A Prevalence-Weighted ICER Approach with Scenario Analyses for HTA without RCT Evidence

EE27

F. T., CHAUDHRY

Norwegian Medical Products Agency (NoMA), Oslo, Norway

INTRODUCTION

From a payer perspective, evaluating the cost-effectiveness analysis (CEA) of treatments across patient subgroups is often constrained by limited randomized control trial (RCT) evidence and modest variation in treatment outcomes.

A single national price commonly applied in multi-indication pharmaceuticals limits the ability to reflect the differing value across patient subgroups[1].

By contrast, indication/population-adjusted pricing offers greater specificity but is constrained by the scarcity of robust real-world evidence.

In such settings, a **weighted ICER approach**—where **subgroup ICERs**[1] are adjusted by **prevalence/**eligible population size can be useful in the decision for overall cost-effectiveness by the decision makers.

OBJECTIVE

1) To construct **a prevalence-weighted ICER** by combining subgroup-specific CEA results derived from external, risk-adjusted data. As an example, we have used data from a pacemaker population[2].

2) To evaluate whether **prevalence-weighted** ICERs yield comparable results to a scenario of **pooled relative-risk (RR)** ICER.

3) To consolidate the ICERs from both scenarios to assist decision makers.

METHOD

Prevalence-weighting: Subgroup ICERs were weighted with respect to their prevalence in order to reflect population-level cost-effectiveness[1].

$$ICER\_pop = (\Sigma(ICER\_i \times P\_i)) / (\Sigma P\_i)$$

where, pop, Population; i = subgroup,; P, Prevalence

Pooled RR: Pooled subgroup RR (mortality) via inverse-variance weighting[3] (confidence intervals (CIs) based) to adjust ICER estimates.

A scenario analysis of the pooled RR adjusted ICER was tested for variation in weights of each subgroup specific RR values based on their CIs.

Lastly, a **credible weighting** was applied for ICERs estimate using **heterogeneity indices, we visualized** and compared ICER outcomes across scenarios within a single, consolidated chart in Figure 1.

$$RR_{index} = \frac{SD(RR)}{Mean(RR)} \text{ and } Prev_{index} = \frac{SD(Prev)}{Mean(Prev)} = \left(\frac{\frac{1}{RRindex}}{\frac{1}{RRi\,ndex} + \frac{1}{Prev\,index}} \right) = w_{RR}$$

