ISPOR Issue Panel

Current Trends in Clinical Endpoint Evaluation Used for Relative Effectiveness Assessments of Pharmaceuticals in Context with EUnetHTA

Sponsor perspectives: Michael Schlichting, Merck Healthcare KGaA

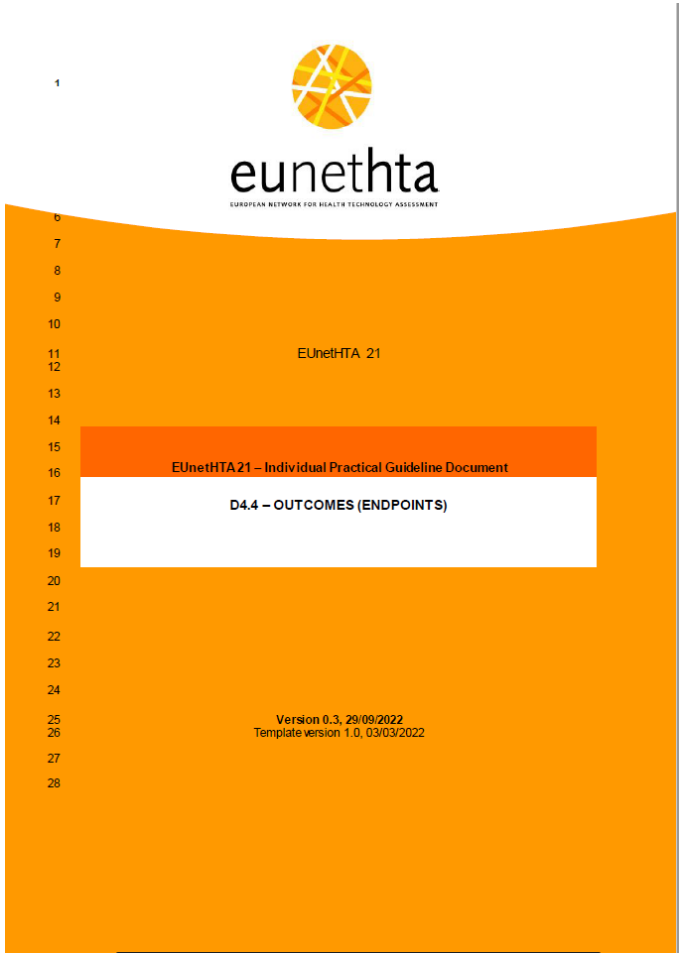
Conflict of Interest

Michael Schlichting is employed by Merck Healthcare KGaA, Darmstadt, Germany.

Outline

Focus: Awareness - Practical Aspects on Endpoint Guidance

1. Definition of outcomes
2. Core set of outcomes
3. Long-term and final outcomes
4. Summary / Conclusion



#1 Definition of outcomes

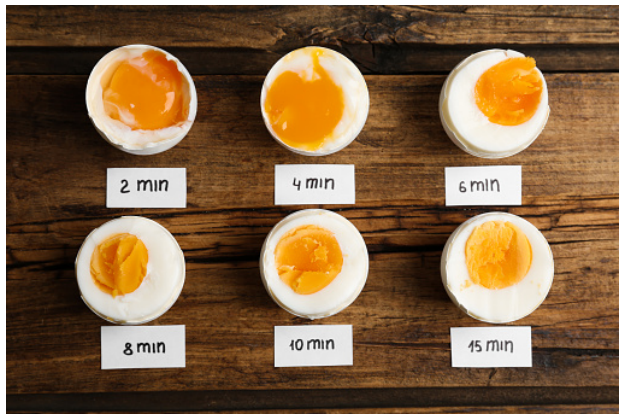
"Definition of outcomes should be as appropriate as possible"

PICOS: Population, Intervention, Comparison, **Outcomes**, Study

*"[Outcome of interest] measured preferably as [**insert measure]"***

*"[Outcome of interest] measured preferably at [**insert timing of assessment]"***

*"[Outcome of interest] with treatment effect expressed preferably as [**insert effect measure]"*.**



#1 Definition of outcomes

"Definition of outcomes should be as appropriate as possible"

Points to consider:

- PICOs prior to study initiation
- PICOs in the scoping process also *incorporating*

