
WHO (2009)	Newborn care until the first week of life: clinical practice pocket guide 2009	2, 3
Wittet (2001)	Hepatitis B vaccine introduction: lessons learned in advocacy, communication and training	1
PATH (2004)	Andhra Pradesh, India: building a model immunization programme	1, 2 Not clear whether birth dose was part of the programme, and whether data is related to birth dose
PATH (2006)	Andhra Pradesh shares lessons with other states on strengthening routine immunization and introducing new vaccines	1, 2 Not clear whether birth dose was part of the programme
PATH (2006)	Protecting children for a health tomorrow: lessons learned from the Andhra Pradesh partnership project on immunization	1, 2
PATH (2006)	Strengthening immunization services through service delivery support: the Andhra Pradesh experience	1, 2
Nelson et al. (2002)	Using Uniject to increase the safety and effectiveness of hepatitis B immunization	2
Lydon (2011)	Outsourcing the vaccine-supply chain and logistics system to the private sector: the Western Cape experience in South Africa	1, 2

A1.6: Data extraction

Data from each of the 64 papers included in this review were analysed and abstracted into a standard tool developed by the authors, comprizing the following categories:

- *first author and year;*
- *study type —*
- randomized control trial (RCT), intervention study, cohort, case-control, survey, qualitative, cost-effectiveness analysis, systematic review, literature review, evaluation, conference/workshop proceedings, opinion piece, or report;
- *study aims;*
- *setting;*
- *definition of birth dose;*
- *group classification;*
- *sub-group classification;*
- *description of the practice, facilitator and/or barrier;*
- *outcome.*

The above information from each paper was recorded by both reviewers and cross-checked for any inconsistencies. A description of the group and sub-group classifications is provided in Table 1 in the main body of the paper.

Annex 2:

Technical consultation participants and programme

1. Consultation on birth dose vaccination for prevention of perinatal transmission of HBV (7–8 December 2010, Melbourne)

Consultation participants

Name	Affiliation	Organization
Dr Salah Al Awaidy	National Government	Department of Communicable Disease Surveillance & Control, Ministry of Health, Oman
Mr David Handojo Muljono	National Government	Ministry of Health and Eijkman Institute, Indonesia
Dr Iwan Ariawan Mihardja	National Government	Centre for Health Research, Universitas Indonesia
Dr Bill Lagani	National Government	Family Health Services, National Department of Health, Papua New Guinea
Dr Cui Fuqiang	National Government	National Immunization Programme, Chinese Centre for Disease Control and Prevention, China
Dr M.A. Silvestre	National Government	University of the Philippines, Manila, Philippines
Dr Karen Hennessy	WHO	EPI Focal Point, WHO Regional Office for the Western Pacific
Dr Howard Sobel	WHO	Country Office, Philippines, WHO Regional Office for the Western Pacific
Dr Siddhartha Datta	WHO	Country Office, Papua New Guinea, WHO Regional Office for the Western Pacific
Dr Severin Von Xylander	WHO HQ	MCH/MPS, WHO
Dr Steven Wiersma	WHO HQ	EPI, WHO, co-convenor
Kye Mohd Hanafiah	WHO HQ	EPI, WHO
Dr Robin Biellik	Partner	IPAC representative
Dr Trudy Murphy	Partner	National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Centers for Disease Control, USA
Dr Linda Quick	Partner	Global Immunization Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control, USA
Dr Minal Patel	Partner	Global Immunization Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control, USA

Name	Affiliation	Organization
Dr Tilman Ruff	Expert	Nossal Institute for Global Health
Dr David Anderson	Partner	Burnet Institute
Dr Chris Morgan	Partner	Burnet Institute, Compass Women's and Children's Health Knowledge Hub, co-convenor
Ms Kylie Carville	Partner	Victorian Infectious Diseases Research Laboratory
Dr Tony Stewart	Partner	Burnet Institute
Dr Ben Cowie	Partner	Victorian Infectious Diseases Research Laboratory
Ms Simona Zipursky	Partner	Project Optimize, PATH
Ms Levinia Crooks AM	Regional partner	Australasian Society for HIV Medicine
Mr Edward Reis	Regional partner	Australasian Society for HIV Medicine
Dr John Clements	Regional partner	Reporting on WHO Regional Office for Africa meeting
Ms Helen Tyrell	Partner	Hepatitis Australia

2. Consultation programme

Day 1: Tuesday 7 December 09:00 to 17:30

Time	Session	Presenters
09:00	1. Introduction and overview	
	Welcome and introductions	WHO and Burnet
	Global context, policy and meeting aims	Steven Wiersma, WHO Geneva
	IPAC introduction	Robin Biellik, Consultant IPAC
	Overview of literature and key themes	Kylie Carville, Ben Cowie, VIDRL
10:45	Break	
11:15	2. Country experiences	
	China	Cui Fuqiang, China CDC
	The Philippines	'Mianne' Silvestre, Philippines General Hospital; Howard Sobel, WHO, the Philippines
	Oman	Salah Al Awaidy, MOH
	Indonesia	David Muljono, Eijkman Institute; Iwan Mihardja, Universitas Indonesia
	WHO Regional Office for Africa	John Clements, Consultant
	United States of America	Trudy Murphy, CDC
	Papua New Guinea	William Lagani MOH, Siddhartha Datta, WHO Papua New Guinea
13:00	Break	

Time	Session	Presenters
13:30	3. Maternal and newborn health (MNH) linkages with birth dose vaccination	
	Global overview of MNH links	Severin Ritter Von Xylander, WHO Geneva
	Postnatal and perinatal care links	Chris Morgan, Burnet
	Innovative newborn care in Africa	Karen Edmond, LSHTM
14:30	4. What should be included in a best-practice guide for birth-dose vaccination	
	Discussion	
17:30	Close	

Day 2: Wednesday 8 December

Time	Session	Presenters
09:00	5. Current state of tools to support countries	
	Frameworks and checklists	Karen Hennessey, WHO Western Pacific Region
	Modelling prevalence	Ben Cowie, VIDRL; Tony Stewart, Burnet
	Discussion on tools available and needed	
10:45	<i>Break</i>	
11:15	6. Future developments, knowledge gaps and capacity development	
	Viewpoints	Simona Zipursky, Project Optimize PATH; Linda Quick, CDC; Tilman Ruff, Nossal Institute for Global Health
	Review of background document	Discussion
13:00	<i>Break</i>	
13:30	7. Continued discussion on best-practice guide, and future work programme	
	Discussion	
15:00	8. Reflections and conclusion	
	Discussion	
	Next steps	Steve Wiersma, WHO; Chris Morgan, Burnet
16:00	<i>Close</i>	

Annex 3:

Grade criteria for appraising the evidence

the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria were used to appraise the evidence in this review, including the few situations where studies could be combined. The criteria and scoring system adopted is detailed below. The original GRADE methodology has been adapted to suit the types of literature identified here, and the topic of this review. Two WHO publications, which used GRADE criteria to appraise evidence, have also been used as a guide to develop the scoring criteria.* For more information on GRADE, see <http://www.gradeworkinggroup.org/index.htm>.

* *Guidelines for the management of postpartum haemorrhage and retained placenta*. Geneva World Health Organization, 2009; *Recommendations for prevention and treatment of pre-eclampsia and eclampsia*. Geneva, World Health Organization, 2011.

Table A3: GRADE criteria used in appraising the evidence

Criterion	Description	Scoring	
		Grade	Characteristic
Before starting appraisal, assign each study a baseline score			
Study design	Assign a starting baseline score depending on study type	High	RCT
		Moderate	Non-randomized intervention study
		Low	Observational study
		Very low	Other evidence (but not grey literature)
For each criterion below, assess and downgrade according to scoring description			
Study design limitations	Overall judgement on the quality of study with respect to biases such as selection bias, performance bias, detection bias, attrition bias, reporting bias, confounding factors not controlled For RCTs this includes, for example, lack of allocation concealment or large loss to follow-up Consider here whether study has looked at impact of one practice on coverage, or multiple practices making it difficult to determine extent of impact	0	All studies have a low risk of bias
		-1	Studies have a moderate or high risk of bias. Majority of studies are of moderate risk of bias
		-2	Studies have a moderate or high risk of bias. Majority of studies are of high risk of bias
Inconsistency	Inconsistencies in direction of the coverage outcome (i.e. increase versus decrease) across studies Plausible explanation not provided by authors for inconsistency in coverage result	0	No severe heterogeneity
		-1	Severe, unexplained heterogeneity *Do not downgrade if heterogeneity could be due to small sample size, downgrade in scoring related to imprecision
Indirectness	Study uses an indirect comparison, population, intervention, comparator or outcome	0	No indirectness
		-1	There is indirect comparison, population, intervention, comparator or outcome
Imprecision	Small sample size Wide confidence intervals Confidence intervals where odds ratios are reported include equal effect (i.e. OR = 1) or appreciable likelihood or non-likelihood	0	No, or neglible imprecision
		-1	One of the conditions related to sample size or confidence intervals is seen
		-2	Small sample size and one of the conditions related to confidence intervals is seen

