HTA Austria
Austrian Institute for
Health Technology Assessment
GmbH

Overview of Health Economic Evaluation Guidelines

International Best Practices and Implications for Austria

Final report

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List of abbreviations

AdViSHE ..... Assessment of the Validation Status of Health-Economic Decision Models
AIHTA ..... Austrian Institute for Health Technology Assessment
AQoL..... Assessment of Quality of Life
BIA ..... Budget Impact Analysis
CBA..... Cost-Benefit Analysis
CCA..... Cost-Consequences Analysis
CEA..... Cost-Effectiveness Analysis
CEAC…….Cost-effectiveness Acceptability Curve
CET..... Cost-Effectiveness Threshold
CHEC..... Consensus on Health Economic Criteria
CHEERS..... Consolidated Health Economic Evaluation Reporting Standards
CMA..... Cost-Minimisation Analysis
CUA ..... Cost-Utility Analysis
DCEA..... Distributional Cost-Effectiveness Analysis

DSA	Deterministic Sensitivity Analysis
EBM	Evidence-Based Medicine
EQ-5D	EuroQol 5 Dimensions Questionnaire
EU	European Union
EUnetHTA	European Network for Health Technology Assessment
EVPI	Expected Value of Perfect Information
EVPPI	Expected Value of Partial Perfect Information
GDP	Gross Domestic Product
GEAR	Guide to Economic Analysis and Research
HAS	Haute Autorité de Santé (France)
HEE	Health Economic Evaluation
HEEG	Health Economic Evaluation Guidelines
HRQoL	Health-Related Quality of Life
HTA	Health Technology Assessment
HUI	Health Utilities Index
ICER	Incremental Cost-Effectiveness Ratio
INFARMED	National Authority of Medicines and Health Products (Portugal)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care, Germany)
ISPOR	International Society for Pharmacoeconomic and Outcomes Research
JCA	Joint Clinical Assessment
KCE	Belgian Healthcare Knowledge Centre
LYG	Life Years Gained
MAUI	Multi-Attribute Utility Instrument
NB	Net Benefit
NHB	Net Health Benefit
NHS	National Health Service
NICE	National Institute for Health and Care Excellence (England & Wales)
NIHO	National Institute for Value and Technologies in Healthcare (Slovakia)
NMB	Net Monetary Benefit
NOMA	Norwegian Medical Products Agency
OWSA	One-Way Sensitivity Analysis
PBAC	Pharmaceutical Benefits Advisory Committee (Australia)
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Probabilistic Sensitivity Analysis
PSS	Personal Social Services
QALY	Quality-Adjusted Life Year
RCT	Randomised Controlled Trial
RWE	Real-World Evidence
SF-6D	Short Form 6D
SFDA	Saudi Food & Drug Authority
VOI	Value of Information
WTP	Willingness to Pay
ZIN	Zorginstituut Nederland (Netherlands)

Country Codes:

AU - Australia
BE - Belgium
CH - Switzerland
CZ-Czech Republic
DE - Germany
EW - England and Wales
FI - Finland
FR - France
HU - Hungary
IT - Italy
JP - Japan
NL - Netherlands
NO - Norway
PT - Portugal
SA - Saudi Arabia
SK - Slovakia

Executive Summary

Background

Growing healthcare demand driven by demographic change and technological innovation has intensified pressure on healthcare budgets worldwide. Health technology assessment (HTA), particularly health economic evaluation, plays a critical role in supporting evidence-based resource allocation decisions. To ensure consistency and methodological quality, many countries have developed health economic evaluation guidelines (HEEGs), which specify standards for conducting and reporting economic evaluations.

demographic change and technological innovation increase budget pressure → high need for health economic evaluation

Austria currently lacks a publicly endorsed national HEEG with detailed methodological specifications. Existing documents address economic considerations only at a high level and remain optional, leaving substantial uncertainty regarding methodological expectations. This need has become increasingly salient following the 2023 establishment of an appraisal board for selected high-cost medicines under § 62d ff of the Federal Hospitals Act, though the applicability of a HEEG could extend beyond this specific context to a wide range of healthcare decisions concerning resource allocation. Against this background, international HEEGs represent an important reference point. By synthesising international methodological preferences, the report generates structured insights to inform the development of a future Austrian HEEG that is both methodologically robust and tailored to the characteristics of the national healthcare system.

