General methodology

Guideline development process

Full details of the guideline development process, including conflict of interest policy, are outlined in the BHIVA guideline development manual which was last updated in 2021 (see https://www.bhiva.org/file/jgCacHqmuxZFL/GuidelineDevelopmentManual.pdf).

The guidelines were commissioned by the BHIVA Guidelines Subcommittee; the Subcommittee nominated the Chair and Vice-chair of the writing group, who then nominated a writing group of experts in the field based on their knowledge, expertise and freedom from conflicts of interest (the conflict of interest statements of members of the writing group have been published along with these guidelines on the BHIVA website). In addition, BHIVA members were asked to volunteer as authors for the guidelines, again based on their knowledge, expertise and freedom from conflicts of interest.

The scope, purpose and guideline topics were agreed by the writing group. Questions concerning each guideline topic were drafted and an independent systematic literature review undertaken. Details of the search questions, including the definition of populations, interventions, comparators and outcomes (PICOs), and of the search strategy are outlined in appendices within each chapter of the guidelines.

Databases (including Medline/PubMed, Embase and the Cochrane Library) were searched between the date of the previous guidelines and the date of the search (see individual chapters). Abstracts from selected conferences were also searched. For each topic and healthcare question, evidence was identified and evaluated by writing group members with expertise in the field. Using the modified GRADE system (see below for summary of the modified GRADE system), writing group members were responsible for assessing and grading the quality of evidence for predefined outcomes across studies and developing and grading the strength of recommendations. All writing group members received training in the use of the modified GRADE criteria before assessing the evidence.

In areas in which there was a lack of data from randomised controlled trials, the writing group was unable to assign high grades; however, recommendations have been given on best practice where decisions need to be made on the balance of available evidence.

Before final approval by the writing group, the guidelines were published online for public consultation and external peer reviews were commissioned.

Summary of the modified GRADE system

BHIVA has adopted the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for the assessment, evaluation and grading of evidence and the development of recommendations [1,2].

1A Strong recommendation High-quality evidence Benefits clearly outweigh risk and burdens, or vice versa. Consistent evidence from well-performed, randomised controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk. Strong recommendations, can apply to most individuals in most circumstances without reservation. Clinicians should follow a strong recommendation unless there is a clear rationale for an alternative approach.	**2A** Weak recommendation High-quality evidence Benefits closely balanced with risks and burdens. Consistent evidence from well-performed randomised controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk. Weak recommendation, best action may differ depending on circumstances or individuals or societal values.
1B Strong recommendation Moderate-quality evidence Benefits clearly outweigh risk and burdens, or vice versa. Evidence from randomised controlled trials with important limitations (inconsistent results, methods flaws, indirect or imprecise), or very strong evidence of some other research design. Further research may impact on our confidence in the estimate of benefit and risk. Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.	**2B** Weak recommendation Moderate-quality evidence Benefits closely balanced with risks and burdens, some uncertainly in the estimates of benefits, risks and burdens. Evidence from randomised controlled trials with important limitations (inconsistent results, methods flaws, indirect or imprecise). Further research may change the estimate of benefit and risk. Weak recommendation, alternative approaches likely to be better for some individuals under some circumstances.
1C Strong recommendation Low-quality evidence Benefits appear to outweigh risk and burdens, or vice versa. Evidence from observational studies, unsystematic clinical experience or from randomised controlled trials with serious flaws. Any estimate of effect is uncertain. Strong recommendation, and applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.	**2C** Weak recommendation Low-quality evidence Uncertainty in the estimates of benefits, risks and burdens; benefits may be closely balanced with risks and burdens. Evidence from observational studies, unsystematic clinical experience or from randomised controlled trials with serious flaws. Any estimate of effect is uncertain. Weak recommendation; other alternatives may be reasonable.
1D Strong recommendation Very low-quality evidence Benefits appear to outweigh risk and burdens, or vice versa. Evidence limited to case studies. Strong recommendation based only on case studies and expert judgement.	**2D** Weak recommendation Very low-quality evidence Uncertainty in the estimates of benefits, risks and burdens; benefits may be closely balanced with risks and burdens. Evidence limited to case studies and expert judgement. Very weak recommendation; other alternatives may be equally reasonable.

References

1. GRADE Working Group. Grading the quality of evidence and the strength of recommendations. Available at: www.gradeworkinggroup.org (accessed June 2019).

2. Guyatt GH, Oxman AD, Kunz R *et al.* Going from evidence to recommendations. *BMJ* 2008; **336**: 1049–1051.