GRADE table 1:

Need for a yellow fever vaccine booster dose in immunocompetent individuals

Population: Immunocompetent individuals
Intervention: Primary yellow fever vaccination
Comparison: No primary vaccination
Outcome: Duration of immunity

Is there evidence that a booster dose of yellow fever vaccine is required to maintain protection in immunocompetent individuals?				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		10/observational [1]	2
	Factors decreasing confidence	Limitation in study design	None serious[2]	0
		Inconsistency	None serious	0
		Indirectness	None serious[3]	0
		Imprecision	None Serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence		**2**	
Summary of Findings	**Statement on quality of evidence**		**Our confidence in the estimate of the effect on the outcome is limited.**	
	Conclusion		Over 540 million doses of yellow fever vaccine have been used (1) with only 12 cases of secondary vaccine failure reported (2-6)[4]. Healthy persons rarely fail to develop neutralizing antibodies after vaccination (7). Neutralizing antibody titres can be found in most vaccines more than 10 years after vaccination (8-19). Immunity might also be cell-mediated (13;15). In endemic settings, high primary vaccination coverage (60-80%) prevents outbreaks. (20). In immunocompetent persons there is no demonstrated need for a booster dose every ten years.	

Reference s

[1] 6 observational studies reported 74.5-100% neutralizing antibody (NTAb) ≥10years after vaccination. One small study reported 65% (n=13/20) with protective NTAb after 10 years (De Melo et al. 2011). One study (Gomez SY et al. 2008) reported NTAb in >68% in vaccinees after ≥4years post vaccination. One study (Veit et al.2009) reported 88% NTAb 1-10 years after vaccination and one study reported 73% with NTAb 3- 4 years after vaccination (Gibney et al. 2012).

[2] Limitations in only 2 of 8 studies/therefore no downgrading: No clear description of method and incomplete medical records of vaccinated (Poland et al. 1981). Non-standardized methods such as mouse-protection test used (Groot et al. 1962).

[3] Serological marker as proxy to assess level of clinical protection, yet overall agreement in the assumption that titre>1:10 in plaque reduction neutralization test is associated with protective immunity (Hepburn at al. 2006; Monath et al. 2005), therefore no downgrading.

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