

A systematic review of effectiveness, immunogenicity, impact and cost effectiveness of paediatric hepatitis A vaccines

Is one dose enough?

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In confidence

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SAGE Hepatitis A WG composition: Secretariat

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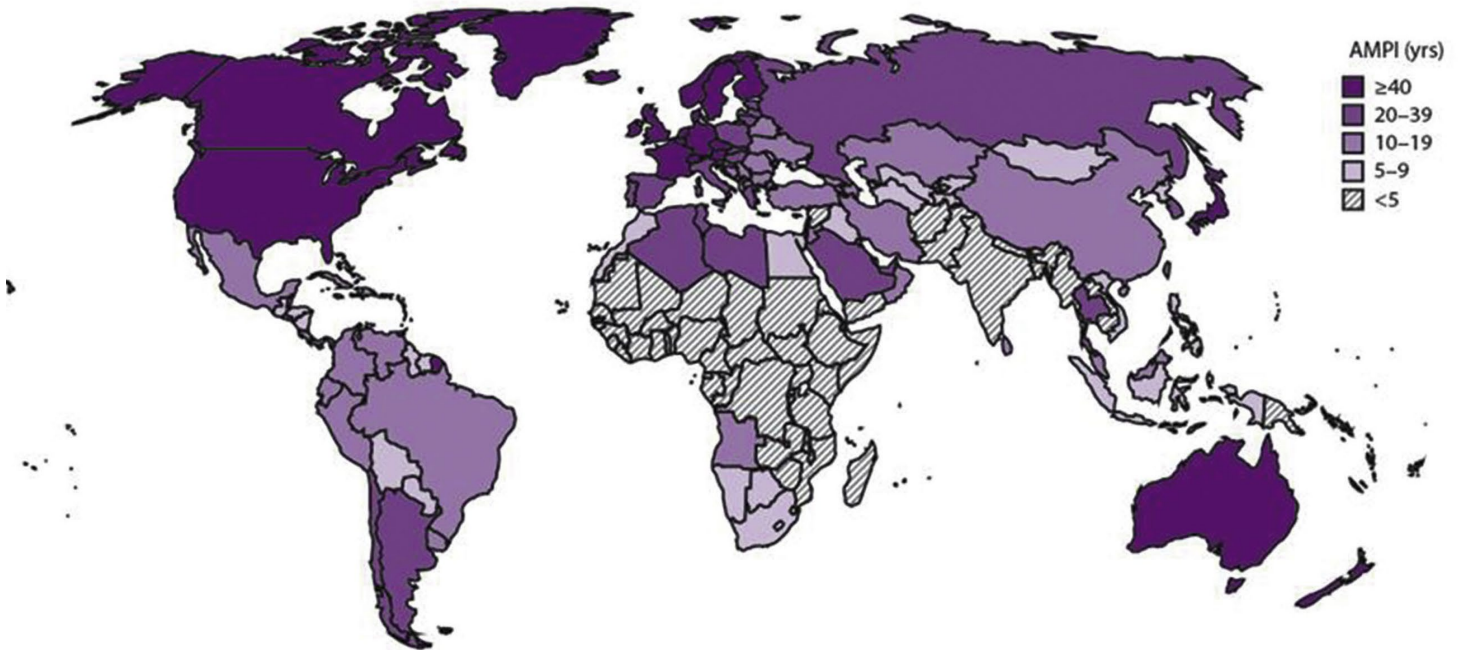
Nick Walsh