$$1 - w_{RR} = w_{Prev}$$

$$ICER_{combined} = (w_{RR} \times ICER_{RR}) + (w_{Prev} \times ICER_{Prev})$$

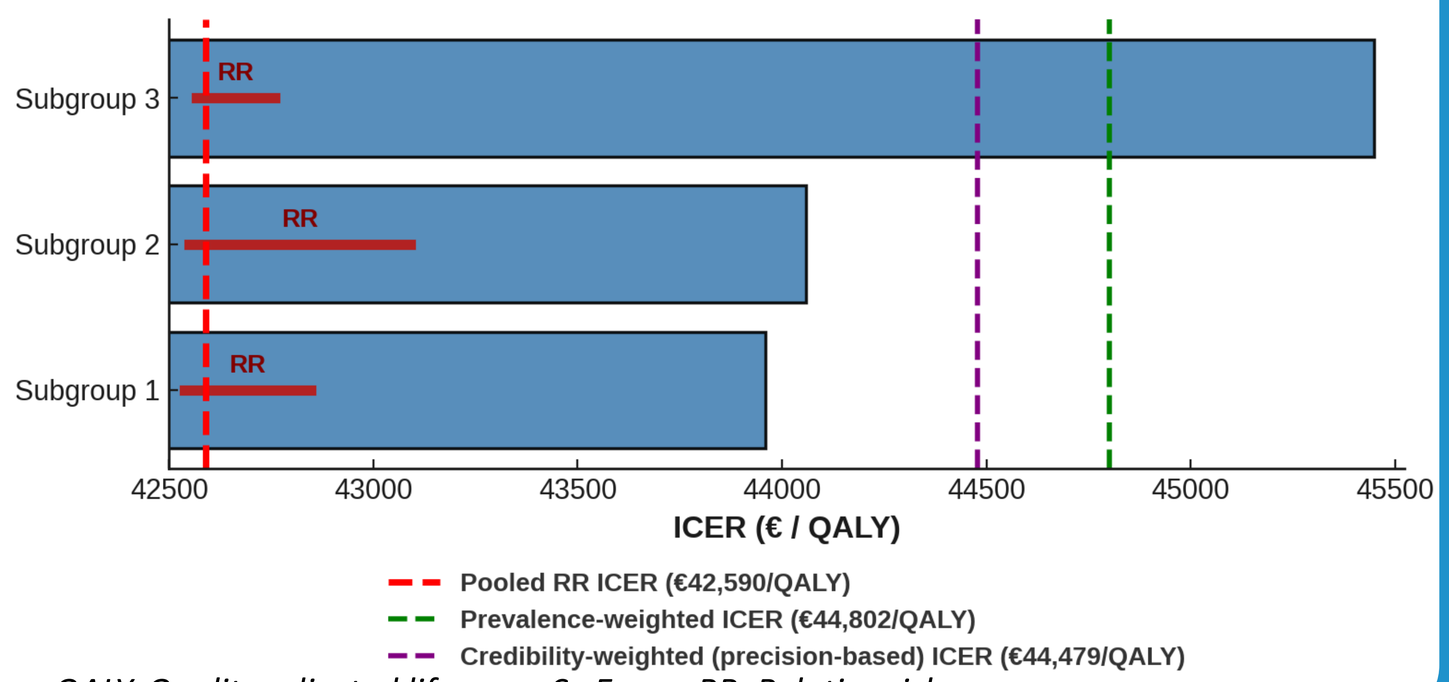
where, Prev, Prevalence: w, weight; SD, standard deviation

RESULTS

Figure 1, presents result summary of weighted ICER and scenario analysis as follows:

1. **Subgroup-specific ICERs** ranged from **€ 43,800 – 45,500/QALY**. **(Blue bars)**
   - ❑ **Subgroup 3** → highest ICER (least cost-effective).
   - ❑ **Subgroup 1** → lowest ICER (most cost-effective).
2. **The prevalence weighted ICER** for all subgroups **≈ € 44,800/QALY** (**green dashed line**).
   - ❑ All subgroup ICERs results are below the prevalence weighted ICER threshold except subgroup 3 ICER.
3. **Pooled RR adjusted ICER** ≈ € 42,600/QALY,
   - ❑ Change (Δ) in ICER due to Δ in weights (Δ CIs of subgroup-specific RR) of the pooled RR **(red bar lines).**
   - ❑ ICER Range lower than prevalence-weighted ICER.
   - ❑ Only **Subgroup 2** has the largest variation in the pooled RR adjusted ICER, suggesting uncertainty (wide CIs).
4. **Credibility-weighted** ICER ≈ **€ 44,500/QALY** (**Purple dashed line**)
   - ❑ **Balances** subgroup ICERs by accounting for both pooled **RR** and **prevalence** variation($w_{RR} = 0.20$ *and* $w_{Prev} = 0.80$).
   - ❑ Narrows the gap between prevalence weighted ICER and pooled RR adjusted ICER.
   - ❑ **Uncertainty Gap** = Prevalence-weighted ICER – Credibility-weighted ICER

Figure 1: Scenario variation frontier illustrating subgroup-specific and weighted ICERs across different approaches, displayed as a bar chart.



QALY, Quality adjusted life year; € , Euros; RR, Relative risk

KEY CONCLUSIONS

- ❑ Pooled RR ICERs are sensitive to parameters with wide CIs, reflecting subgroup uncertainty for the risk estimates such as overall survival and complications.
- ❑ Prevalence-weighted ICERs account for population mix, demographics, and costs.
- ❑ Credibility-weighted ICER balances pooled RR and prevalence variation due to different source for evidence such as expert inputs.
- ❑ Prevalence-weighted ICERs should guide interpretation when subgroup proportions are credible and drive most of the variation in outcomes.
- ❑ The difference between prevalence-weighted and credibility-weighted ICERs may be used to guide **uncertainty-based price discounts**.

