

# Lessons Learned from Confounder Identification

Insights from **German HTA Procedures**

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## INTRODUCTION

In the **absence of randomized** controlled trial (RCT) **data**, comparisons between populations from different studies are necessary to assess the efficacy of medicinal products, e.g. by **indirect treatment comparisons**.

Confounding factors have to be incorporated into these comparative analyses as covariates to adjust for baseline parameters in order to **receive unbiased results**, e.g. via the use of PS (propensity score) methods.

### Challenges

Health technology assessment (HTA) bodies, such as IQWiG and G-BA (Germany), acknowledge the importance of systematic literature reviews and expert judgment in confounder identification.

**However, no clear guidance on how to conduct confounder identification is given.**

## METHODS

- Derivation of **methodological requirements** for confounder identification from official documents of German HTA authorities.
- Review of **German HTA submissions** employing confounder identification as well as subsequent **authorities' assessments**.
- Evaluation of **applied methods** and identification of **potential pitfalls**.

## CONCLUSION

Identifying confounding factors for inclusion as covariates in HTA analyses of non-randomized comparisons demands substantial effort in literature reviews and expert judgments, incurring high costs.

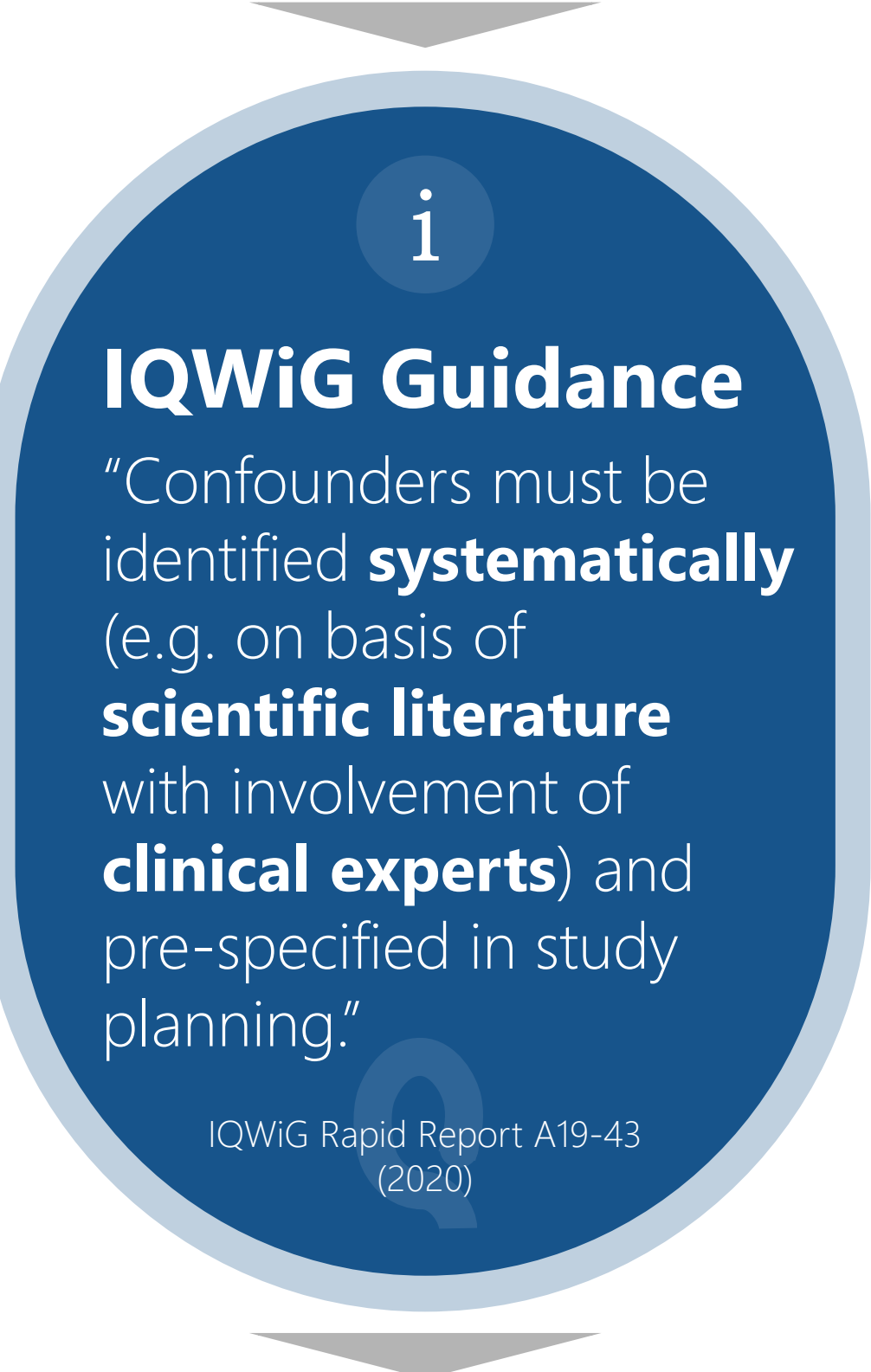
The lack of detailed guidance on methodology from HTA authorities raises uncertainty about the appropriateness of implemented methods.