Johanna Torres



Global epidemiology

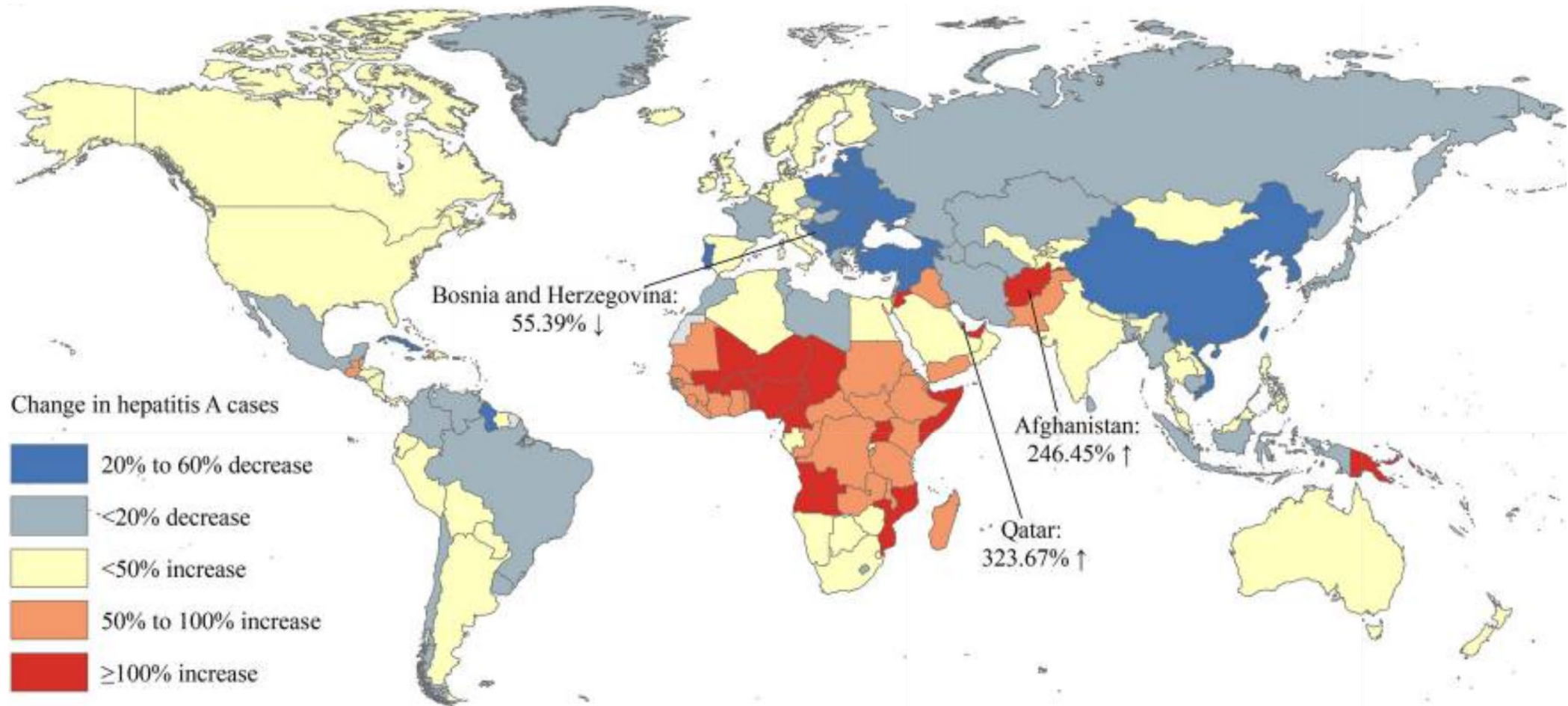
- In 2019, according to Global Burden of Disease Study (GBDS)
 - 159 million acute infections
 - 39 000 deaths
 - 2.3 million DALYs
- LIC and LMIC account for
 - 66% of cases
 - 97% of deaths
- **Australia**
 - **248 notifications in 2025**
 - **Mostly male, < 35**



Map of estimated age (in years) at midpoint of population immunity (AMPI) to hepatitis A by country in 2015.

From: Jacobsen KH. Globalization and the Changing Epidemiology of Hepatitis A Virus. Cold Spring Harb Perspect Med. 2018 Oct 1;8(10):a031716.

Hepatitis A – change in incidence (ASIR), 1990 - 2019



Cao G, Jing W, Liu J, Liu M. The global trends and regional differences in incidence and mortality of hepatitis A from 1990 to 2019 and implications for its prevention. *Hepatol Int.* 2021 Oct;15(5):1068-1082. doi: 10.1007/s12072-021-10232-4. Epub 2021 Aug 3. PMID: 34345993; PMCID: PMC8514357.

The evidence review

Should single dose hepatitis A vaccine - inactivated or live attenuated- (vs two dose inactivated) be used in national paediatric programs to prevent hepatitis A disease?

