

Strategic Advisory Group of Experts (SAGE) on Immunization Evidence to recommendations frameworkⁱ

Question: Should rotavirus vaccine be administered to children to prevent rotavirus-related disease.						
Population: Children (<24 month of age)						
Intervention: Rotavirus vaccination (according to recommended schedule)						
Comparison(s): No vaccination						
Outcome: Rotavirus-associated diarrhoeal disease						
Background: Rotaviruses are the most common cause of severe diarrhoeal disease in infants and young children worldwide, predominantly in developing countries. Currently, four oral, live, attenuated rotavirus vaccines, Rotarix™, RotaTeq™, Rotavac™ and RotaSiil™ are available internationally and WHO prequalified. The public health impact of rotavirus vaccination has been demonstrated in several countries, with measurable decrease in the number of rotavirus-related hospitalizations and deaths.						
	CRITERIA	JUDGEMENTS			RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a public health priority?	No	Un-certain	Yes	Varies by setting	Before rotavirus vaccines first became available in 2006, rotaviruses infected nearly every child by the age of 3–5 years. Globally, rotavirus was the leading cause of severe, dehydrating diarrhoea in children aged <5 years, resulting in an estimated >500 000 childhood deaths and >2 million hospitalizations worldwide in 2000. Between 2013 and 2017, an estimated 122 000–215 000 child deaths due to rotavirus occurred annually, representing a decline of 59%–77% since 2000. In most low income countries in Asia and Africa, the
		<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	

BENEFITS & HARMS OF THE OPTIONS

VALUES & PREFERENCES						of follow-up, ranging from 48% to 57%. ^{ii,iii}		
	<u>Harms of the intervention</u>	<i>No</i>	<i>Un-certain</i>	<i>Yes</i>	<i>Varies</i>		Each of the WHO prequalified rotavirus vaccines has demonstrated a good safety profile. Intussusception has been associated with rotavirus vaccines; no other serious adverse event has been identified. ⁱⁱ	
	Are the undesirable anticipated effects small?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			
	Balance between benefits and harms	<i>Favours intervention</i>	<i>Favours comparison</i>	<i>Favours both</i>	<i>Favours neither</i>	<i>Unclear</i>	Balancing benefits and harms, rotavirus vaccination is favoured over no vaccination.	
	What is the overall quality of this evidence for the critical outcomes?	Effectiveness of the intervention <i>No included studies</i> <i>Very low</i> <i>Low</i> <i>Moderate</i> <i>High</i> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> Safety of the intervention <i>No included studies</i> <i>Very low</i> <i>Low</i> <i>Moderate</i> <i>High</i> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>					The GRADE tables are published within the systematic review. Please see “Update of a systematic review and meta-analysis of the safety, effectiveness and efficacy of childhood schedules using Rotavirus vaccines”. ⁱⁱ	
How certain is the relative importance of the desirable and undesirable outcomes?	<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>	No global evidence available, though it is assumed that there is no important uncertainty or variability in respect to the desirable and undesirable outcomes.		

RESOURCE USE	Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?	No	Probably No	Uncertain	Probably Yes	Yes	Varies	No global evidence available, though it is assumed that there is no important uncertainty or variability in respect to the desirable and undesirable effects. It is assumed that the target population (their caregivers) assign more weight to the desirable effects than to the undesirable effects related to rotavirus vaccination.	
	Are the resources required small?	No	Uncertain	Yes	Varies			Additional resources may be needed to introduce rotavirus vaccine, though existing platforms for infant immunization could be leveraged and support by funding agencies may be available to certain countries.	
	Cost-effectiveness	No	Uncertain	Yes	Varies			Rotavirus vaccination is cost-effective in most low- and middle-income countries when compared to no vaccination, with multiple studies in these settings finding rotavirus vaccination to be highly cost-effective or even cost-saving. ⁱⁱⁱ	
EQUITY	What would be the impact on health inequities?	Increased	Uncertain	Reduced	Varies			Providing protection against the most common diarrheal disease is critically important, regardless of place of birth, in particular given the limited treatment options in low-resource	