Annex 4:

Summary of included studies

abbreviations used in the table

BD = Birth dose, SD = Service delivery, HW = Health workforce, HIS = Health information systems, T = Medical products, vaccines and technologies, FN = Financing, GL = Governance & leadership, OR = Odds ratio, CI = Confidence interval, P = Practice, F = Facilitator, B = Barrier

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/I/B	Outcome
1	Aiken et al. (2002)	Qualitative	USA	Random national sample of 296 hospital nurseries Low-risk infants	To explore why some hospitals do not offer the hepatitis B vaccine to low-risk newborns	"At birth"	HW	Knowledge, attitudes and training	Perceptions that the population was at low risk of HBV infection (B)	Decreased coverage in birth dose vaccination
							HW	Knowledge, attitudes and training	Perceptions that infants' parents are compliant and will come to hospital for the first dose of the hepatitis B vaccine when the infant is two months old (B)	
							HIS	Vaccination records	Difficulties in transferring vaccination records to primary physicians (B)	
							FN	Funding for birth dose programmes	Difficulties in obtaining reimbursement for the birth dose vaccine (B)	
2	Bascom et al. (2005)	Cohort	USA	Birth cohort of year 2000 in 25 delivery hospitals in New Hampshire	To evaluate current performance on recommended perinatal HBV and rubella prevention practices in New Hampshire	Within 12 hours of birth	GL	Policies and guidelines	Change in national policy regarding administration of the hepatitis B birth dose (B)	Children born during the months right after the policy change were 8.2 times less likely to be vaccinated with the birth dose compared to children born in subsequent months
3	Bialek et al. (2010)	Survey	Micronesia (Federated States of) and Marshall Islands (the)	Children born before and children born after implementation of routine hepatitis B vaccination	To evaluate the impact of routine hepatitis B vaccination on the prevalence of chronic HBV infection among children in Pacific Island countries	On the day of birth	SD	Location of service delivery	Implementation of a policy on universal birth dose vaccination (P)	Birth dose coverage among children born after implementation of the policy was 76%, as opposed to 29% among children born before implementation (p < 0.001)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
4	Biroschak et al. (2003)	Survey	USA	75 children before, 81 born during, and 60 children born after change in policy	To assess the impact of the USPHS/AAP policy on birth dose coverage for infants who are born to women with unknown HBsAg status	Before discharge Within 12 hours	GL	Polices and guidelines	Change in national recommendations on administration of birth dose vaccine (B)	Proportion of infants vaccinated with the birth dose before the change in recommendations was 53%, 7% during the period of changed recommendations ($p<0.001$) and 57% after original recommendations were reinstated Proportion of infants vaccinated within 12 hours of birth was 19% before the change in recommendations, 1% during the period of changed recommendations ($p<0.001$) and 14% after original recommendations were reinstated (difference for latter not significant)
5	Brayden et al. (2000)	Survey & qualitative	USA	Nine hospitals providing obstetric services in two regions of rural Colorado	To assess hospital policies for administering the hepatitis B vaccine and for communicating administration of the vaccine, and the extent of apparent under-vaccination accounted for by ineffective communication to the primary-care clinicians and information sources used to determine neonatal HBV vaccine status	Before discharge	HIS	Vaccination records	No written policy for acquisition of or acceptable documentation of neonatal birth dose vaccination (B)	Newborns not being vaccinated in cases where vaccination was assumed (no figure provided)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
6	Cabana, Aiken et al. (2002)	Survey	USA	Directors of a national random sample of 207 nurseries	To examine the association between newborn hepatitis B vaccination in hospital nurseries and state-financing strategies	"At birth"	GL	Policies and guidelines	Change in national recommendations on the hepatitis B birth dose (B)	Of 120 nurseries that had a strict policy to vaccinate all low-risk babies with the birth dose, 31% changed policies towards less strict immunization policies after changes in national recommendations, even after thimerosal-free vaccines were available
7	Cabana, Aiken & Clark (2002)	Survey	USA	Directors of a national random sample of 207 nurseries	To describe how hospital nurseries develop hepatitis B vaccination policies	"At birth"	GL	Policies and guidelines	Different sources of information on change in national recommendations on birth dose vaccination (B/F)	A significant number of nurseries received information on changes in national recommendations from pharmaceutical companies (16–28%), as well as from nurses (5%) and pharmacists (7–10%)
8	Chunsubutwat (1997)	Review	Thailand	Children aged 12–23 months in the Provinces of Chonburi and Chiangmai	To report on the successful integration of hepatitis B vaccination into EPI and present results of immunogenicity and efficacy of the hepatitis B vaccine when used for routine immunization	"At birth"	SD	Integration within the EPI	Integration of hepatitis B vaccination, including the birth dose, within the EPI (P)	Coverage with three doses of the hepatitis B vaccine (including the birth dose) increased from 0% at the start of the project to 90% after four years

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
9	Clark et al. (2001)	Survey	USA	Random sample of 773 hospitals across the country	To explore changes in hepatitis B vaccination practices for newborns related to the revised recommendations	Before discharge	HW	Knowledge, attitudes and training	Resistance from physicians to vaccinate newborns with the hepatitis B birth dose (B)	38% of hospitals that reported physician resistance vaccinated all low-risk infants, compared to 62% of hospitals where there was no resistance ($p < 0.05$)
								Policies and guidelines	Increase in inappropriate practices following a change in national recommendations on administration of the birth dose vaccine (B)	Following the change in policy, 69% of hospitals surveyed administered the birth dose to infants born to HBsAg-positive mothers and 39% of hospitals to infants born to mothers of unknown status, as opposed to 88% and 69% respectively of hospitals prior to the change in policy
							GL	Policies and guidelines	Confusion around change in national recommendations on administration of the birth dose vaccine (B)	45% of hospitals that reported confusion around the policy change vaccinated all low-risk infants, as opposed to 55% of hospitals that did not report confusion ($p < 0.05$)
10	Clements (2006)	Review	Western Pacific Region	Infants born within the Western Pacific Region	To summarize the progress of HBV control in the Western Pacific Region and to discuss the issues which continue to have an impact on the achievement of the goal set by the WHO Regional Committee	Within 24 hours of birth	SD	Access to a trained health worker	Home birth (B)	Hepatitis B birth dose vaccine not administered to newborn within 24 hours of delivery
							HW	Delineation of responsibilities	Birth attendant is not responsible for immunization and therefore has no access to the vaccine (B)	Hepatitis B birth dose vaccine not administered to newborn even when delivery is in a health facility
							T	Vaccine storage and access to the cold chain	Lack of cold storage facilities in rural areas (B)	Difficulties in administering the hepatitis B birth dose within 24 hours of delivery

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
11	Connors et al. (1998)	Survey	Australia	Infants born in two hospitals that provide maternity services for women in Darwin	To compare live births with vaccine usage to determine the uptake of the first dose of hepatitis B vaccine under this new policy and to identify hospital factors that influenced this rate	"At birth"	GL	Policies and guidelines	Recommending hepatitis B vaccination for low-risk neonates (P)	Birth dose coverage was 96% and 93% in 1993 and 1994 respectively in the hospital that had a standing order and recommended hepatitis B vaccination, compared to 71% and 77% in 1993 and 1994 respectively in the hospital that did not have the standing order and did not recommend vaccination (no p-value provided)
							GL	Standing orders	Having a standing order on hepatitis B vaccine for neonates in postnatal ward (P)	
12	Cooper et al. (2001)	Survey	USA	National sample of 600 practicing paediatricians	To evaluate the attitudes and practices of paediatricians in the USA regarding the hepatitis B birth dose vaccine	"At birth"	SD	Location of service delivery	Location of physician's practice at a hospital or a non-profit clinic (F)	75% of paediatricians based at a city or county hospital, or a non-profit clinic, and 74% of paediatricians based at a medical school-based hospital administered the birth dose, as opposed to less than 50% of paediatricians working in group or individual practices ($p < 0.05$)
							HW	Knowledge, attitudes and training	Paediatricians' belief in the importance of the birth dose (F)	