CONTEXT:

- *The WHO vaccine position paper is from 2012, when evidence on single- dose immunization was quite limited*
- *Since then, single-dose national programmes have expanded and further epidemiologic data are available to support the use of such programmes.*

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The answer:

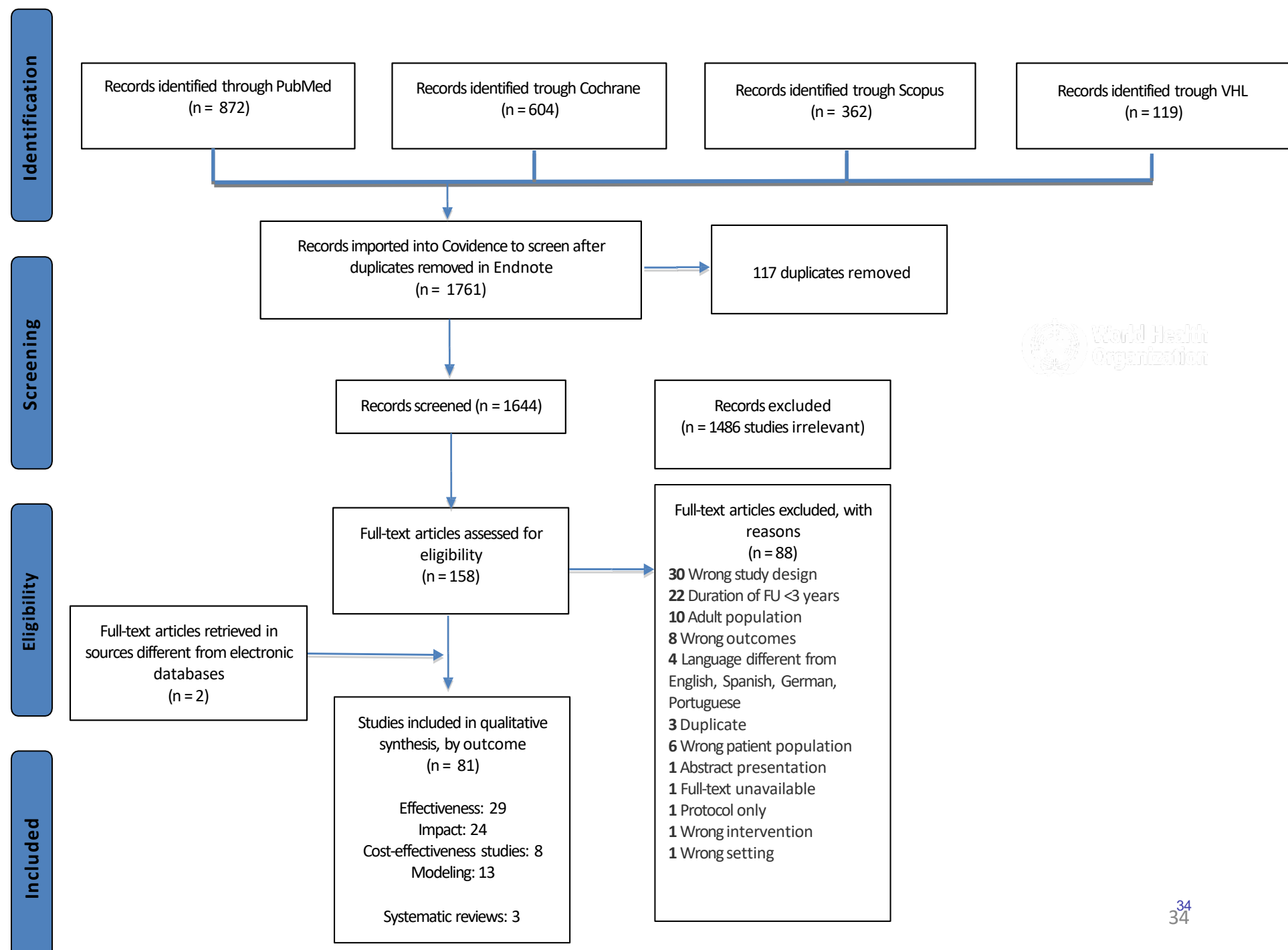
Yes

Walsh, N., Torres, J., & Curtis, S. (2022). *Hepatitis A childhood and adolescent vaccination: A systematic review of the effectiveness, immunogenicity, impact, safety and cost-effectiveness of pediatric vaccines: Final report to the World Health Organization Strategic Advisory Group of Experts on Immunization Working Group on hepatitis A vaccines*. https://cdn.who.int/media/docs/default-source/immunization/sage/vpp-background-documents/sage_hepatitisa_wg_systematic_review_09mar22.pdf?sfvrsn=26166494_1_4