Austria without a binding HEEG – introduction of the Appraisal board process in 2023 as an impetus for national HEEG development

Methods

We conducted a comparative analysis of national HEEGs from countries with healthcare systems comparable to Austria's. Through a comprehensive manual search, we identified guidelines that met the following inclusion criteria: mandatory regulatory status in the given national jurisdiction; published or updated by June 2025; originating in a high-income country; and available in English or a European Union language. The guidelines were analysed using a structured comparative framework covering key aspects of HTA and health economic evaluation (HEE), comprising scope, comparator selection, evidence requirements, analytical methods, perspective, costing, discounting, handling of uncertainty and reporting standards. A qualitative synthesis was used to identify areas of methodological convergence, divergence, and emerging trends. The endorsed methodological choices and their implications were then critically examined in the light of their possible implementation in the Austrian context.

comparative analysis of national HEEGs based on structured criteria

inclusion: mandatory HEEGs from high-income countries

Results

Sixteen HEEGs, predominantly from EU countries, were included in the final analysis: Australia, Belgium, the Czech Republic, England and Wales, Finland, France, Germany, Hungary, Italy, Japan, the Netherlands, Norway, Portugal, Saudi Arabia, Slovakia, and Switzerland.

final analysis set: 16 HEEGs predominantly from EU countries

aspects with strong international convergence: CUA, QALYs, EQ-5D, ICER, time horizon, and modelling details

The analysis revealed a strong international convergence across core aspects of HEEs. Cost-utility analysis using quality-adjusted life years (QALYs) is the preferred analytical approach in most countries, supporting comparability across disease areas and interventions. The incremental cost-effectiveness ratio (ICER) is widely used as the primary summary measure, and randomised controlled trials are consistently identified as the preferred source of evidence on health effects, with acceptance of lower-level evidence when necessary. Furthermore, there is consensus on the necessity of employing decision-analytic modelling in nearly all cases of HEE, with associated requirements for model type justification, validation, and submission of unlocked electronic models. The EQ-5D instrument dominates the measurement of health-related quality of life, although preferences differ regarding the three-level versus five-level versions and the use of national versus foreign value sets. In addition, there is a universal consensus that the time horizon should be long enough to capture all relevant differences in costs and outcomes between the compared interventions.

comparator, BIA, and perspective: economically informed choice, integration, and healthcare payer

Comparator selection relies on the standard-of-care status, though there is an increasing emphasis on economically informed choices, with several HEEGs explicitly requiring the inclusion of the most cost-effective intervention and comparisons via the fully incremental analysis. Budget impact analysis guidelines are integrated into most HEEGs, as the parallel conduct of both analysis types is encouraged, with time horizons ranging from two to six years. While most countries require adopting a healthcare payer perspective in the reference case, several HEEGs extend the strict payer perspective by including specified categories of costs and outcomes, and one HEEG opts for the most comprehensive societal perspective. Uncertainty analysis requirements generally depend on the type of uncertainty present; however, there are differences in the wording of HEEGs regarding the mandatory or recommended probabilistic sensitivity analysis.

divergence on scope, inclusion of equity, discount rates, cost-effectiveness thresholds, and guidance on modelling

Meaningful differences emerge in aspects that reflect national policy priorities, institutional capacity, and value judgements. While there is an observable shift in the HEEG scope to extend to all health interventions, a number of HEEGs is still applicable only to medicinal products, with some extensions. Discount rates cluster around 3-4% annually, though a minority of HEEGs employ differential and time-declining rates. Equity considerations are addressed by only half of the HEEGs and should be primarily incorporated through a qualitative discussion rather than quantitative weighting. Explicit cost-effectiveness thresholds are referenced in some guidelines, whereas others rely on efficiency frontier approach or context-dependent decision-making. Greater variation was also observed in the level of guidance provided for modelling, as well as in the overall comprehensiveness of the HEEGs.

Discussion and implications for Austria

discussion: transferability and implementation requirements for Austria

The analysis indicates that while no single, universally preferred methodological approach exists, there is substantial consensus on the core elements of good practice in HEE. For Austria, these areas of convergence – particularly the preference for cost-utility analysis, standardised outcome measurement, and transparent incremental analysis – provide a robust foundation for developing a national HEEG. The implementation requirements of the identified methodological preferences in the context of the Austrian health care system were also critically evaluated. Certain aspects, such as the regulatory status and scope of the HEEG, the acceptable cost-effectiveness threshold, the preferred perspective, and the discount rate, are strategic in nature. Other aspects, such as the valuation of costs and outcomes, or the complexity of modelling and uncertainty analyses, depend on the availability of relevant data and analytical capacity. Further best practices of HEE, such as selecting suitable comparator(s) and conducting a fully incremental analysis, rely on prior knowledge of the costs and benefits of the interventions used. Such methodological sophistication is observed especially in HEEGs from established HTA systems, likely reflecting years of iterative refinement and investment in analytical infrastructure. The upcoming Austrian HEEG will need to find pragmatic solutions to these methodological challenges.