REFERENCES

1. Jakobsen M, Holst-Kristensen A. The potential of a weighted average ICER as a supplementary decision tool when assessing the cost-effectiveness of multi-indication pharmaceuticals. *Value Health.* 2020;23(Suppl 2):S526.
2. Direktoratet for medisinske produkter. *Pacemaker uten elektroledning (Micra™ Transcatheter Pacing System)* -: Direktoratet for medisinske produkter; 2023.
3. Lee CH, Cook S, Lee JS, Han B. Comparison of two meta-analysis methods: inverse-variance-weighted average and weighted sum of Z-scores. *Genomics Inform.* 2016;14(4):173-180. doi:10.5808/gi.2016.14.4.173

CONTACT

Fawaz Tariq Chaudhry | Health Economist| Norwegian Medical Products Agency (NoMA), Oslo, Norway
Email: fawaz.chaudhry@noma.no
Scan QR for full contact information

Direktoratet for medisinske produkter

Understanding the Methodology

A Prevalence-Weighted ICER Approach with Scenario Analyses for HTA without RCT Evidence

Fawaz Tariq Chaudhry | Health Economist | Norwegian Medical Products Agency (NoMA), Oslo, Norway
Email: fawaz.chaudhry@noma.no
LinkedIn: www.linkedin.com/in/fawaztariq

Background

In health technology assessment (HTA), evaluating cost-effectiveness across patient subgroups is often difficult when randomized controlled trial (RCT) evidence is limited. A single national price for multi-indication drugs ignores variation in value across patient subgroups. This methodology introduces a prevalence-weighted ICER that combines subgroup results to reflect population-level cost-effectiveness.

Objectives

- Combine subgroup-specific ICERs into a prevalence-weighted ICER.
- Compare it to pooled relative-risk (RR) ICERs from meta-analytic adjustment.
- Develop a credibility-weighted ICER that balances uncertainty and population mix.

Method Overview

Step 1: Prevalence-Weighted ICER
Each subgroup ICER is weighted by its prevalence:
$ICER_{pop} = (\Sigma(ICER_i \times P_i)) / (\Sigma P_i)$

Step 2: Pooled RR Adjustment
Subgroup relative risks (RR) for mortality were combined using inverse-variance weighting based on confidence intervals.

Step 3: Credibility-Weighted ICER
A hybrid ICER was derived combining both sources of uncertainty:
$ICER_{combined} = w_{RR} \times ICER_{RR} + w_{Prev} \times ICER_{Prev}$
Weights were assigned based on heterogeneity indices of RR and prevalence.

Results Summary

- Subgroup ICERs: €43,800–€45,500 per QALY
- Prevalence-weighted ICER: ≈ €44,800/QALY
- Pooled RR adjusted ICER: ≈ €42,600/QALY
- Credibility-weighted ICER: ≈ €44,500/QALY

• The difference between methods reflects the uncertainty gap and can guide uncertainty-adjusted pricing in HTA.

Key Insights

• Prevalence-weighted ICERs better represent population-level cost-effectiveness when subgroup data are credible.

• Pooled RR ICERs highlight uncertainty when subgroup data have wide confidence intervals.

• Credibility-weighted ICER integrates both real-world variation and parameter uncertainty.

• The difference between methods can inform uncertainty-adjusted pricing in HTA.

References

1. Jakobsen M, Holst-Kristensen A. Value Health 2020;23(Suppl 2):S526.
2. Direktoratet for medisinske produkter. Pacemaker uten elektroledning (Micra System). 2023.
3. Lee CH et al. Genomics Inform 2016;14(4):173–180.

Scan to view my LinkedIn profile