2026 analysis updated to June 2026

Results

PRISMA chart



Overall results

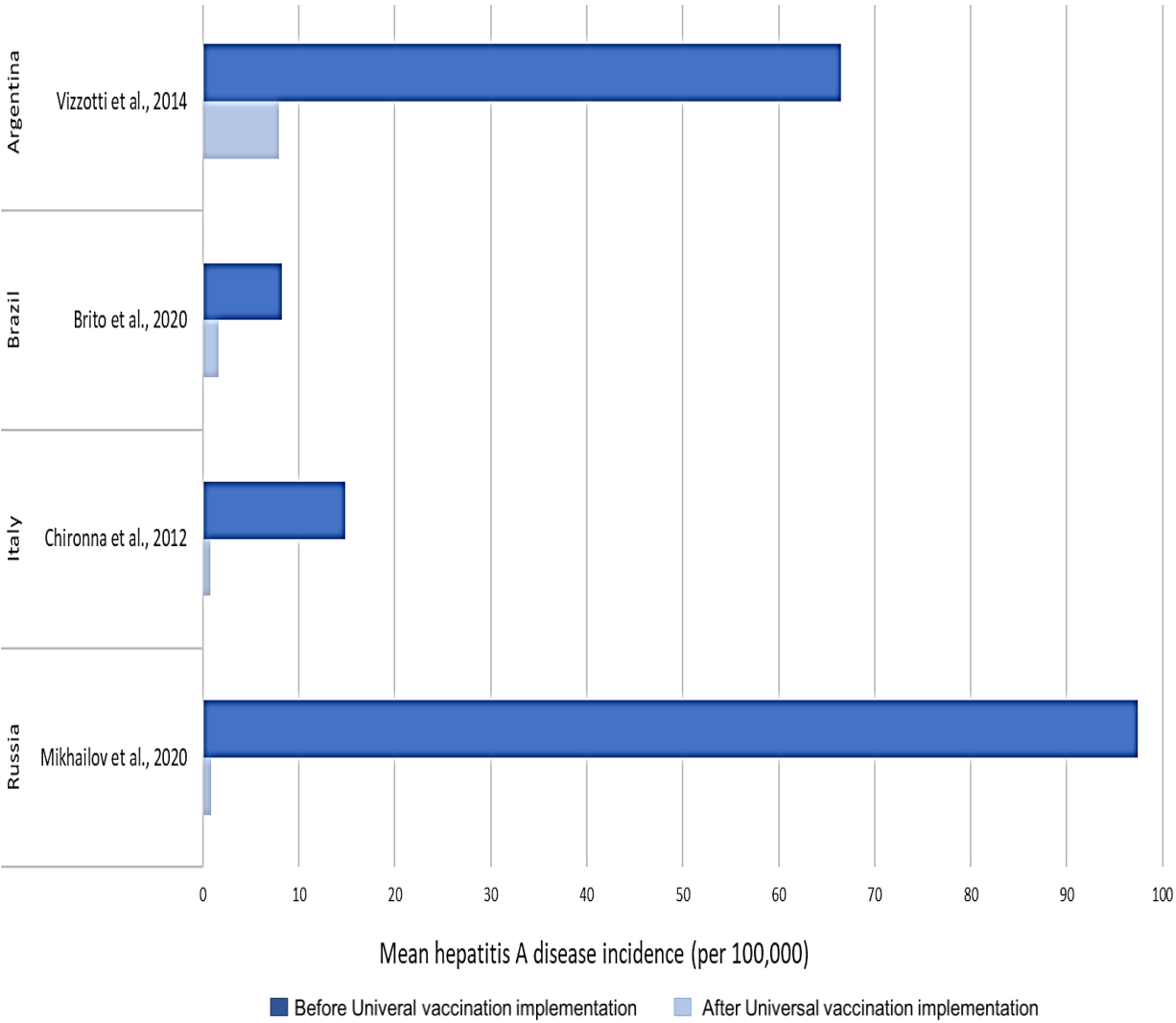
- HAV vaccination is **highly effective in preventing clinical disease**.
- **No difference in the short (< 7 years) or over long-term (>7 years)** comparing HAV single- dose vaccine and two-dose schedules in:
 - **Clinical disease incidence**
 - **Seroprotection**
- However, **GMC (antibody titre) is lower for single dose schedules**.
- **HAV vaccines are safe**. Adverse events are generally mild and infrequent.
- **Both** one and two-dose **schedules** show **substantial population level impact** on reported new cases of clinical disease
- **Both** one and two-dose **schedules** are **cost-effective but single dose are cost-saving**.
- Limited data on long term cellular immunity; however **suggests single-dose confers strong cellular immunity over the long-term**, even where antibody titres are below seroprotection thresholds.