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
12	Cooper et al. (2001) Continued	As in previous row	As in previous row	As in previous row	As in previous row	As in previous row	HIS	Vaccination records	Difficulties in tracking immunizations in the hospital (B)	29% of paediatricians who strongly agreed, or agreed that tracking vaccines given in the hospital was difficult administered the birth dose, as opposed to 45% of paediatricians who were neutral and 66% of paediatricians who strongly disagreed, or disagreed that there were difficulties (p < 0.001)
							FN	Financing for birth dose	Increased cost to vaccinating in the hospital (B)	25% of paediatricians who strongly agreed, or agreed that there was an increased cost to vaccinating in the hospital administered the birth dose, as opposed to 43% of paediatricians who were neutral and 67% of paediatricians who disagreed, or strongly disagreed that there was an increased cost (p < 0.001)
							FN	Financing for birth dose	No reimbursement from insurance companies for hepatitis B birth dose administered in the hospital (B)	24% of paediatricians who strongly agreed, or agreed that the insurance company may not reimburse for vaccination administered the birth dose, as opposed to 48% of paediatricians who were neutral and 66% of paediatricians who disagreed, or strongly disagreed that the insurance company many not reimbursement the costs (p < 0.001)
							GL	Policies and guidelines	Having a universal immunization distribution policy (P)	80% of paediatricians based in a state with a universal vaccination policy administered the birth dose, as opposed to less than 50% of paediatricians in states with no universal policy (p < 0.001)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
13	Creati et al. (2007)	Review	Indonesia	Infants born in districts where demonstration projects were implemented	To identify and discuss operational issues key to the successful delivery of a timely birth dose vaccine	Within seven days of birth	HW	Delineation of responsibilities	Reluctance from immunization staff to give vaccines to midwives due to mistrust (B)	Decreased coverage Study outcome: 7% of infants born at home were immunized on the day of delivery, 16% within 24 hours and 39% within one week
							HW	Attitudes, knowledge and training	Anxiety among village midwives that if an infant died after vaccination, midwives would be blamed by the community (B)	
							GL	Policies and guidelines	The national policy on hepatitis B birth dose stated that the birth dose should be given within the first seven days rather than within 24 hours (B)	
							T	Vaccine storage and access to the cold chain	Greater storage requirements for ten doses of the hepatitis B vaccine in Uniject devices (B)	
							T	Vaccine presentation	Reluctance to open hepatitis B 10-dose vials to immunize a few infants due to fears of wastage (B)	

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
14	Centers for Disease Control and Prevention (CDC) (2007)	Review	China	Infants who have been immunized against HBV	To describe China's progress in increasing coverage among infants with hepatitis B vaccine and timely administration of the birth dose	Within 24 hours	SD	Demand for vaccination	Increasing the awareness of the importance of timely birth dose administration among providers and parents (P)	Timely birth dose coverage increased from 29.1% among children born in 1997 to 75.8% among children born in 2003
							SD	Access to a trained health worker	Increasing the percentage of births that occur in hospitals (P)	
							SD	Linkages between immunization and maternity services	Building collaboration among delivery services and between vaccination services (P)	
							HW	Knowledge, attitudes and training	Intensifying training, supervision and monitoring of county, township and village health workers (P)	
							T	Procurement, supply and distribution systems	Improving vaccine availability in hospitals and township health facilities (P)	As in previous row
15	Danielsson et al. (2009)	Survey	Tonga	449 children aged 6–59 months who were admitted to one hospital or visiting the outpatient clinic from Dec 2004–April 2007	To measure the impact of improved immunization practices on the prevalence of HBV infection in preschool children, and to assess the progress towards HBV elimination in Tonga	Within 24 hours, and within seven days	HW	Task-shifting	Transfer of responsibility for delivering the birth dose vaccine from EPI staff to midwives and nurses who attend deliveries (P)	Of 445 children for whom immunization data was available, 92% (CI: 89 – 94) received the first dose within 24 hours after birth. In contrast, only 14% (CI: 11 – 18) of children received the first dose of BCG within 24 hours after birth

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
16	de la Hoz et al. (2005)	Survey	Columbia	3044 children between the ages of one and 12 years in four areas of the Amazon Department	To measure vaccine coverage with hepatitis B and other EPI vaccines, and to identify individual factors and health-service characteristics that influenced coverage	Within 72 hours	SD	Location of service delivery	Child having siblings (F)	In multivariate analysis, odds of non-complete vaccination compared to children with no siblings (reference): OR for children with 2/3 siblings = 2.9 (CI: 1.0 – 8.6) OR for children with 4/5 siblings = 3.3 (CI: 1.2 – 10.6) OR for children with 4/20 siblings = 2.8 (CI: 0.9 – 9.1) (p < 0.05)
							HW	Knowledge, attitudes and training	Higher number of years that health worker had worked at the health centre (F)	In multivariate analysis, odds of non-complete vaccination compared to health workers who had worked for 0/14 years (reference): OR if the health workers had worked for 15/21 years: = 0.4 (CI: 0.2 – 0.6)
									Health workers' belief that there were contraindications to hepatitis B vaccination (B)	In multivariate analysis, odds of non-complete vaccination compared to if worker believed there were no contraindications (reference): OR if worker believed there were contraindications = 2.3 (CI: 1.1 – 5.1)
							T	Procurement, supply and distribution systems	Lack of vaccine supplies (B)	In multivariate analysis, odds of non-complete vaccination compared to if there was a supply of vaccines (reference): OR if there were no vaccine supplies = 3.2 (CI: 1.8 – 5.5)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
17	Downing et al. (2008)	Qualitative	Papua New Guinea	Willing maternity unit health-care workers in five main hospitals in four regions	To examine hepatitis B birth dose coverage, the attitudes and practices of staff, and the barriers to delivery of a hepatitis B birth dose in five major hospitals	Within 24 hours	HW	Knowledge, attitudes and training	Incorrect practices observed in relation to administration of the birth dose vaccine (B)	Birth dose not routinely offered or administration delayed Coverage of timely birth dose was 79% across five hospitals (range 40% to 96%)
							HW	Knowledge, attitudes and training	Poor knowledge among health workers on hepatitis B birth dose and contraindications (B)	
							HW	Delineation of responsibilities	Designated immunization nurse in one hospital (P)	Coverage of timely birth dose in the hospital increased from less than 40% to over 80%
							T	Procurement, supply and distribution systems	Lack of a hepatitis B vaccine stock in the labour ward due to storage of the vaccine in another ward (B)	
18	Government of Indonesia (2008)	Report	Indonesia	Newborns	Annual Progress Report 2007 submitted to GAVI on GAVI-funded programmes	Within seven days	SD	Demand for vaccination	Low awareness among mothers for the need of hepatitis B birth dose (B)	Low coverage of timely birth dose (no figure provided)
19	Government of the People's Republic of China (2006)	Report	China	Newborns	Annual Progress Report 2005 submitted to GAVI on GAVI-funded programmes	Within 24 hours	SD	Demand for vaccination	Information, education and communication (IEC) activities to increase awareness of the hepatitis B birth dose (P)	Coverage of timely birth dose increased from 40% in 2004 to 70% in 2005 in Qinghai
							HW	Knowledge, attitudes and training	Training provided to village doctors and birth attendants in Qinghai (P)	Timely birth dose coverage increased from 40% in 2004 to 70% in 2005 in Qinghai
							HW	Knowledge, attitudes and training	Inadequately trained staff, particularly at the county level and below (B)	Low coverage of timely birth dose (below the target of 75%), particularly in counties with high rates of home births

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
19	Government of the People's Republic of China (2006) Continued	As in previous row	As in previous row	As in previous row	As in previous row	As in previous row	T	Procurement, supply and distribution systems	Poor management of vaccine supplies (B)	Low coverage of timely birth dose (below the target of 75%), particularly for counties with high rates of home births
							HIS	Registries	Registration of pregnant women (P)	Coverage of timely birth dose increased from 40% in 2004 to 70% in 2005 in Qinghai. Coverage of home births with timely birth dose increased from 20% to 60%
							FN	Funding for birth dose programmes	Insufficient operational funds at the county level, particularly in the poorest counties with low timely birth rates (B)	Low timely birth dose (well under the target of 75%) in certain counties of China
20	Government of the People's Republic of China (2008)	Report	China	Newborns	Annual Progress Report 2007 submitted to GAVI on GAVI-funded programmes	Within 24 hours	SD	Access to a trained health worker	Low rate of deliveries in hospitals, at 53.3% (B)	Infants requiring birth dose were not being vaccinated
							T	Procurement, supply and distribution systems	Inadequate number of vaccines stored at the village level (B)	Between January to August 2007, coverage of the third dose of the hepatitis B vaccine was 98.2% compared to 74.1% for timely birth dose
							T	Procurement, supply and distribution systems	Poor management of vaccines and auto-disposable syringes (B)	545 counties have not met the goal of 75% coverage of timely birth dose in China
							HIS	Registries	Floating and migrating populations (B)	Inaccurate data on target population for birth dose In Wushan County and Xigu District of Gansu Province, coverage of timely birth dose was 74.1%, below the target of 75%
							FN	Funding for birth dose programmes	Insufficient funds for operational activities (B)	545 counties have not met the goal of 75% coverage of timely birth dose in China