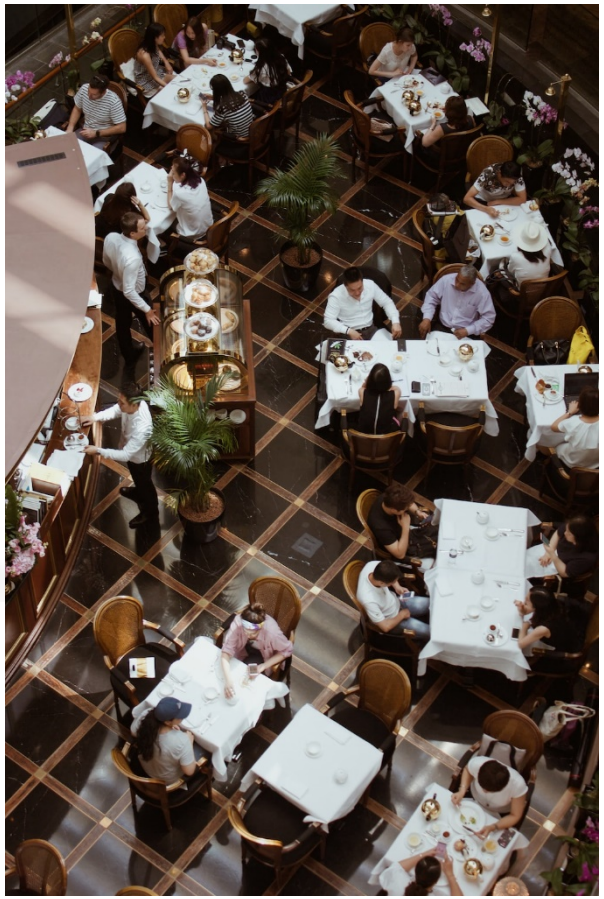
  the intercurrent events *and*

  international recommendations / standards e.g.

  SISAQOL-IMI, InSPiRe, Asterix

#2 Core set of outcomes (COS)

"Well established core outcome sets should be considered, if COS are available"



Pragmatism

- Missing COS for carcinoma
- Too many outcomes for different purposes
- Relevant outcomes from prescribing information

#2 Core set of outcomes (COS)

"Well established core outcome sets should be considered, if COS are available"

Surrogates - Multiple roles of PFS / OR / duration of response

- (Too) Strict validation criteria for surrogate outcomes ?
- Candidate surrogates, likely to predict OS
- Biomarker outcome to indicate tumor growth
- Intermediate outcome that could inform about life expectancy
- Novel, digital, composite endpoints ?

#3 Long-term or final outcomes

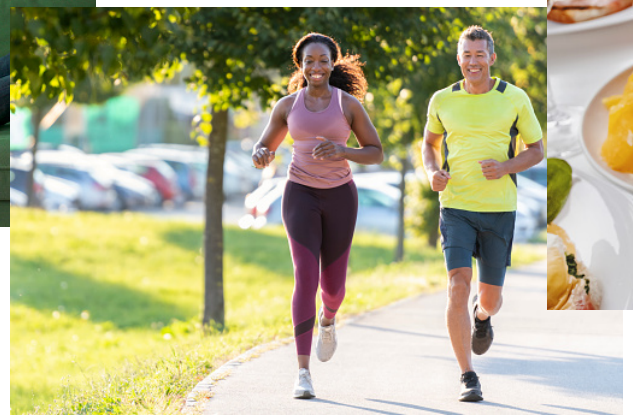
“ … outcomes relevant for HTA should be long-term or final, where possible “

…*where not possible* e.g., when marketing authorization is based on planned interim analysis

- Use of surrogate or candidate surrogates, biomarker or intermediate endpoints
- Statistical approaches to predict, extrapolate outcomes

#3 Long-term or final outcomes

" … outcomes relevant for HTA should be long-term or final, where possible "



Long-term / final = Data collection after treatment discontinuation?

- Interpretability
- Feasibility / Practical barriers
- Clinical most important periods generally covered

#3 Long-term or final outcomes

… provide data for all outcomes requested … regardless of how immature they are

Provision of too immature data could compromise study integrity

- Consultation to align regulatory and HTA needs
- Candidate surrogates
- Modelling

#4 Summary/Conclusion

New EU HTA outcome guidance provide directions how to deal with the several issues encountered around the assessment of endpoints

Appropriate uptake of current methodological practices

PICOs to include intercurrent events

SISAQOL-IMI for PRO; InSPiRe, Asterix for small populations

Pragmatism and constructive dialogue to innovative methodologies / technologies / designs while mitigating uncertainties by statistical reasoning and clinical judgement

Announcement Statistics in EU HTA – PICOs, Estimands & More!

Webinar November 14th, 2022: register https://psi.glueup.com/event/62576/register/

Joint PSI & EFSPI HTA SIG Webinar: Statistics in EU HTA - PICOs, Estimands & More! (WEB292)

Event Details

Starting in 2025, a system for HTA, not entirely unlike that of EMA for regulatory assessments, will apply to new medicinal products submitted for EMA regulatory review. The system will require manufacturers to submit an HTA evidence dossier broad enough to support each member state's evaluation of relative effectiveness within the context of their specific healthcare system.

Is this a ripple that will matter mostly for statisticians specializing in HTA – or is it a splash that should be on all pharmaceutical statisticians radar?

Who is this event intended for? Statisticians who either work on regulatory or HTA submissions, or are involved in evaluating HTA submissions. Non-statisticians who want to understand statistical dimensions of HTA.
What is the benefit of attending? We hope this webinar will provide a deeper awareness and understanding of how the new EU HTA regulation may affect not only HTA but regulatory processes.

12:00-14:00 GMT | 13:00-15:00 CET