Summary of Findings – effectiveness (6)

Single dose HAV vaccine (LIVE attenuated) compared to 2 dose HAV vaccine (inactivated) 7 -25 years follow up

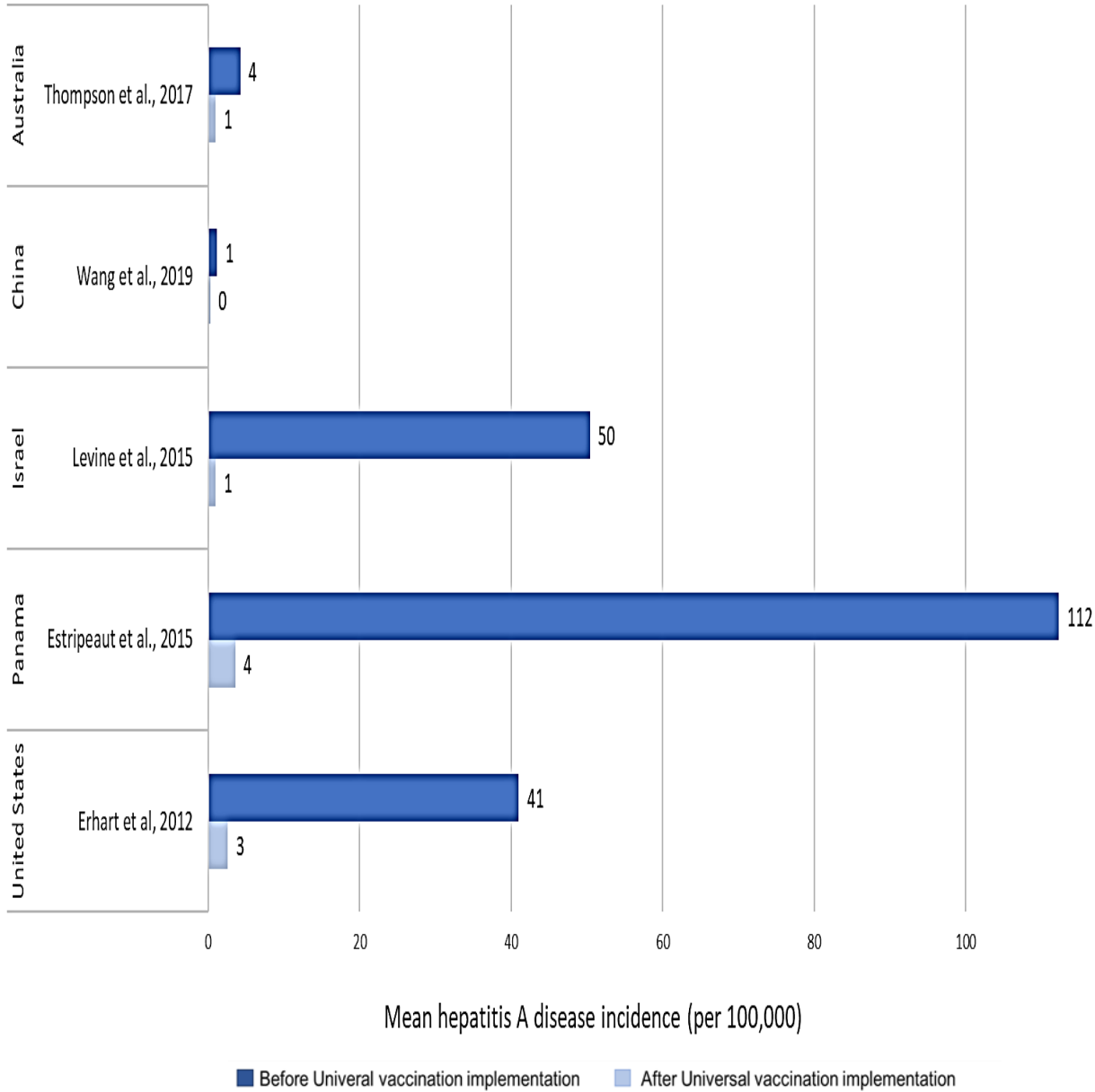
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)
	Risk with 2 dose HAV vaccine (inactivated)	Risk with Single dose HAV vaccine (live attenuated)			
hepatitis A disease incidence (Incidence) assessed with: Cases of HAV clinical disease follow up: range >7 years to 25 years	0 per 1,000	0 per 1,000 (0 to 0)	RR 1 (1 to 1)	149 (2 observational studies)	 ⊕○○○ VERY LOW 1,2,a,b,c
hepatitis A seroprotection (Seroprotection) assessed with: Anti HAV Ab titre > study cut-off follow up: range 7 years to 25 years	980 per 1,000	980 per 1,000 (950 to 1,000)	RR 1.00 (0.97 to 1.03)	1026 (7 observational studies)	⊕○○○ VERY LOW 1,2,3,4,5,6,7,a,b,c,d,e
Geometric mean concentration (GMC) assessed with: Anti HAV Ab titre IU/mL follow up: range 7 years to 25	The mean geometric mean concentration was 145.0 IU/mL	MD 65.4 IU/mL lower (68 lower to 62.9 lower)	-	774 (7 observational studies)	⊕○○○ VERY LOW 1,2,3,4,5,6,7,a,b,c ^{4,0} ₄₀