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
20	Government of the People's Republic of China (2008) Continued	As in previous row	As in previous row	As in previous row	As in previous row	As in previous row	GL	Policies and guidelines	Strict standards on vaccine contraindications (B)	Premature or low-birth-weight infants were not being vaccinated within 24 hours Coverage of the third dose of the hepatitis B vaccine was 98.2% compared to 74.1% for timely birth dose between January to August 2007
21	Hu et al. (2001)	Survey	China	2632 children born 2008–2009 above the age of 12 months in Zhejiang Province	To assess the immunization coverage for the primary vaccination series and the determinants of this coverage in Zhejiang	"At birth"	SD	Political commitment Demand for vaccination	Insufficient attention to timely birth dose from prefectures and counties; lack of supervision (B) Parents' satisfaction with clinical immunization services (F)	545 counties have not met the goal of 75% coverage of timely birth dose in China In multivariate analysis, odds of being vaccinated compared to infants whose parents were not satisfied with services (reference): OR for infant being vaccinated if parents were satisfied = 2.1 (CI: 1.5 – 4.3, $p < 0.05$)
							SD	Demand for vaccination	Family's high socio-economic status (F)	In multivariate analysis, odds of being vaccinated compared to infants from low-income families (reference): OR for infant being vaccinated if from a high-income family = 2.3 (CI: 1.3 – 2.9, $p < 0.05$)
							SD	Demand for vaccination	Mother's high level of education (F)	In multivariate analysis, odds of being vaccinated compared to infants whose mother had middle-school level education (reference): OR for infants being vaccinated if mothers had college or higher-level education = 2.8 (CI: 1.1 – 7.3, $p < 0.05$).

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
21	Hu et al. (2001) Continued	As in previous row	As in previous row	As in previous row	As in previous row	As in previous row	HIS	Registries	Registration of household (F)	In multivariate analysis, odds of being vaccinated compared to infants from a household that was not registered with the local authorities (reference): OR for infant being vaccinated if household was registered = 2.7 (CI: 1.8 – 4.1, $p < 0.05$)
22	Hurie et al. (2001)	Survey	USA	98 nursery nurse managers in hospitals in Wisconsin	To determine the extent to which hospital infant hepatitis B vaccination policies have changed in response to the thimerosal concern	Before discharge	GL	Policies and guidelines	Change in national recommendations on administration of the birth dose (B)	Number of hospitals offering routine birth dose vaccination decreased by percentage in the range of 11% to 72%, depending on the region
23	Jacques-Carroll et al. (2009)	Survey	USA	56 federally funded immunization city and state grantees	To compare newborn hepatitis B vaccination coverage for infants born in jurisdictions with universal vaccination policies, with those born in jurisdictions without these policies	Within 48 hours of birth	GL	Policies and guidelines	Having a universal policy to provide hepatitis B vaccines to delivery hospitals for a birth dose to all infants (P)	Median coverage of hepatitis B birth dose among programmes with a universal policy was 65% (21.4% – 83.3%), compared to a coverage rate of 43% (9.9% – 65.4%) for programmes without such policies ($p < 0.05$)
24	Kuruvilla et al. (2009)	Survey	India	202 infants in rural areas of Thiruvallur district and 205 infants in Chennai, aged 12–24 months	To analyse the rural/urban difference in the timing of the first dose of hepatitis B, OPV and BCG vaccines among infants in Tamil Nadu	Day of birth	SD	Location of service delivery	Birth in rural areas (B)	Coverage of the hepatitis B birth dose vaccine was lower in rural areas, at 3.5%, compared to a coverage of 11% in urban areas ($p < 0.05$)
25	Levin et al. (2005)	Cost-effective analysis	Indonesia	Children born in three provinces; West Nusa Tenggara, Yogyakarta, East Java	A retrospective cost-analysis of delivering the vaccine at birth using the Uniject prefill injection device	Within seven days of birth	T	Vaccine delivery technologies and disposal	Hepatitis B birth dose provided through single-dose auto-disposable Uniject devices (P)	Two years after using Uniject to deliver the birth dose, coverage of birth dose increased from 68% to 80% in West Nusa Tenggara, from 0% to 86% in Yogyakarta and from 0 to 38% in East Java

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
26	Liang et al. (2009)	Survey	China	40 219 children born during period 1 January 1992 to 31 December 2005 in 160 national disease surveillance points in 31 provinces	To describe immunization coverage among children born after integration of the hepatitis B vaccine into routine immunization, to identify risk factors for under-immunization and to evaluate impact of the hepatitis B vaccine	Within 24 hours	SD	Access to a trained health worker	Home birth (B)	In multivariate analysis, odds of low timely birth dose coverage compared to infants born in county hospitals (reference): OR for infants born at home = 7.6 (CI: 5.7 – 10.2), $p < 0.01$
							SD	Demand for vaccination	Residence in a rural location (B)	In multivariate analysis, odds of low timely birth dose coverage compared to infants born in urban areas (reference): OR for infants born in rural areas = 2.6 (CI: 2.1 – 3.3, $p < 0.01$)
							FN	Cost to recipient	Birth before 2001 when policy to provide vaccination free-of-cost was implemented	In multivariate analysis, odds of low timely birth dose coverage compared to infants born after 2001 (reference): OR for infants born before 2001 = 5.5 (CI: 4.8 – 6.3, $p < 0.01$)
27	Luman et al. (2004)	Cohort	USA	41 589 American children born before, during and after the recommendation to suspend birth dose in July 1999	To determine the effects of changes in recommendations regarding administration of a hepatitis B birth dose on vaccination coverage	Within 48 hours of birth	SD	Linkages between immunization and private health services	Having a private provider (B)	In multivariate analysis, odds of being vaccinated with the birth dose compared to infants with private providers: OR for infants with a public provider = 1.3 (CI: 1.2 – 1.5)
							SD	Location of SD	Residence in a suburban area (B)	In multivariate analysis, odds of being vaccinated with the birth dose compared to infants living in rural areas: OR for infants living in suburban areas = 0.8 (CI: 0.7 – 0.9)
							GL	Policies and guidelines	Change in national recommendations on the hepatitis B birth dose (B)	Prior to the change, 47% of infants received the birth dose; during suspension of the policy, coverage decreased to 11%

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27	Luman et al. (2004) Continued	As in previous row	As in previous row	As in previous row	As in previous row	As in previous row	SD	Demand for vaccination	One-child household (B)	In multivariate analysis, odds of being vaccinated with the birth dose compared to infants from households with two or more children: OR for infants who were the only child = 0.9 (CI: 0.8 – 1)
								Demand for vaccination	Age of mother is above 30 years (B)	In multivariate analysis, odds of being vaccinated with the birth dose compared to infants whose mother was above the age of 30 years: OR for children whose mothers were under the age of 19 or between the ages 20–29 = 1.2 (CI: 1 – 1.6)
28	Maayan-Metzger et al. (2005)	Survey	Israel	Mothers of healthy term singleton babies who gave birth at a large tertiary hospital in Israel, January to September 2003	To compare the characteristics of mothers who refused to administer the hepatitis B vaccine to their newborn infants to characteristics of those mothers who complied	"At birth"	SD	Demand for vaccination	Mother's perception that vaccination was not required or would cause harm to the baby (B)	Hepatitis B birth dose vaccine not administered to newborn
								Demand for vaccination	Mother not intending to comply with the full series of hepatitis vaccination for their child (B)	Hepatitis B birth dose vaccine not administered to newborn
								Demand for vaccination	High socio-economic status (B)	Hepatitis B birth dose vaccine not administered to newborn
								Demand for vaccination	Mother's high level of education (B)	Mothers whose newborns were not vaccinated had more years of education than mothers whose newborns were vaccinated (p < 0.001)
29	Madlon-Kay et al. (2011)	Cohort	USA	857 newborns born at Fairview Riverside Hospital from January to June 2007 and from January to June 2008	To determine the effect of changing routine nursery orders on hepatitis B birth dose coverage	Before discharge	GL	Standing orders	Having a nursery order requiring physicians to opt out of hepatitis B birth dose vaccination (P)	Coverage of hepatitis B birth dose vaccination increased from 73% in 2007 to 84% in 2008 (p < 0.001)
								Vaccination records	Use of existing vaccination records and forms to report on hepatitis B birth dose vaccination (F)	Increase in birth dose coverage

