

Supplemental Material 4 - Grading of Recommendations, Assessment, Development and Evaluation – GRADE

Question: Is the use of chloroquine/hydroxychloroquine associated with hearing impairment?

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hearing loss	Without hearing loss	Relative (95% CI)	Absolute (95% CI)	
6	Observational studies	Serious ^a	Not serious	Very serious ^b	Serious ^c	None	90/302 (29.8%)	212/302 (70.2%)	OR 0.7600 (0.4154 to 1.3987)	-	⊕○○○ Very low

CI: confidence interval; **OR:** odds ratio

Explanations

a. Inclusion of a study with moderate risk of bias, and no control for confounding factors

b. Impossibility of using direct comparison between chloroquine/hydroxychloroquine users in the synthesis to establish the association

c. Wide prediction interval [PI95% = 0.3226 - 1.8012]