

ONLINE SUPPLEMENTARY CONTENT

Table S1 - Strength of recommendations and levels of evidence according to the GRADE methodology¹¹, with their significance regarding quality of evidence*

Grade of recommendation (1-2) Level of evidence (A-B-C)	Benefit vs risk and burdens	Methodological quality of supporting evidence	Significance
1A	Benefits clearly outweigh risk and burdens	Data arising from numerous RCT or meta-analyses of RCT	Strong recommendation, high quality of evidence
1B	Benefits clearly outweigh risk and burdens	Data arising from RCT with important limitations or large non-RCT	Strong recommendation, moderate quality of evidence
1C	Benefits clearly outweigh risk and burdens	Data arising from small non-RCT, case-series or registries	Strong recommendation, low or very low quality of evidence
2A	Benefits closely balanced with risks and burden	Data arising from numerous RCT or meta-analyses of RCT	Weak recommendation, high quality of evidence
2B	Benefits closely balanced with risks and burden	Data arising from RCT with important limitations or large non-RCT	Weak recommendation, moderate quality of evidence
2C	Uncertainty in the estimates of benefits, risks and burden	Data arising from small non-RCT, case-series or registries	Weak recommendation, low or very low quality of evidence

*Definitions of quality of evidence - *High quality*: Further research is very unlikely to change our confidence in the estimate of effect. *Moderate quality*: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. *Low quality*: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. *Very low quality*: Any estimate of effect is very uncertain.

RCT: randomised controlled trials.