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
30	Manea et al (1992)	Intervention study	Micronesia (Federated States of)	Newborns up to children aged six years	To carry out a HBV campaign to immunize children with three doses of the vaccine	Before discharge	HW	Delineation of responsibilities	Experienced immunization nurses coordinating the vaccination campaign	Coverage of all three doses (including birth dose) of the hepatitis B vaccine increased from 67% in 1988 to 92% in 1990 across the Federated States of Micronesia
31	Mercier et al. (2007)	Intervention study	USA	Healthy, newborn infants born at 12 Vermont hospitals with obstetric services	To examine the effects of a quality improvement intervention on the delivery of newborn preventive health-care services during the birth hospitalization in a statewide sample of community hospitals delivering obstetric care	"At birth"	HIS	Vaccination records	Use of existent forms and records to monitor hepatitis B vaccination	Hepatitis B birth dose coverage decreased from 45% pre-intervention to 30% post-intervention ($p = 0.19$)
							SD	Quality improvement	Specific quality improvement interventions (P)	

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
32	Morgan et al. (2010)	Evaluation	Papua New Guinea	Newborns born within the catchment areas of seven health centres in Angoram District of the East Sepik Province	To test the feasibility of reaching newborns on the first day of life with a simple package of services, including vaccination, by rural health staff and trained community health volunteers	Within 24 hours	SD	Linkages between immunization and early newborn care services	Hepatitis B birth dose vaccination integrated within a package of early newborn care services (P)	Overall coverage of timely birth dose vaccination was 83%, specifically 65% for home births and 93% for health-centre births at the end of the project compared to 18% for the district average and likely to be close to zero for home births at baseline in 2008
							HW	Task-shifting	Deploying village health workers to deliver birth dose vaccination (P)	
							T	Vaccine delivery technologies and vaccine disposal	Use of Uniject as the device to deliver the birth dose vaccine	
							T	Storage and access to the cold chain	Uniject birth dose vaccine stored out-of-the-cold-chain (P)	Overall coverage of timely birth dose vaccination was 83%, specifically 65% for home births and 93% for health-centre births at the end of the project compared to 18% for the district average and likely to be close to zero for home births at baseline in 2008
							HIS	Birth notification	For each birth, the VHVs completed a birth record form, collecting a variety of information, including when the VHVs visited the baby and mother, whether the visit was within 24 hours of birth and what health and education interventions were given (P)	

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33	Murakami et al. (2008)	Qualitative	Viet Nam	60 commune EPI staff, and 52 mothers of infants at the commune level in four provinces	To assess the operational mechanisms and cost of providing birth dose of hepatitis B in Viet Nam, and to identify the major influences on birth dose coverage	Within 72 hours	SD	Linkages between immunization services and private health-care services	Weak linkages between private health facilities and the national EPI programme (B)	Birth dose coverage in the district with the highest percentage of deliveries in private facilities, at 47%, within the sample surveyed, had the lowest coverage of birth dose (within 72 hours) at 52% compared to 87%–97% in other districts
							HIS	Registries	Tracking of pregnancies by village health workers and community health workers (P)	In districts where pregnancies were tracked, coverage of birth dose administered within 72 hours was 96.9% and 89.6%, compared to 87.3%, 51.7% and 44.5% in districts where there was no tracking
							GL	Policies and guidelines	Large hospitals in Viet Nam can establish their own clinical guidelines which do not need to comply with national policy (B)	Birth dose coverage in two districts of Ho Chi Minh, where there are large hospitals, was 87.3% and 44.5%
									Out-dated policies regarding vaccination of underweight and sick neonates (B)	Delayed birth dose due to fear of deaths or adverse events being linked to vaccination
							SD	Demand for vaccination	Traditional practices of sequestering newborns at home during the first month after delivery (B)	Hepatitis B birth dose vaccine not administered to newborn

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
34	O'Leary et al. (2012)	Survey	USA	64 425 infants born in Colorado in 2008	To (1) describe and determine the effects of hospital policies on newborn HBV prevention, and (2) determine maternal characteristics associated with non-receipt of birth dose	Before discharge	SD	Demand for vaccination	High socio-economic status (B)	In multivariate analysis, odds for non-receipt of birth dose vaccination compared to infants whose mother's income was < \$15 000 (reference): OR for mother's income in the range of \$50 000–\$74 999 = 1.31 (CI: 1.22 – 1.41) OR for mother's income above \$75 000 = 1.21 (CI: 1.13 – 1.30)
							SD	Demand for vaccination	Mother's high level of education (B)	In multivariate analysis, ORs for non-receipt of birth dose vaccination compared to infants whose mother had middle-school education (reference): OR if mother had a Bachelors degree = 1.38 (CI: 1.25 – 1.52) OR if mother had a Masters degree = 1.66 (CI: 1.49 – 1.85) OR if mother had a Doctorate/professional degree = 1.51 (CI: 1.31 – 1.74)
							GL	Policies and guidelines	Having a policy to offer hepatitis B birth dose vaccine to newborns (P)	In multivariate analysis, ORs for non-receipt of birth dose vaccination compared to if born in a hospital with a policy (reference): OR if born in a hospital with no policy = 1.39 (CI: 1.32 – 1.47) OR if born in a hospital with a policy to review maternal status but no birth dose policy = 2.21 (CI: 2.13 – 2.30)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
35	Oram et al. (2001)	Survey	USA	46 general nurseries in Cook County, Illinois that provided obstetric services and routine medical care to healthy, full-term infants	To determine hospital hepatitis B vaccination policy before the recommendation for delay of hepatitis B vaccination and one year later	"At birth"	GL	Policies and guidelines	Change in national recommendations regarding administration of the hepatitis B birth dose (B)	Before the change in policy, 74% of hospital nurseries surveyed offered the hepatitis B birth dose vaccine to all neonates; only 39% did so following changes in policies
36	PATH (1998)	Report	Indonesia	Newborns in selected villages of Lombok, Mataram, Sumbawa and Bali	To provide an overview of the Healthy Start for Healthy Life Project	Within seven days of birth	SD	Linkages between immunization and postnatal care services	Birth dose vaccination integrated within a package of postnatal care services delivered at home (P)	Coverage of birth dose delivered within seven days of birth increased from baseline to endline in all three districts. In Lombok, coverage increased from 33% to 83%. In Mataram from 24% to 51% and in Sumbawa from 3% to 90%

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/I/B	Outcome
37	PATH (2003)	Report	Indonesia	Newborns in four districts of East and West Java	To provide an overview of the Healthy Start for Healthy Life Project	Within seven days of birth	HW	Knowledge, attitudes and training	Providing training to midwives on postnatal care services, including communication skills (P)	Between baseline and endline, coverage of birth dose administered within seven days of birth increased by around 25% in the four project districts, compared to an increase of 7% in control districts Midwives were responsible for 78% of this increase (supporting evidence not provided)
							SD	Demand for vaccination	Raising awareness within the community on birth dose vaccination within seven days of birth (P)	Mothers' knowledge on early hepatitis B immunization increased by around 12%–13% ($p < 0.001$) in project districts after one year of the project, compared to an increase of 4% in control districts Between baseline and endline coverage of birth dose administered within seven days of birth increased by around 25% in the four project districts, compared to an increase of 7% in control districts
							HIS	Birth notification	Community-based birth notification systems where community volunteers were designated to inform midwives of pregnancies and new births, or coloured flags were used to announce births (P)	Between baseline and endline coverage of birth dose administered within seven days of birth increased by around 25% in the four project districts, compared to an increase of 7% in control districts
38	PATH (2003)	Report	Indonesia	Newborns	To provide an overview of the Healthy Start Project	Within seven days of birth	HIS	Birth notification	TBAs filled out colour-coded cards that informed midwives of each birth, so that they could then visit homes within one day of birth to administer the birth dose (P)	Increase in birth dose coverage after three years of the project (no figure provided)

