

Supplemental File 5A: Illustrations of the GRADE approach

Table SF5A-1: The outcome-centric approach in GRADE

| Source | PICO question | Outcomes evaluated ^a | Outcome importance ^b | Systematic review | Recommendation formulation |
|--|--|---|---------------------------------|--|--|
| | | | | Certainty of a body of evidence ^c | Overall certainty of evidence ^d |
| Hanson 2019 ¹ and Crocket 2012 ² | Should lubiprostone be used in the management of opioid-induced constipation in patients with non-cancer pain? | Spontaneous bowel movement response | Critical | Low ⊕⊕○○ | Low |
| | | Reduction in severity of straining | Important | Moderate ⊕⊕⊕○ | |
| | | Adverse effects leading to discontinuation of treatment | Important | Moderate ⊕⊕⊕○ | |
| Lantos 2021 ³ | In patients following a high-risk tick bite, should prophylactic antibiotic therapy be used <i>versus</i> observation? | Clinical evidence of Lyme disease after treatment | Critical | Moderate ⊕⊕⊕○ | Moderate |
| | | Seroconversion | Important | Low ⊕⊕○○ | |
| | | Serious adverse events | Important | Moderate ⊕⊕⊕○ | |

^aSee original citations for a complete list of outcomes that are reported in the GRADE evidence profiles;

^bMultiple stakeholders participate in defining which outcomes are critical and important. This is an early step in the process for developing clinical recommendations;

^cDetermined by consideration of factors that affect confidence in an estimate of effect.⁴ See Table 5.1 in main text for the specific reasons for upgrading and downgrading the certainty of evidence;

^dFor recommendations, overall certainty across outcomes is determined by the lowest certainty of evidence for any outcome rated as critical.⁵

Table SF5A-2: Statement of conclusions on evidence certainty reached with and without application of GRADE^a

| Topic of interest: <i>Should treatment (X) be used to treat (condition) in (population)?</i> Critical outcomes: <i>Quality of Life (QoL), significant adverse events (AEs)</i> Systematic review research question: <i>Is treatment X more effective than usual care for improving QoL in (condition)?</i> | |
|--|--|
| Without application of GRADE | With application of GRADE |
| Treatment X compared to usual care leads to statistically significant improvements in QoL. | There is (<i>high, moderate, low, very low</i>) certainty evidence that Treatment X compared to usual care improves QoL in (population) with (condition). |
| Treatment X was not associated with significant AEs compared to usual care. | There is (<i>high, moderate, low, very low</i>) certainty evidence that Treatment X does not cause more frequent AEs compared to usual care in (population) with (condition). |
| There is sufficient evidence to suggest Treatment X over usual care for improving QoL in (condition). | There is (<i>high, moderate, low, very low</i>) certainty evidence that Treatment X is more effective for improving QoL compared to usual care in (population) with (condition). |

^aThe example is a hypothetical systematic review. Adapted from Samuniak and colleagues.⁶

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