

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: Is there the need for a hepatitis B vaccine booster dose following primary immunization?</p> <p>Population: Immunocompetent individuals. Intervention: Administration of a hepatitis B vaccine booster dose. Comparison(s): Primary immunization only without booster dose. Outcome: Immunogenicity</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 systematic review assessed the benefits and harms of a booster dose hepatitis B vaccination, more than five years after the primary vaccination, for preventing HBV infection in healthy individuals previously vaccinated with the hepatitis B vaccine, and with hepatitis B surface antibody levels (anti-HBs) below 10 mIU/ml.</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> Are the desirable anticipated effects large?	No <input checked="" type="checkbox"/> Uncertain <input type="checkbox"/> Yes <input type="checkbox"/> Varies <input type="checkbox"/>	2 systematic reviews concluded that individuals adequately vaccinated in a 3-dose or 4- dose primary schedule do not require additional booster dose. The results from a meta-analysis show that protection provided by HBV vaccine persists for at least two decades in the great majority of immunocompetent adequately vaccinated individuals.	
	<u>Harms of the intervention</u> Are the undesirable anticipated effects small?	No <input type="checkbox"/> Uncertain <input type="checkbox"/> Yes <input checked="" type="checkbox"/> Varies <input type="checkbox"/>	Evidence suggests that hepatitis B vaccine is well tolerated, when administered as primary immunization or booster dose.	
	Balance between benefits and harms	Favours intervention <input type="checkbox"/> Favours comparison <input checked="" type="checkbox"/> Favours both <input type="checkbox"/> Favours neither <input type="checkbox"/> Unclear <input type="checkbox"/>	The comparison is favored when balancing the benefits and harms.	
	What is the overall quality of this evidence for the critical outcomes?	Effectiveness of the intervention No included studies <input type="checkbox"/> Very low <input type="checkbox"/> Low <input type="checkbox"/> Moderate <input type="checkbox"/> High <input checked="" type="checkbox"/> Safety of the intervention No included studies <input checked="" type="checkbox"/> Very low <input type="checkbox"/> Low <input type="checkbox"/> Moderate <input type="checkbox"/> High <input type="checkbox"/>	There is high quality evidence that hepatitis B vaccine confers long-term protection	

VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 25%;"><i>Important uncertainty or variability</i></td> <td style="text-align: center; width: 25%;"><i>Possibly important uncertainty or variability</i></td> <td style="text-align: center; width: 25%;"><i>Probably no important uncertainty or variability</i></td> <td style="text-align: center; width: 25%;"><i>No important uncertainty or variability</i></td> <td style="text-align: center; width: 25%;"><i>No known undesirable outcomes</i></td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> </table>	<i>Important uncertainty or variability</i>	<i>Possibly important uncertainty or variability</i>	<i>Probably no important uncertainty or variability</i>	<i>No important uncertainty or variability</i>	<i>No known undesirable 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>Important uncertainty or variability</i>	<i>Possibly important uncertainty or variability</i>	<i>Probably no important uncertainty or variability</i>	<i>No important uncertainty or variability</i>	<i>No known undesirable 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 style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 16.6%;">No</td> <td style="text-align: center; width: 16.6%;">Probably No</td> <td style="text-align: center; width: 16.6%;">Uncertain</td> <td style="text-align: center; width: 16.6%;">Probably Yes</td> <td style="text-align: center; width: 16.6%;">Yes</td> <td style="text-align: center; width: 16.6%;">Varies</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> </table>	No	Probably No	Uncertain	Probably Yes	Yes	Varies	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	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.	
No	Probably No	Uncertain	Probably Yes	Yes	Varies											
<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
RESOURCE USE	Are the resources required small?	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 33.3%;">No</td> <td style="text-align: center; width: 33.3%;">Uncertain</td> <td style="text-align: center; width: 33.3%;">Yes</td> <td style="text-align: center; width: 33.3%;">Varies</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> </table>	No	Uncertain	Yes	Varies	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Additional resources will be needed for the administration of a booster dose.					
	No	Uncertain	Yes	Varies												
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
Cost-effectiveness	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 33.3%;">No</td> <td style="text-align: center; width: 33.3%;">Uncertain</td> <td style="text-align: center; width: 33.3%;">Yes</td> <td style="text-align: center; width: 33.3%;">Varies</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> </table>	No	Uncertain	Yes	Varies	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	No evidence available, though it is assumed that the administration of a booster dose, in light of the limited benefit of this intervention, is not cost-effective.						
No	Uncertain	Yes	Varies													
<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
EQUITY	What would be the impact on health inequities?	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 33.3%;">Increased</td> <td style="text-align: center; width: 33.3%;">Uncertain</td> <td style="text-align: center; width: 33.3%;">Reduced</td> <td style="text-align: center; width: 33.3%;">Varies</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> </table>	Increased	Uncertain	Reduced	Varies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	No expected impact of the intervention on health inequities.					
Increased	Uncertain	Reduced	Varies													
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													

ACCEPTABILITY	Which option is acceptable to key stakeholders (Ministries of Health, Immunization Managers)?	<i>Intervention</i> <input type="checkbox"/> <i>Comparison</i> <input checked="" type="checkbox"/> <i>Both</i> <input type="checkbox"/> <i>Neither</i> <input type="checkbox"/> <i>Unclear</i> <input type="checkbox"/>					The administration of a booster dose is likely not acceptable to the key stakeholders given this increased costs and limited additional benefit for the target population.	
	Which option is acceptable to target group?	<i>Intervention</i> <input type="checkbox"/> <i>Comparison</i> <input checked="" type="checkbox"/> <i>Both</i> <input type="checkbox"/> <i>Neither</i> <input type="checkbox"/> <i>Unclear</i> <input type="checkbox"/>					Ensuring adequate protection with the least number of injections is likely the most acceptable option to the target population.	
FEASIBILITY	Is the intervention feasible to implement?	<i>No</i> <input checked="" type="checkbox"/> <i>Probably No</i> <input type="checkbox"/> <i>Uncertain</i> <input type="checkbox"/> <i>Probably Yes</i> <input type="checkbox"/> <i>Yes</i> <input type="checkbox"/> <i>Varies</i> <input type="checkbox"/>					Given the limited benefit of the intervention, it is not advisable to implement the intervention but to focus resources on the administration of the primary hepatitis B vaccine series.	
Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings		The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings		
Type of recommendation	We recommend the intervention	We suggest considering recommendation of the intervention			We recommend the comparison	We recommend against the intervention and the comparison		
	<input type="checkbox"/>	<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			<input checked="" type="checkbox"/>	<input type="checkbox"/>		

<p>Recommendation (text)</p>	<p>There is no evidence to support the need for a booster dose of hepatitis B vaccine in routine immunization programmes. No changes were proposed by SAGE in the current recommendations related to booster doses.</p>
<p>Implementation considerations</p>	
<p>Monitoring and evaluation</p>	
<p>Research priorities</p>	<p>Three primary doses of hepatitis B vaccine ensure a good protection against infection for up to 20 years. However, additional longer-term studies should be conducted to explore vaccine efficacy and the need of booster doses in different subgroups of the population</p>