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39	PATH (2005)	Report	China	Newborns requiring birth dose in 81 townships in three counties in Hunan Province	To evaluate the safety and effectiveness of using village doctors to provide hepatitis B birth dose, through Uniject or single-dose vials stored OCC	Within 24 hours	T	Storage and access to the cold chain	Comparison of three vaccination strategies: Delivery of the birth dose as single-dose vials stored within the cold chain in township hospitals Delivery of the birth dose using Uniject stored OCC Delivery of the birth dose using single-dose vials stored OCC (P)	Compared to baseline, in the survey following implementation of the intervention, coverage of timely birth dose increased: From 2% to 25% in township hospitals From 3% to 52% using single-dose vials stored OCC From 1% to 67% using Uniject stored OCC
40	PATH et al. (2006)	Intervention study	Viet Nam	10 000 children in four study districts of Viet Nam who were immunized with the birth dose	To evaluate the safety, coverage, immunogenicity and logistics of OCC delivery for hepatitis B birth dose in areas where the cold chain does not function	Within 24 hours	T	Storage and access to the cold chain	Comparison of two strategies: Vaccination with single-dose vials stored in the cold chain to newborns born at district hospitals Vaccination with single-dose vials stored OCC in community health facilities for infants born at community health centres and at home (P)	Coverage of birth dose for children born in all four districts increased from 45% (within three days) before the study to 90% coverage for vaccination within 24 hours after the study Timely birth dose coverage was 83% for infants born in health centres where the vaccine was stored OCC, and 82% in hospitals where vaccines were stored in the cold chain
41	PATH (2007)	Report	Viet Nam	Newborns in study areas of Thanh Hoa Province	To model a new strategy to increase coverage rates for the birth dose vaccine in Thanh Hoa Province	Within 24 hours	T	Storage and access to the cold chain	Lack of fridges in the community health centres or insufficient budgets to continuously operate fridges (B)	Low birth dose coverage (figure not provided)
							T	Storage and access to the cold chain	Storing single-dose vials with vaccine vial monitors OCC in community health centres for up to two weeks (P)	Coverage of birth dose increased from 45% of neonates vaccinated < 72 hours before implementation of the intervention, to 89% vaccinated within < 72 hours and 83% vaccinated < 24 hours (indicator on within 24 hours not available at baseline)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
42	PATH (2008)	Intervention study	Indonesia	Newborns in study districts of Bali, Mataram and Lombok	To increase mothers' and infants' immunization coverage (among other objectives related to maternal and child health)	Within seven days of birth	SD	Linkages between immunization and postnatal care services	Birth dose vaccination integrated in a package of postnatal services delivered at homes (P)	Coverage of birth dose delivered within seven days of birth increased from baseline to endline from 33% to 83% in Lombok, from 24% to 51% in Mataram and from 3% to 90% in Sumbawa
43	PATH (2010)	Report	Viet Nam	Newborns	To increase the coverage and timeliness of birth dose coverage	Within 24 hours	SD	Demand for vaccination	Reports of adverse events (AE) following provision of the birth dose (B)	Coverage of timely birth dose decreased from 64.3% in 2006 to 20.4% by the end of 2008
44	Pearce et al. (2008)	Qualitative	Australia	Six midwives from two teaching hospitals in metropolitan Sydney	To gain a clear perspective on perceptions held by local midwives about the neonatal dose of hepatitis B vaccine and their role in its promotion and administration	"At birth"	GL	Political commitment	Highly publicized adverse events from hepatitis B vaccination resulted in high levels of anxiety within the government resulting in the MoH halting administration of the lot of vaccines from which AE had been reported (B)	Newborn not administered the birth dose
45	Ruff et al. (1995)	Intervention study	Indonesia	Newborns in Lombok, Indonesia	To present results of final sero-survey after implementation of the Lombok model project	Within seven days of birth	HW	Knowledge, attitudes and training	Midwives' belief that parents' sovereignty was important when making a decision on the birth dose vaccine (B)	Birth dose coverage increased to reach above 95% in 1989 and 1991
							HW	Knowledge, attitudes and training	Midwives' reservations about the safety and necessity of the neonatal hepatitis B vaccine programme (B)	
							HIS	Birth notification	Community-based birth notification systems (P)	

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
46	Ruff et al. (2009)	Review	Indonesia	No specific population	To review the current situation, challenges and recommended priorities for HBV control	Within 24 hours	SD	Access to a trained health worker	Lack of timely contact between a health-care provider and the newborn within 24 hours of delivery (B)	Hepatitis B birth dose vaccine not administered to newborn
							T	Vaccine procurement, supply and distribution systems	Unavailability of vaccine when there is a contact between a health-care provider and the newborn (B)	
47	Sobel et al. (2010)	Qualitative and intervention study	the Philippines	Senior pharmacist, neonatal practitioner, nurse or midwife at 150 hospitals	To assess the implementation, coverage, documentation, logistic systems, policies and awareness of hepatitis B vaccination at birth in 150 hospitals in the Philippines	Before discharge	GL	Policies and guidelines	Having a copy of national policies or guidelines (P)	Odds of having >50% coverage of birth dose compared to hospitals who did not have a copy of the national hepatitis B vaccine policy or immunization policy (reference): OR for hospitals who had a copy of the vaccine policy = 4.7 (CI: 1.2 – 18) OR for hospitals who had a copy of the immunization policy = 3.9 (CI: 0.7 – 21.2)
							GL	Standing orders	Hospitals having standing orders on birth dose vaccination (P)	Odds of having >50% coverage of birth dose compared to hospitals which did not have standing orders (reference): OR for hospitals with standing orders = 4.8 (CI: 1.3 – 18.1)
				45 health centre staff, 120 community health workers and 23 private practitioners in nine health centres of metropolitan Manila			HW	Knowledge, attitudes and training	Training for neonatal practitioners on the hepatitis B vaccination policy (P)	Odds of having >50% coverage of birth dose compared to hospitals where neonatal practitioners had not been trained: OR for hospitals where practitioners had been trained = 14.4 (CI: 3.1 – 87.9)
									Training for health workers on aspects related to HBV and vaccination (P)	Coverage of timely birth dose increased from 19% before implementation of the intervention to 74% during the two months after the intervention

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/I/B	Outcome
48	Sun et al. (2002)	Review	China	Newborns in China	Review of universal neonatal hepatitis B vaccination in China	"At birth"	SD	Location of service delivery	Residence in suburban areas (B)	In a sample of 1271 children in four capital cities and suburbs, the coverage rate for the birth dose was 92% in cities compared to 77% in the suburbs
49	Thomas et al. (2004)	Cohort	USA	Infants born to women, whose HBV surface antigen (HBsAg) status was unknown, during April to June 1999, August to October 1999 and April to June 2000 at 34 hospitals in Oregon	To determine whether infants born to mothers of unknown HbsAg status received appropriate immunization	Before discharge	GL	Policies and guidelines	Change in national recommendations on administration of the birth dose (B)	Before the change in policy, 27% of infants born to mothers of unknown status were vaccinated, as opposed to 1% who were vaccinated during the policy change (p < 0.001)
50	Wang et al. (2007)	RCT	China	1202 infants from 957 villages in the counties of Sangzhi, Longshan and Fenghuang in the province of Hunan	To explore the feasibility and effectiveness of a village-based, out-of-cold-chain strategy for improving timely administration of the hepatitis B vaccine birth dose in rural areas of Hunan Province, China	Within 24 hours	HW	Training	Raising awareness of the importance of the hepatitis B birth dose through meetings with public-health officials and health workers (P)	Coverage of birth dose increased by at least 50% in all study groups Percentage of parents reporting not being informed by a provider about the importance of timely birth dose decreased from 79% to 49% for those of children born at home, and from 78% to 26% for those of children born in the hospital
							T	Storage and access to the cold chain	Use of single-dose vial vaccines stored OCC in villages and administered by village health workers (P)	Coverage of timely birth dose increased from 11.3% (CI: 7.3 – 15.2) to 67.8% (CI: 61.5 – 74.2)
							T	Vaccines delivery technologies and disposal	Use of Uniject vaccines stored OCC in villages and administered by village health workers (P)	Coverage of timely birth dose increased from 6.8% (CI: 4.1 – 5.9) to 77.3% (CI: 71.5 – 83.0)
							T	Storage and access to the cold chain	Single-dose vial vaccines stored in hospitals within the cold chain (P)	Coverage of timely birth dose increased from 8% (CI: 4.7 – 11.2) to 57.9% (CI: 50.3 – 65.4)

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
51	White et al. (2009)	Survey	USA	103 birthing hospitals in Minnesota	To assess (1) perinatal hepatitis B vaccination practices for hospitals in Minnesota; (2) immunization information systems hepatitis B birth dose rates for participating hospitals, and to compare these rates with charts for a subset of hospitals; (3) to identify barriers to capturing hepatitis B birth dose administration on birth certificates and submitting data into information systems	Within three days of birth	GL	Policies and guidelines	Having a standing order or policy for giving the birth dose (P)	Odds of having a birth dose coverage rate of >50% compared to hospitals with no standing order or policy on giving the birth dose: OR for hospitals with a standing order or policy = 36.4 (CI: 7.7 – 330), p < 0.001
							HIS	Vaccination records	Incorrect or no recording of birth dose vaccination on the birth certificate (B)	Reported birth dose coverage rates before discharge were higher when examining data from hospital charts (74%, 87% and 82% in three hospitals), compared to birth dose rates obtained (0.1%, 0% and 38% for the same hospitals respectively) from reviewing data in birth certificates
52	WHO (2002)	Workshop proceedings	China	Newborns	To advise on how to improve HBV control through immunization	Within 24 hours	FN	Cost to recipient	Halving of user fees for the hepatitis B birth dose vaccine (P)	Coverage of timely birth dose increased to 76% by 2002
53	WHO (2006)	Guidelines	Mongolia	Newborns	An operational manual to plan, implement and monitor the delivery of the timely birth dose of hepatitis B vaccine	Within 24 hours	HW	Knowledge, attitudes and training	Poor knowledge of the importance and purpose of the hepatitis B birth dose (B)	Decreased coverage of timely birth dose, vaccine administered with delay — 2 to 3 days after birth

