eAPPENDIX 3 Risk of bias assessments

Randomized control trials used as data sources for the included health economic evaluation were assessed using the Cochrane Collaboration Risk of Bias (ROB) tool (Appendix Supplemental Table 4A). We examined the following domains: selection bias (adequate sequence generation, allocation concealment), performance bias (blinding of participants/study personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data addressed), reporting bias (free from selective reporting), and other bias. Assessment used an ordinal scale of low, medium/unknown and high ROB for RCTs.[20]

Non-randomized trials were assessed for ROB using the Newcastle-Ottawa Scale (NOS), examining the following domains: selection (max score of 4), comparability (max score of 2) and exposure (max score of 3) (Appendix Supplemental Table 4B) for cohort and case-control studies (Appendix Supplemental Table 4C).[21]

Quality of the studies were based on either good (3-4 stars in selection domain and 1-2 stars in comparability domain and 2-3 stars in outcome/exposure domain), fair (2 stars in selection domain and 1-2 stars in comparability domain and 2-3 stars in outcome/exposure domain) or poor (0-1 star in selection domain or 0 stars in comparability domain or 0-1 stars in outcome/exposure domain) quality. Each of the criteria for the NOS scales for cohort/case-control studies are found in the footnotes of Appendix Supplemental Tables 4B & 4C.[21]

Surveys were assessed using the ROB tool from the McMaster University Clinical Advances Through Research and Information Translation (CLARITY) group examining the following domains: source population, response rate, missing data, clinical sensibility of the survey and reliability/validity of the survey instrument (Appendix Supplemental Table 4D). Each of the criteria for the NOS scales for cohort/case-control studies are found in the footnotes of Appendix Supplemental Table 4D. Assessment used an ordinal scale of "no, probably no, probably yes and yes" for surveys.[22,23]

For model-based designs, we assessed ROB in each of the multiple contributing source studies in the models. If one the contributing types (RCTs to surveys) of studies had an unknown/high ROB (identified as the weakest link), we concluded that the entire economic evaluation would be assessed an unknown/high ROB. For source articles drawn from SRs, guideline documents or health economic evaluations, we did not assess ROB given that the sources previously assessed in Appendix Supplemental Table 4A-D. We did not assess risk of bias when data were derived from an externally established public database (i.e. Consumer Price Index, etc.).