							settings. The intervention would contribute to reducing health inequities by ensuring protection of children against a potentially life-threatening disease.		
ACCEPTABILITY	Which option is acceptable to key stakeholders (Ministries of Health, Immunization Managers)?	<i>Inter-venti on</i>	<i>Com paris on</i>	<i>Both</i>	<i>Neit her</i>	<i>Un-clear</i>	In light of the balance of benefits vs harms, it is assumed that the intervention is acceptable to most key stakeholders.		
		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
	Which option is acceptable to target group?	<i>Inter-venti on</i>	<i>Com paris on</i>	<i>Both</i>	<i>Neit her</i>	<i>Un-clear</i>	Vaccine acceptability in general varies between (sub)population groups and may be correlated with the perceived risk posed by the disease. In general, it is assumed that the target population (their caregivers) strongly favour the intervention-induced protection. Further, this vaccine is given orally, which is likely more acceptable than an additional injection.		
		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
FEASI BILIT	Is the intervention	<i>No</i>	<i>Pro bab ly</i>	<i>Un-cer</i>	<i>Pro ba bly</i>	<i>Yes</i>	<i>Varie s</i>	The vaccine is assumed to be easily implementable in settings – including	

	feasible to implement?	<div> <div>No</div> <div>tain</div> <div>Yes</div> </div> <div> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> </div>	<p>low- and middle-income-countries – with existing vaccine logistics and delivery infrastructure.</p> <p>Storage and distribution requirements of the rotavirus vaccines are the same as those of many other vaccines currently in use globally. The oral administration route of the vaccine may be easily implementable, although administration-related challenges remain (see background document ⁱⁱⁱ).</p>		
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 <input checked="" type="checkbox"/>	We suggest considering recommendation of the intervention <input type="checkbox"/> Only in the context of rigorous research	We recommend the comparison <input type="checkbox"/>	We recommend against the intervention and the comparison <input type="checkbox"/>	

	<input type="checkbox"/> Only with targeted monitoring and evaluation <input type="checkbox"/> Only in specific contexts or specific (sub)populations
Recommendation (text)	Please see the Rotavirus vaccines: WHO position paper – July 2021 (www.who.int/publications/i/item/weekly-epidemiological-record-vol.-28-2021-96-301-320 , accessed May 2022)
Implementation considerations	Please see the Rotavirus vaccines: WHO position paper – July 2021 (www.who.int/publications/i/item/weekly-epidemiological-record-vol.-28-2021-96-301-320 , accessed May 2022)
Monitoring and evaluation	Please see the Rotavirus vaccines: WHO position paper – July 2021 (www.who.int/publications/i/item/weekly-epidemiological-record-vol.-28-2021-96-301-320 , accessed May 2022)
Research priorities	Please see the Rotavirus vaccines: WHO position paper – July 2021 (www.who.int/publications/i/item/weekly-epidemiological-record-vol.-28-2021-96-301-320 , accessed May 2022)

References

ⁱThis Evidence to Recommendation table is based on the DECIDE Work Package 5: Strategies for communicating evidence to inform decisions about health system and public health interventions. Evidence to a recommendation (for use by a guideline panel). (www.decide-collaboration.eu, accessed May 2022)

ⁱⁱ Update of a systematic review and meta-analysis of the safety, effectiveness and efficacy of childhood schedules using Rotavirus vaccines. (https://terrance.who.int/mediacentre/data/sage/SAGE_eYB_October_2020.pdf, accessed May 2022)

ⁱⁱⁱ Rotavirus epidemiology and rotavirus vaccines, including economic evidence for use and programmatic considerations for vaccine implementation (https://terrance.who.int/mediacentre/data/sage/SAGE_eYB_October_2020.pdf?ua=1, accessed May 2022)