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Appendix A

Grade of Recommendation & Level of Evidence Summary Table for CAN-ADAPTT Summary Statements

GR/LOE*	CLARITY OF RISK/BENEFIT	QUALITY OF SUPPORTING EVIDENCE	IMPLICATIONS
1A Strong Recommendation High Quality Evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well performed randomized, 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 patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1B Strong Recommendation Moderate Quality Evidence	Benefits clearly outweigh risk and burdens, or vice versa	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	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.
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 randomized, 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.
2A Weak Recommendation High Quality Evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well performed randomized, 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 patients or societal values
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 randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances
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 randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable.

^{*} GR- Grade of Recommendation, LOE – Level of Evidence
** Adapted from: UpToDate. Grading guide. No date. Available from: http://www.uptodate.com/home/about/policies/grade.html; and
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