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
54	WHO (2007)	Meeting proceedings	WHO Western Pacific Region	Newborns	To review and make recommendations on the WHO Western Pacific Region regional plan for HBV control	Within seven days	SD	Access to a trained health worker	Home births (B)	In 2006, coverage of birth dose administered within 7 days was 52% in Cambodia
						Within 24 hours	T	Storage and access to the cold chain	Absence of vaccine vial monitors (B)	Coverage of timely provision of birth dose increased to 64% by the end of 2006 in Viet Nam
									Ensuring vaccine storage in labour rooms in public hospitals in Viet Nam (P)	Increase in timely birth dose coverage in public hospitals in Viet Nam Coverage of timely birth dose in the entire country was 64% in 2008
54	WHO (2007) Continued	As in previous row	As in previous row	As in previous row	As in previous row	Within 24 hours	T	Storage and access to the cold chain	Vaccine provided OCC for hepatitis B birth dose in four districts (P)	Coverage of timely provision of birth dose increased to 64% by the end of 2006 in Viet Nam
							T	Vaccine presentation	Use of single-dose vials for birth dose vaccination in public hospitals in Viet Nam (P)	Increase in timely birth dose coverage in public hospitals in Viet Nam Coverage of timely birth dose in the entire country was 64% in 2008
							FN	Cost to the recipient	Hepatitis B birth dose covered under the National Insurance Act in the Republic of Korea since 2002 (P)	94.6% of newborns received birth dose before discharge in the Republic of Korea
55	WHO (2008)	Meeting proceedings	Viet Nam	Newborns	To review progress made, constraints faced and strategies followed for achieving HBV control in the WHO Western Pacific Region	Within 24 hours	GL	Policies and guidelines	Lack of guidelines on storing vaccines OCC and on explicit vaccine labelling that would support such use (B)	Low coverage of timely hepatitis B birth dose in the region (did not give a figure)
							SD	Demand for vaccination	Reports of adverse events following provision of the birth dose (B)	Coverage of timely birth dose declined from 64.3% in 2006 to 28.6% at the end of 2007

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
56	WHO (2008)	Epidemiological report	Worldwide	Newborns	To assess the status of immunization schedules with regard to the hepatitis B birth dose	Within 24 hours	SD	Access to a trained health worker	Home births (B)	Hepatitis B birth dose vaccine not administered to newborns
							SD	Linkages between maternity and private health-care services	Coordination between immunization services and maternal health services (P)	Increased coverage of the hepatitis B birth dose
							T	Procurement, supply and distribution systems	Inadequate supply of hepatitis B birth dose vaccines (B)	Hepatitis B birth dose vaccine not administered to newborns
57	WHO (2011)	Meeting proceedings	WHO Western Pacific Region	Newborns	To review and discuss the certification process, and to identify strategies for increasing hepatitis B vaccination coverage in priority countries	Within 24 hours	SD	Access to a trained health worker	Home births (B)	Timely birth dose coverage was under 60% in 2009 in Cambodia
57	WHO (2011) Continued	As in previous row	As in previous row	As in previous row	As in previous row	As in previous row	SD	Access to a trained health worker	Births occurring without attendants (B)	Birth dose coverage of under 20% in 2008 in Lao People's Democratic Republic
								Demand for vaccination	Lack of public demand (B)	Birth dose coverage of under 20% in 2008 in Lao People's Democratic Republic
							HIS	Procurement, supply and distribution systems	Vaccine stock-outs (B)	Birth dose coverage of under 20% in 2008 in Lao People's Democratic Republic
							FN	Funding for birth dose programmes	Lack of funding (B)	

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
58	Willis et al. (2010)	Survey	USA	190 random hospitals across the United States, including District of Columbia and Puerto Rico	To assess hospital policies and practices pertaining to perinatal HBV prevention	"At birth"	SD	Location of service delivery	Location of hospital in a rural area (F)	82% of infants born in rural hospitals were vaccinated with the hepatitis B birth dose as opposed to 62% of infants born in urban hospitals ($p < 0.05$)
							GL	Polices and guidelines	State having a universal policy on hepatitis B birth dose supply, i.e. to provide the birth dose at no cost to all infants regardless of insurance status (P) Hospital has a policy to offer hepatitis B birth dose vaccine to newborns (P)	84% of infants born in states with a universal policy were vaccinated with the hepatitis B birth dose compared to 58% of infants born in states without a universal policy ($p < 0.001$) 87% of infants born in hospitals with a policy were vaccinated with the hepatitis B birth dose compared to 38% of infants born in hospitals without a policy ($p < 0.001$).
59	Wood et al. (2008)	Cohort	Australia	1061 women who delivered 1 July 2002 to 30 June 2004	To examine how routine HBsAg testing of antenatal women (as identified on the Northern Territory (NT) Midwife's Data Collection System) can be used to track the impact of hepatitis B vaccination on the prevalence of chronic HBV infection in the NT	"At birth"	HIS	Monitoring performance, equity and scale-up	Tracking the impact of hepatitis B vaccination on the prevalence of chronic HBV infection through use of state data- collection systems (P)	The impact of HBV vaccination can be workably monitored through linking data from state data-collection systems and HBsAg results

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
60	Yusuf et al. (1999)	Survey	USA	32 742 children across 78 geographic survey areas in the country	To assess progress in hepatitis B vaccination of children from 1994 to 1997	"At birth"	GL	Policies and guidelines	State having a policy that vaccination with three doses of the hepatitis B vaccine was required for entry into day care (P)	In states where vaccination with three doses of the hepatitis B vaccine was required for day-care entry, coverage was 87% (CI: 86 – 88) as opposed to a coverage of 83% (CI: 82 – 84) in states where there was no such policy ($p < 0.01$)
							SD	Demand for vaccination	Family's income was below the poverty line (B)	Coverage of three doses of the hepatitis B vaccine was 85% (CI: 84 – 86) for infants from families whose income was at, or above, the poverty level, compared to a coverage of 81% (CI: 79 – 82) for infants whose family income was below the poverty line ($p < 0.01$)
61	Zeng et al. (1999)	Survey	China	Infants born from 1 January 1993 to 31 December 1994 in 112 disease surveillance points from 25 provinces, autonomous regions and municipalities across the country	To conduct an epidemiological survey in the national disease surveillance points (DSPs) between December 1995 and January 1996	"At birth"	SD	Location of service delivery	Residence in a rural area (B)	Coverage of birth dose was 97% in urban areas compared to 51% in rural areas in 1993–1994

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
62	Zhao et al. (2011)	Cohort	USA	Children born in the birth year cohorts of 1998 to 2007	To investigate the progress in newborn hepatitis B vaccination and the impact of the changes in Advisory Committee on Immunization Practices recommendations on hepatitis B birth dose vaccination coverage by birth year cohort	"At birth"	GL	Policies and guidelines	Change in national recommendations regarding administration of the hepatitis B birth dose (B)	Hepatitis B birth dose coverage decreased from 56.3% before the policy suspension to 32.9% during the suspension, and only increased by 1.5% in the year after the suspension was removed
63	Zhou et al. (2008)	Review	China	Infants across China	To review the implementation of mass vaccination of hepatitis B vaccine and its critical role in prevention of HBV infection in China	Within 24 hours	FN	Cost to recipient	Vaccination provided free-of-charge to all neonates in 12 western provinces and the poorest counties in 10 other provinces (P)	Across the 11 western provinces surveyed, average coverage of timely birth-dose increased from 46.5% to 88.6% in township hospitals and from 61.2% to 89.8%–96.6% in city and province hospitals between 1998/1999 and 2005
							FN	Cost to recipient	Hepatitis B vaccine provided free-of-charge to all neonates and infants across China (P)	Coverage of timely birth dose maintained at around 95% in cities, coverage increased to 83.5%–96.5% in rural areas after 2005 (year not specified) compared to 18.1%–50% in 1993–1994

