

EVIDENCE TO RECOMMENDATIONS TABLE AND GRADE TABLE

Detailed evidence related to the evidence to recommendation table can be found in the background papers presented to the Strategic Advisory Group of Experts (SAGE) on Immunization in October 2016 (<http://www.who.int/immunization/sage/meetings/2016/october/en/>)

<p>Question: Should the first dose of a hepatitis B vaccine (birth dose) be given to infants within ≤ 24 hours after birth vs at the time of the first dose of diphtheria tetanus and pertussis (DTP) vaccine?</p> <p>Population: Infants.</p> <p>Intervention: First dose of hepatitis B vaccines given at ≤ 24 hours.</p> <p>Comparison(s): First dose given at the same time as the first dose of DTP vaccine.</p> <p>Outcome: Seroconversion to antibody against hepatitis B surface antigen (anti-HBs).</p>							
<p>Background:</p> <p>HBV is a major cause of liver cancer cases worldwide, with wide geographical variations in the attributable fraction. In 1992, the WHO set a goal for all countries to integrate HBV vaccination into the Expanded Program on Immunization (EPI). In September 2015, the United Nations General Assembly adopted the 2030 Agenda for Sustainable Development. A goal is to combat viral hepatitis. In May 2016, the Global Health Sector Strategy on Viral Hepatitis was endorsed by Member States and has set a 2020 target to reduce the new cases of chronic hepatitis B virus (HBV) infection by 30%, which is equivalent to for 2020 a 1% prevalence of hepatitis B surface antigen (HBsAg) among children less than 5 years of age, and a 2030 target of achieving a 0.1% prevalence of HBsAg among children 5 years of age. WHO recommends that all infants receive their first dose of hepatitis B vaccine as soon as possible after birth. The birth dose should then be followed by two or three additional doses with a minimum interval of four weeks.</p> <p>A literature review was conducted to evaluate whether the timing of administration of birth dose of hepatitis B vaccines for infants induces higher levels of anti-HBs seroconversion (from negative to positive), presented as the absolute geometric mean concentration of antibodies (GMCs) and the percentage with anti-HBs seroconversion with a threshold of ≥ 10 IU/ml, and clinical outcomes.</p>							
	CRITERIA	JUDGEMENTS		RESEARCH EVIDENCE	ADDITIONAL INFORMATION		
PROBLEM	Is the problem a public health priority?	No <input type="checkbox"/>	Uncertain <input type="checkbox"/>	Yes <input type="checkbox"/>	Varies by setting <input checked="" type="checkbox"/>	Vaccinating against hepatitis B has been associated with substantial reductions in the incidence of acute and chronic HBV infections and mortality from hepatocellular carcinoma.	1
BENEFITS & HARMS OF THE OPTIONS	<u>Benefits of the intervention</u>	No <input type="checkbox"/>	Uncertain <input type="checkbox"/>	Yes <input checked="" type="checkbox"/>	Varies <input checked="" type="checkbox"/>	Infant hepatitis B vaccination achieves substantial protection against chronic HBV infection, which will ultimately result in significant reductions of cirrhosis and hepatocellular carcinoma.	

Are the desirable anticipated effects large?			
<u>Harms of the intervention</u> Are the undesirable anticipated effects small?	<p>No <input type="checkbox"/> Uncertain <input type="checkbox"/> Yes <input checked="" type="checkbox"/> Varies <input type="checkbox"/></p>	Evidence showed no difference with regard to serious adverse events, all-cause deaths and clinical outcomes among infants who received a birth dose compared with those who began vaccination after one month of life.	
Balance between benefits and harms	<p>Favours intervention <input checked="" type="checkbox"/> Favours comparison <input type="checkbox"/> Favours both <input type="checkbox"/> Favours neither <input type="checkbox"/> Unclear <input type="checkbox"/></p>	The intervention is favored when balancing the benefits and harms.	
What is the overall quality of this evidence for the critical outcomes?	<p>Effectiveness of the intervention</p> <p>No included studies <input type="checkbox"/> Very low <input type="checkbox"/> Low <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> High <input type="checkbox"/></p> <p>Safety of the intervention</p> <p>No included studies <input type="checkbox"/> Very low <input type="checkbox"/> Low <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> High <input type="checkbox"/></p>	<p>There is moderate quality evidence to support the effectiveness of hepatitis B vaccine given within 24 hours of birth to prevent HBV infection.</p> <p>Low quality evidence also showed no difference with regard to serious adverse events, all-cause deaths and clinical outcomes among infants who received a birth dose compared with those who began vaccination after one month of life.</p>	

VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	<table border="0"> <tr> <td><i>Importan t uncertain ty or variabilit y</i></td> <td><i>Possibly importan t uncertain ty or variabilit y</i></td> <td><i>Probably no importan t uncertain ty or variabilit y</i></td> <td><i>No importan t uncertain ty or variabilit y</i></td> <td><i>No known undesirab le outcomes</i></td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	<i>Importan t uncertain ty or variabilit y</i>	<i>Possibly importan t uncertain ty or variabilit y</i>	<i>Probably no importan t uncertain ty or variabilit y</i>	<i>No importan t uncertain ty or variabilit y</i>	<i>No known undesirab le outcomes</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	No evidence available though it is assumed that in general there is no important uncertainty or variability.			
<i>Importan t uncertain ty or variabilit y</i>	<i>Possibly importan t uncertain ty or variabilit y</i>	<i>Probably no importan t uncertain ty or variabilit y</i>	<i>No importan t uncertain ty or variabilit y</i>	<i>No known undesirab le outcomes</i>												
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>												
VALUES & PREFERENCES	Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?	<table border="0"> <tr> <td><i>No</i></td> <td><i>Probably No</i></td> <td><i>Uncertain</i></td> <td><i>Probably Yes</i></td> <td><i>Yes</i></td> <td><i>Varies</i></td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	<i>No</i>	<i>Probably No</i>	<i>Uncertain</i>	<i>Probably Yes</i>	<i>Yes</i>	<i>Varies</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<p>A review of literature retrieved no evidence on the values and preferences of the caregivers. Assessment of the values and preferences is very context specific and, in case no data are available, countries are asked to conduct these assessments in their specific setting.</p> <p>A random sample of 600 paediatricians obtained from the American Academy of Pediatrics membership database was surveyed by mail. Of 270 paediatricians who vaccinated children with hepatitis B vaccine and indicated their practice regarding the birth dose, 50% offered the first dose of hepatitis B vaccine at birth to all infants; the rest either offered the vaccine at birth only to infants of anti-HBs positive mothers and mothers whose serostatus is unknown, or did not offer the birth dose to any infants at all. Practicing in the inner city, working for a medical school or government hospital, and living in a state with universal immunization supply policies were associated with the respondent giving the birth dose. The strongest perceived barriers to giving the birth dose in the hospital were the difficulty tracking these vaccines (39%), the increased cost (27%), and the lack of reimbursement from insurance companies (26%).</p>	
<i>No</i>	<i>Probably No</i>	<i>Uncertain</i>	<i>Probably Yes</i>	<i>Yes</i>	<i>Varies</i>											
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											

RESOURCE USE	Are the resources required small?	No <input type="checkbox"/>	Uncertain <input type="checkbox"/>	Yes <input type="checkbox"/>	Varies <input checked="" type="checkbox"/>	Resources will be needed for the administration of the birth dose. Outreach services will need to be put in place to reach those children not born in a health care facility.		
	Cost-effectiveness	No <input type="checkbox"/>	Uncertain <input type="checkbox"/>	Yes <input checked="" type="checkbox"/>	Varies <input type="checkbox"/>	Six studies investigating birth dose hepatitis vaccination showed that it was cost-effective		
EQUITY	What would be the impact on health inequities?	Increased <input type="checkbox"/>	Uncertain <input type="checkbox"/>	Reduced <input checked="" type="checkbox"/>	Varies <input type="checkbox"/>	Implementing hepatitis B vaccine birth dose, in particular in resource-constrained settings, is expected to reduce health inequities.		
ACCEPTABILITY	Which option is acceptable to key stakeholders (Ministries of Health, Immunization Managers)?	Intervention <input checked="" type="checkbox"/>	Comparison <input type="checkbox"/>	Both <input type="checkbox"/>	Neither <input type="checkbox"/>	Unclear <input type="checkbox"/>	Administering the birth dose within 24 hours is assumed to be an acceptable option to key stakeholders.	
	Which option is acceptable to target group?	Intervention <input checked="" type="checkbox"/>	Comparison <input type="checkbox"/>	Both <input type="checkbox"/>	Neither <input type="checkbox"/>	Unclear <input type="checkbox"/>	Ensuring early protection of infants is likely to be acceptable to the target group.	

FEASIBILITY	Is the intervention feasible to implement?	No <input type="checkbox"/> Probably No <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably Yes <input checked="" type="checkbox"/> Yes <input type="checkbox"/> Varies <input type="checkbox"/>					Certain barriers to implementing the birth dose exist in a variety of settings, such as being born at home, health systems with less access to health care facilities, the need for health workers training.	
	Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings <input type="checkbox"/>	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings <input type="checkbox"/>	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i> <input type="checkbox"/>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings <input type="checkbox"/>	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings <input checked="" type="checkbox"/>		
Type of recommendation	We recommend the intervention <input checked="" type="checkbox"/>	We suggest considering recommendation of the intervention <input type="checkbox"/> Only in the context of rigorous research <input type="checkbox"/> Only with targeted monitoring and evaluation <input type="checkbox"/> Only in specific contexts or specific (sub)populations		We recommend the comparison <input type="checkbox"/>	We recommend against the intervention and the comparison <input type="checkbox"/>			
Recommendation (text)	All infants should receive the first dose of hepatitis B vaccine as soon as possible after birth, preferably within 24 hours. If administration within 24 hours is not feasible, the birth dose can still be effective in preventing perinatal transmission if given within 7 days, particularly within 3 days, although somewhat less than if given within 24 hours, but with declining effectiveness with each passing day. Even after 7 days, a late birth dose can be effective in preventing horizontal transmission and therefore remains beneficial. Thus, SAGE recommends that all infants receive the birth dose during the first contact with health facilities at any time up to the time of the first primary dose. The birth dose given after 24 hours should be reported as a late birth dose vaccination.							

Implementation considerations	SAGE reemphasized the importance of the birth dose and urged all countries to introduce the universal birth dose without further delay. Guidance on how to improve coverage of the hepatitis B vaccine birth dose vaccine can be found in the following document: “Practices to improve coverage of the hepatitis B birth dose vaccine” http://apps.who.int/iris/bitstream/10665/78616/1/WHO_IVB_12.11_eng.pdf?ua=1
Monitoring and evaluation	
Research priorities	