Establishing an official, pragmatic, and transparent approach for confounder identification is crucial, especially considering the upcoming EU HTA.

## RESULTS

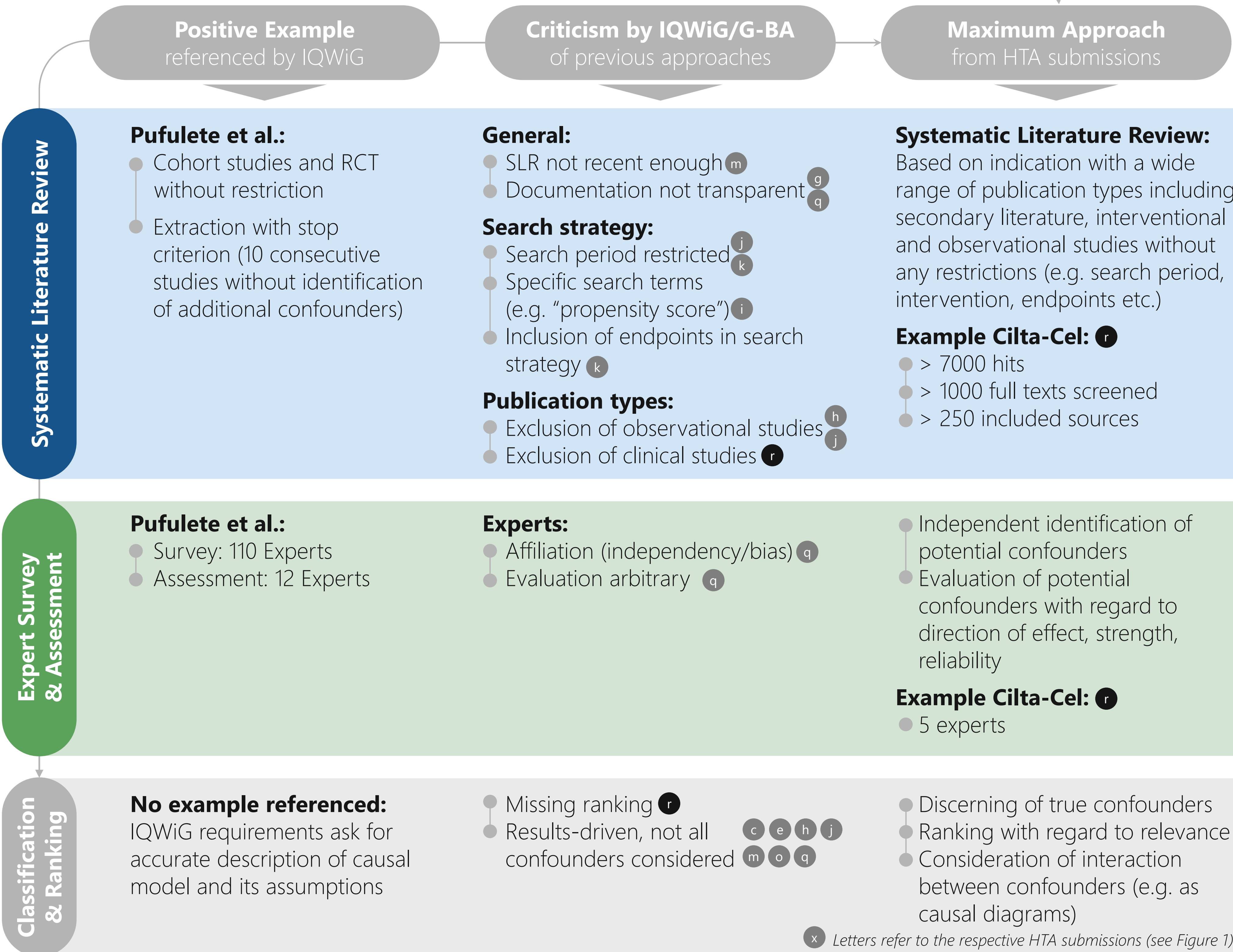
**Despite great efforts, confounder identification was seen as appropriate in only 1 of 18 German HTA submissions.**

Figure 1 Overview of German HTA submissions reporting confounder identification.



**Lack of detailed methodology and strong criticism lead to extensive approaches with huge effort in systematic literature reviews (SLR) and expert judgments.**

Table 1 Requirements vs. approach for confounder identification.



Letters refer to the respective HTA submissions (see Figure 1)

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**References**  
HTA submissions <https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/> (German)  
IQWiG Guidance <https://www.iqwig.de/en/projects/a19-43.html> (English)  
Pufulete et al. Confounders and co-interventions identified in non-randomized studies of interventions. J Clin Epidemiol. 2022 Aug;148:115-123.

**Abbreviations**  
PS: Propensity Score  
IPTW: Inverse Probability of Treatment Weighting  
MAIC: Matching Adjusted Indirect Treatment Comparison