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
64	Zhou et al. (2009)	Survey	China	3390 infants born in 2004 in four counties of the provinces of Guangxi, Guizhou, Tibet and Shaanxi	To assess the status of, and major factors influencing, timely administration of the hepatitis B birth dose	Within 24 hours	SD	Demand for vaccination	Parents unaware of the importance or availability of the birth dose vaccine (B)	In multivariate analysis, the odds of receipt of timely birth dose compared to newborns whose parents or guardians knew that the birth dose should be given within 24 hours (reference): OR for newborns with parents or guardians who did not know = 0.62 (p = 0.002)
									Parents concerned about an adverse event from vaccination (B)	Hepatitis B birth dose vaccine not administered to newborn
									Parents not having the time to take the infant for vaccination (B)	Hepatitis B birth dose vaccine not administered to newborn
			SD					Access to a trained health worker	Home birth (B)	In multivariate analysis, odds of being vaccinated with the birth dose compared to children born at home (reference): OR for being born in a county hospital = 6.5 (CI: 5.3 – 8), p < 0.0001 OR for being born in a township-level hospital = 7.1 (CI: 5.7 – 9), p < 0.0001 OR for being born in a private clinic = 5.6 (CI: 3.7 – 8.6), p < 0.0001
			HIS					Vaccination records	Family not having an immunization registration book or card at home (B)	In multivariate analysis, odds of being vaccinated with the birth dose compared to children who had an immunization registration book or card (reference): OR for children who lack an immunization registration book or card = 0.64 (CI: 0.5 – 0.8), p < 0.0001

#	First author (Year)	Study/paper type	Setting	Population	Study aims	Definition of BD	Group	Sub-group	Description of P/F/B	Outcome
65	Zola et al. (1997)	Survey	USA	76 physicians providing obstetric services in San Francisco	To survey the current knowledge, attitudes and practices of obstetric providers regarding the education of pregnant women about infant hepatitis B vaccination	Before discharge	HW	Knowledge, attitudes and training	Antenatal education not provided to mothers (B)	Of the physicians who believed that it was feasible to educate expectant mothers on infant hepatitis B vaccination, only 53% actually provided this education

Annex 5:

Grade tables

Note: These tables only record the appraisals done for those studies that reported practices (rather than barriers or facilitators) and indicated a plausible contribution of the practice to increased birth dose coverage. As noted in the main report, this was a subset of included studies, and there were few instances where studies could be combined.

Having a facility policy to offer the birth dose

Quality assessment						Summary of findings			Importance
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Coverage* (range across studies)		Quality	
						No policy	Policy		
3	Observational study	Serious limitations ¹	No serious inconsistencies ²	No serious indirectness	No serious imprecision	15%–58%	41%–87%	Very low	Critical

* Could not combine coverage across studies due to the different populations surveyed, and population figures not provided across all studies. Range provided includes lowest and highest coverage figures across the studies, $p < 0.05$ in all studies for difference in coverage.

¹ Serious limitations due to biases from self-reported data in one study, low response rate in one study and no control of confounding factors in one study.

² No serious inconsistencies, even though definition of birth dose varied across the studies — “at birth”, “within 2 days” and “before discharge” — as the outcome of the practice in question, having a policy, is unlikely to change based on timing of the birth dose.

Training for health workers on the hepatitis B birth dose

Quality assessment						Summary of findings				Importance
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants		Coverage		Quality
						Before	After	Before	After	
1*	Intervention study	Serious limitations ¹	Not relevant	No serious indirectness	No serious imprecision	1231	294	19%	74%	Low (p < 0.01)
										Critical

* Although another study, which was a RCT, reported on an activity of raising awareness of the birth dose among health workers, this was deemed as the highest level of evidence, as one of the main aims of the RCT was not to determine the effect of awareness-raising. This intervention study specifically looked at impact of a training intervention on coverage.

¹ Study did not control for confounding factors of infants born before and after the intervention.

Having standing orders to offer the birth dose

Quality assessment						Summary of findings				Importance
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Have standing orders		Odds ratio	Quality	
						Percentage of hospitals with > 50% coverage of the birth dose (before discharge) (n = 14)	Percentage of hospitals with ≤ 50% coverage of the birth dose (before discharge) (n = 71)			
1*	Observational study	Serious limitations ¹	Not relevant	No serious indirectness	No serious imprecision	100%	70%	4.8 (1.3 – 18.1)	Very low	Important

* Although there were two other observational studies which looked at birth dose coverage based on presence of a standing order, the observational study deemed to have the most rigorous design was selected for GRADE appraisal, as findings from the studies could not be aggregated or easily compared.

¹ Serious limitations because study did not control for confounding factors.

Use of the Uniject device to deliver the birth dose vaccine

# of studies		Quality assessment					Summary of findings				Importance
		Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants	Increase in coverage (within 7 days)		Quality	
								Before	After		
1	Other (cost-effective analysis)	No serious limitations ¹	Not relevant	No serious indirectness	No serious imprecision	364 159 (in study districts in 3 provinces)	0%	86%	Very low	Important	
							0%	38%			
							68%	80%			

¹ The focus of this study is on cost-effectiveness of using Uniject; however data was provided on coverage. Given that the study is “other” evidence and already rated as ‘very low’, further downgrading was not done even though the study did not provide adequate detail on how coverage estimates were derived.

Linkages between immunization and postnatal care services in the home

# of studies	Quality assessment					Summary of findings		Importance
	Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants	Coverage (within 7 days)	
1	Other (review)	Serious ¹	Not relevant	No serious indirectness	No serious imprecision ²	Not provided	7% born at home vaccinate on the day of birth, 16% within 24 hours and 39% within one week	Very low
								Critical

¹ Serious limitations because the study reviews several different practices undertaken as part of birth dose programmes in Indonesia and hence it cannot be determined the extent to which integration of birth dose vaccination within the package of postnatal services had an effect on improving coverage of birth dose for home births.

² No serious imprecision determined even though confidence intervals or number of infants (denominator) not provided.

Hepatitis B birth dose vaccine stored OCC

Quality assessment						Summary of findings*				Importance	
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants		Increase in coverage			Quality
						Before	After	Single-dose vial stored within cold chain	Single-dose vial stored OCC		
1	RCT	Serious1	Not relevant	No serious indirectness	No serious imprecision	792	802	50%	57%	Moderate	Critical
						p < 0.05					

* Study also looked at birth dose delivered through Uniject OCC; this is not included here as it is not a direct comparison to a single-dose vial stored within the cold chain. The increase in coverage was highest for Uniject OCC (p < 0.05).

¹ Details on allocation concealment not provided. Even though control and comparison are not strictly matched, given that the comparison (OCC) involved administration by village health workers at homes (and not in hospitals), this was not deemed to be an important limitation as administration by village health workers at homes is only likely to underestimate the effect of OCC on coverage.

Tracking of pregnancies

Quality assessment						Summary of findings			Importance	
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants	Coverage (within 72 hours)			Quality
							No tracking (3 provinces)	Tracking (2 provinces)		
1	Observational	Serious limitations ¹	Not relevant	No serious indirectness	No serious imprecision ²	Not provided	87% 52% 45%	97% 90%	Very low	Important

¹ Serious limitations, as data was collected through focus group discussion and key informant interviews — article does not mention whether there was cross-checking with vaccination records. Also, confounding factors were not controlled for, so difficult to determine whether meticulous tracking of pregnancies can explain the difference in coverage between districts that tracked pregnancies, and those that did not.

² No serious imprecision determined even though confidence intervals or number of infants (denominator) not provided.

Community-based birth notification systems for home births

Quality assessment						Summary of findings			Importance	
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants	Coverage (within 7 days)			Quality
							Before	After		
1	Intervention study	Serious limitations ¹	Not relevant	No serious indirectness	No serious imprecision ²	Not provided	Not provided	Above 95%	Low	Important

¹ Serious limitations because the study reviews the Lombok birth dose programme in Indonesia overall, with a focus on vaccine efficacy. Does not examine the extent to which community-based birth dose notification had an effect on improving coverage of birth dose for home births — there is no comparator.

² No serious imprecision determined even though confidence intervals or number of infants (denominator) not provided.

Providing birth dose vaccine free-of-charge

Quality assessment						Summary of findings				Importance	
# of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	# of infants	Increase in coverage (between 1998/1999 and 2005; between 1993/1994 and after 2005 for rural areas)				Quality
							Township hospitals	City & province hospitals	Rural areas		
1	Other (review)	Serious limitations ¹	Not relevant	No serious indirectness	No serious imprecision ²	Not provided	42%	29%	34%*	Very low	Critical

* This is the minimum increase in coverage as a range was provided, coverage was in the range of 18%–50% in 1993/1994 and 84%–97% after 2005 (year not specified).

¹ Serious limitations because the study does not control for confounders and so cannot determine the extent to which providing birth dose vaccination free-of-cost had an effect on improving coverage of birth dose.

² No serious imprecision determined even though confidence intervals or number of infants (denominator) not provided.

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