**NCPE requirements for conducting and reporting**

**clinical evidence synthesis analyses**

This document outlines the NCPE requirements for the conduct and reporting of clinical evidence synthesis analyses submitted to the NCPE as part of a full pharmacoeconomic assessment. Section 3.ii) of the Applicant Submission must be completed according to these requirements. This document may be updated periodically. Please refer to www.ncpe.ie to obtain the most recent version prior to submission.

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*This guidance document should be followed if evidence synthesis methods were used to combine multiple sources of evidence to estimate comparative effectiveness e.g. a pairwise meta-analysis, indirect comparison or network meta-analysis. If not applicable, write “N/A”.*

*All evidence included in the evidence synthesis must be selected following a systematic review which is conducted and reported in accordance with* [*PRISMA*](http://www.prisma-statement.org/) *guidelines. Analysis, reporting and interpretation of the results of evidence synthesis analyses should follow good practice principles.*

## Background

Describe the context of the analysis and the rationale for conducting the evidence synthesis.

## Objective

Describe the objective of the analysis, clearly defining each of the PICOS elements (i.e. population, interventions, comparators, outcomes, study design). The objective should correspond with the decision problem outlined in the Applicant Submission in terms of population, intervention and comparators. Any deviations from the decision problem should be justified. Outcomes should include important clinical and safety outcomes. Provide the rationale for inclusion/exclusion of specific clinical and/or safety outcomes.

## Methods

* 1. ***Eligibility criteria***

Clearly define the inclusion and exclusion criteria. Justify any deviation from the PICOS definitions described above.

* 1. ***Systematic search methods***

Studies should be identified and selected following a systematic review of the published peer-reviewed and grey literature, in addition to any relevant unpublished data available to the applicant. Provide a clear description of the data sources used, and the search strategies used for all electronic databases. *(This may be included in an appendix and a summary included in the main submission).*Database searches must be conducted within six months of the date of HTA submission.

* 1. ***Study selection and data extraction***
* Describe the process of study selection and data extraction, including a flowchart of the study selection process.
* Provide a clear list of excluded studies with reasons for exclusion.
* Where direct and indirect evidence were combined, present a diagram of the evidence network.
* Tabulate the details of each study selected for inclusion including study identifier, design, interventions, population, outcome definitions, analysis methods, baseline characteristics and results*.* Tabulate the individual study data extracted for inclusion in the evidence synthesis analysis *(This may be included in an appendix and a summary included in the main submission).*
* Assess the similarity of studies within the evidence network and discuss any implications for the evidence synthesis methodology, sensitivity analysis, results or interpretation.
	1. ***Quality assessment***
* Complete a quality assessment of each study, including a risk of bias assessment, using a validated quality assessment tool *(This may be included in an appendix and a summary included in the main submission).*
* Discuss the quality of the evidence network and any implications for the evidence synthesis methodology, sensitivity analysis, results or interpretation.
	1. ***Data synthesis methodology***

Clearly describe the evidence synthesis methodology.

* Describe the type of analysis conducted i.e. pairwise meta-analysis, indirect comparison, adjusted indirect comparison, network meta-analysis or other type of analysis. Provide the rationale for the type of analysis.
* Define the outcome measure(s) used in the analysis. Where more than one outcome measure exists, justify the exclusion of alternative measures.
* Describe the statistical model(s) used for each outcome. Specify if a fixed-effects or random-effects model was used and justify the choice of model(s).
* For Bayesian analyses, provide details on priors, convergence and number of iterations.
* Describe how statistical heterogeneity was measured.
* Describe how consistency between the direct and indirect evidence was assessed.
* Outline the approach taken to sensitivity analysis and scenario analysis in order to explore uncertainty in the evidence and/or the analysis base, including uncertainty related to bias, heterogeneity and/or inconsistency.
* Discuss the role for bias adjustment in the presence of imbalances in potential treatment effect modifiers, or heterogeneity in relative treatment effects.
* Provide details of the statistical software and code used to conduct the analysis *(This may be included in an appendix and a summary included in the main submission).*

## Results

* Tabulate and present forest plots and/or posterior distributions of the mean treatment effects and 95% confidence/credible intervals of each treatment versus the common/reference comparator for each outcome, including measures of between-study heterogeneity for random effects models.
* Tabulate and present forest plots and/or posterior distributions of the mean treatment effects and 95% confidence/credible intervals of the intervention versus the comparator(s) for each outcome.
* If absolute treatment effects parameters are required for the economic model, tabulate the absolute treatment effects and 95% confidence/credible intervals for each treatment and outcome.
* Tabulate a comparison of the direct and indirect evidence – present results of pairwise comparisons from the evidence synthesis alongside corresponding results from direct comparative studies, and pairwise meta-analysis if appropriate.
* Present results of model diagnostics to justify model selection.
* Provide the results of the statistical assessment of heterogeneity in the relative treatment effects and inconsistency in the evidence network.
* Present the results of sensitivity analyses, including any adjustments to the analysis as a result of bias, heterogeneity and/or inconsistency.

## Discussion

Discuss the results of the analysis, including the internal and external validity of the analysis, and the assumptions regarding study similarity and evidence consistency.