Population impact: 1 and 2 dose



Mean change in in all-ages HAV incidence before and after

universal HAV vaccination program with **single-dose Inactivated** vaccine schedule.
Inactivated



Mean change in in all-ages HAV incidence before and after

universal HAV vaccination program with **two-dose** vaccine schedule.

Modeling: the duration of vaccine immune response

- Espul 2025 (1 vs 2 dose study, n = 438/101):
 - Modeling of both single and two-dose antibody longevity (based on 15 years of post vax follow up data in toddlers)
→ no difference at 40 years in antibody persistence.
 - Impact of natural boosting on seropositivity at 30 years resulted ~ 5% difference in seropositivity (both schedules)
- Yu 2020 (2-dose study):
 - Seroprotection (>20mIU/mL) persistence at least 60 years

Espul, C., Cuello, H., Lo Castro, I., Bravo, C., Thollot, Y., Voznica, J., Vigne, C. & Coudeville, L. 2020. Statistical modeling alongside observational data predicts long-term immunogenicity of one dose and two doses of pediatric hepatitis A vaccine in the Mendoza province of Argentina. *Vaccine*, 38, 1715-1722.

Espul C, Cuello HH, Saravia A, Vargas ME, Bravo C, Augard C, Coudeville L. Long-Term Antibody Persistence After Hepatitis A Vaccination in Healthy Toddlers: Insights from Modeling. *Infect Dis Ther*. 2026 Feb;15(2):527-538. doi: 10.1007/s40121-025-01278-0. Epub 2025 Dec 12. PMID: 41385061; PMCID: PMC12855680.

Yu, Y. P., Chen, J. T., Jiang, Z. W., Wang, L., Yu, C. K., Yan, X. Y., Yao, C. & Xia, J. L. 2020. Modeling the Long-term Antibody Response and Duration of Immune Protection Induced by an Inactivated, Preservative-free hepatitis A Vaccine (Healive) in Children. *Biomed Environ Sci*, 33, 484-492.

Modeling: vaccine epidemiologic impact

- **Universal immunization programs** have early and substantial epidemiological impact, especially where endemicity is higher.
- **Both single and 2 dose schedules are effective** and the impact difference is determined by assumptions on rate of waning immune protection.
- **Herd immunity is substantial contributor** to overall impact
- Decisions on committing extra resources necessary to initiate a catch-up vaccine program in low endemicity settings require country- and context - specific investigation and analysis

Modeling: cost-effectiveness

- **Single-dose schedules are more cost-effective than two-dose,** even when some reduced efficacy was factored into the single-dose analysis.
 - **Single dose schedules were cost saving.**
- Higher endemicity, lower cost of vaccine and longer seroprotection assumptions resulted in improved cost-effectiveness.
- Assumptions of vaccine coverage were highly heterogeneous across studies.

Implications

Consideration of single dose HAV vaccine for currently recommended paediatric populations Australia

1. Single dose hepatitis A vaccine
2. Routine for national paediatric programs – *where epidemiologically indicated*
3. Measure epidemiologic impact