Lumanity

How to: Perform a Feasibility Assessment

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In the fifth installment of our "How to" series, Lumanity's Ketsia Habimana, Hollie Pilkington, Tracy Westley and Sarah Smith outline why and how to conduct a feasibility assessment for indirect treatment comparisons and focus on whether network meta-analyses (NMAs) can or should be performed.

What is a feasibility assessment?

A feasibility assessment is a process designed to determine whether it is appropriate to perform indirect treatment comparisons (ITCs) of treatments not directly compared in head-to-head randomized control trials (RCTs). The key questions in any feasibility assessment are:

- Can we perform ITCs? If yes, how?
- Given what we know about the evidence base, should we perform ITCs?

There are multiple types of ITCs including standard (Bucher), Network Meta-Analyses (NMAs) and population-adjusted approaches. This guide focuses on the feasibility of conducting NMAs. This method synthesizes results from multiple RCTs at once, estimating differences in treatments for the same indication through direct and indirect comparisons across a connected network of studies.

Why do you need a feasibility assessment?

A formal feasibility assessment provides a framework to systematically identify underlying assumptions, potential biases and robustness of interpretation associated with synthesizing the results of multiple studies to inform a specific research question. This helps to ensure the transparency and validity of the NMA, which is crucial for making informed decisions regarding the comparative efficacy and safety of alternative treatments. The three main assumptions for conducting an NMA are:

Homogeneity:

- In a standard head-to-head meta-analysis of randomized trials, it is assumed that different trials are sufficiently homogeneous
- Trials should estimate the same single treatment effect (fixed effect model) or different treatment effects distributed around a typical value (random effects model)
- This homogeneity assumption should be fulfilled in NMA when multiple trials are involved

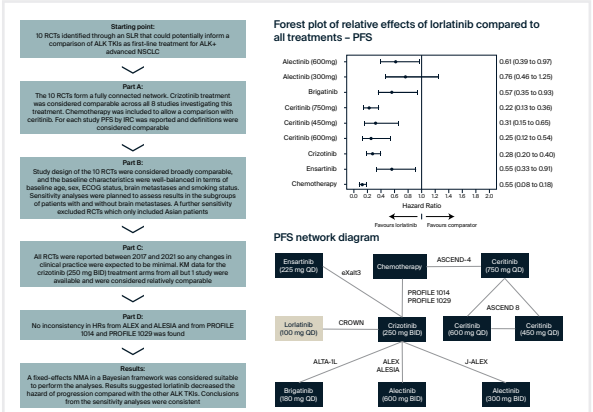
Similarity:

- Characteristics which are treatment effect modifiers should be similarly balanced across trials
- Trial similarity consists of clinical and methodological aspects
- **Clinical similarity:** Trials should be similar in terms of the patients' characteristics, interventions, settings, length of follow-up, and outcomes measured
- **Methodological similarity:** Trials should have similar aspects related to the risk of bias, such as randomization, blinding of participants and assessors, trial length, and design

Consistency:

- Indirect evidence should be consistent with evidence from direct, head-to-head trials, considering clinically meaningful heterogeneity

An example of conducting a thorough feasibility assessment has been portrayed here[2]:



Key: ALK, anaplastic lymphoma kinase; ALK+, anaplastic lymphoma kinase-positive, BID, twice daily; HR, hazard ratio; IRC, independent review committee; KM, Kaplan-Meier; NSCLC, non-small-cell lung cancer; PFS, progression-free survival; QD, once daily; SLR, systematic literature review; TKI, tyrosine kinase inhibitor

How do we develop a feasibility assessment?

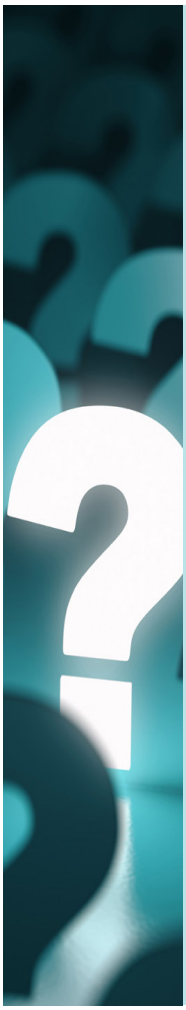
Once the evidence base for the feasibility assessment has been identified, ideally systematically to ensure all relevant information is considered, a feasibility assessment can be divided into two main steps. Step 1 involves an assessment of the clinical and methodological heterogeneity in terms of treatment, outcome, study and patient characteristics. Step 2 consists of an evaluation of the differences within and across the direct pairwise comparisons in terms of baseline risk and observed treatment effects. During any step, it may be decided that an NMA is not feasible.

The key steps, as described in Cope et al. 2014, outline the process for conducting a feasibility assessment[1].

Key principles for consideration:

For Step 2, there are no universally prescribed methods. However, the literature shares common emphasis on certain key principles for consideration:

- **Magnitude of treatment effects:** Evaluating the size of the effects observed in the studies
- **Uncertainty in the estimates:** Assessing the confidence or precision of the effect estimates
- **Risk of bias:** Considering the quality of the RCTs and identifying potential biases
- **Differences in treatment effect modifiers:** Investigating any variations in the distribution of treatment effect modifiers across direct treatment comparisons



Key steps in conducting a feasibility assessment:

1. **Assess clinical heterogeneity:**
   a. Assess differences in treatment and outcome characteristics. Is there a common comparator treatment arm to connect the treatments of interest for each outcome? Only studies which include interventions of interest that connect into the evidence network will be considered for the feasibility assessment
   b. Evaluate study design and patient characteristics to assess clinical and methodological similarity
2. **Evaluate baseline risk and treatment effects:**
   c. Examine differences in baseline risk across studies (from the comparator arms)
   d. Assess observed treatment effects and identify any heterogeneity or inconsistencymodifiers across direct treatment comparisons

About the authors

Have a question for our authors? Use the links below to contact them directly on LinkedIn or by email.

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References

1. Cope S, Zhang J, Saletan S, Smiechowski B, Jansen JP, Schmid P. A process for assessing the feasibility of a network meta-analysis: a case study of everolimus in combination with hormonal therapy versus chemotherapy for advanced breast cancer. BMC medicine. 2014 Dec;12:1-7.
2. Ou SH, Kilvert H, Candlish J, Lee B, Polli A, Thomaidou D, Le H. Systematic review and network meta-analysis of lorlatinib with comparison to other anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitors (TKIs) as first-line treatment for advanced ALK-positive non-small-cell lung cancer (NSCLC). Lung Cancer. 2024 Sep 29:107968.

We hope you enjoyed the fifth in our series explaining how to undertake early HEOR evidence generation activities.

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