

11. Appendices

Appendix 1. Levels of evidence and grades of recommendation (SIGN)²¹⁴

Levels of evidence

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1 +	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendations

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

Studies classified as 1- and 2- should not be used in the process of preparing recommendations due to the high possibility of bias.

$\sqrt{1}$	Recommended best practice based on the clinical experience of the guideline development group
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1. In some cases, the guide-preparation team observes that there are important practical aspects that they would like to emphasize and for which there is probably no supporting scientific evidence. In general, these cases are related to some aspect of the treatment that is considered to be good clinical practice and that is not normally questioned. These aspects are classified as points of good clinical practice. These messages are not alternatives to the recommendations based on scientific evidence, but rather should be considered only when there is no other way to highlight the aspect in question.