strategic decisions and capacity building as priorities

some best practices require prior knowledge of cost-effectiveness– a challenge for Austria

limitations: manual search, guideline selection, potential interpretative variation

The review's findings should be interpreted with several limitations in mind. The analysis relied on a manual search rather than systematic literature research, though this approach appropriately addresses the grey literature nature of official guideline documents and should not introduce systematic bias. When multiple HEEGs existed within a jurisdiction, only the primary mandatory HEEG with the broadest scope was included. Further inaccuracies can be attributed to the authors' interpretation of guideline contents, with potential for interpretive variation, especially in translated documents. While the categorisation of HEEGs based on the endorsed methodological preferences was cross-checked against primary sources, minor inconsistencies may persist.

Conclusion

planning of the Austrian HEEG: strategic decisions and capacity building as priorities

The analysis demonstrates that while substantial international consensus exists around core methodological aspects of conducting HEE, there is a scope for tailoring a new HEEG to the circumstances, priorities, and capacities of the national healthcare systems. The development of the Austrian HEEG should prioritise capacity-building in the identified areas requiring pre-existing infrastructure, while involving policymakers in decisions on methodological requirements that reflect societal values and normative preferences.

Zusammenfassung

Hintergrund

demografischer Wandel und technologische Innovation erhöhen Budgetdruck → gesundheitsökonomische n Evaluation gewinnt an Bedeutung

Die wachsende Nachfrage nach Gesundheitsleistungen, bedingt durch den demografischen Wandel und technologische Innovationen, hat den Druck auf die Gesundheitsbudgets weltweit verstärkt. Health Technology Assessment (HTA), insbesondere die gesundheitsökonomische Evaluation, spielt daher eine zentrale Rolle bei der Unterstützung evidenzbasierter Ressourcenallokationsentscheidungen. Um Konsistenz und methodische Qualität solcher Evaluationen zu gewährleisten, haben viele Länder gesundheitsökonomische Evaluationsleitlinien (Health Economic Evaluation Guidelines, HEEGs) entwickelt, die Standards für die Durchführung und Berichterstattung ökonomischer Evaluationen festlegen.

Österreich ohne verbindliche HEEG – Einführung des Bewertungsboardprozesses 2023 fundierte als Impuls für nationale HEEG-Entwicklung

Österreich verfügt derzeit über keine öffentlich anerkannte nationale HEEG mit detaillierten methodischen Spezifikationen. Bestehende Dokumente behandeln ökonomische Aspekte nur auf übergeordneter Ebene und sind nicht verbindlich, was zu erheblicher Unsicherheit hinsichtlich der methodischen Erwartungen führt. Dieser Bedarf hat durch die Einrichtung eines Bewertungsboards für ausgewählte hochpreisige Arzneimittel gemäß § 62d ff. des Krankenanstalten- und Kuranstaltengesetzes im Jahr 2023 an Bedeutung gewonnen, wobei der Anwendungsbereich einer HEEG über diesen spezifischen Kontext hinaus auf ein breites Spektrum von Entscheidungen zur Ressourcenallokation im Gesundheitswesen ausgeweitet werden könnte. Vor diesem Hintergrund stellen internationale HEEGs einen wichtigen Referenzpunkt dar. Durch die Synthese internationaler methodischer Präferenzen liefert der vorliegende Bericht strukturierte Erkenntnisse zur Unterstützung der Entwicklung einer künftigen österreichischen HEEG, die sowohl methodisch fundiert als auch auf die Besonderheiten des nationalen Gesundheitssystems zugeschnitten sein sollte.

Methoden

Methodik: Vergleichende Analyse nationaler HEEG anhand strukturierter Kriterien

Einschluss: Verbindliche HEEG aus Hocheinkommensländern

Es wurde eine vergleichende Analyse nationaler HEEGs aus Ländern mit zu Österreich vergleichbaren Gesundheitssystemen durchgeführt. Mittels einer umfassenden manuellen Suche wurden Leitlinien identifiziert, die folgende Einschlusskriterien erfüllten: verpflichtender regulatorischer Status in der jeweiligen nationalen Jurisdiktion; Veröffentlichung oder Aktualisierung der Leitlinie bis Juni 2025; Herkunft aus einem Hocheinkommensland; Verfügbarkeit in englischer Sprache oder in einer Sprache der Europäischen Union. Die Leitlinien wurden anhand strukturierter Kriterien analysiert, die wesentliche Aspekte von HTA und gesundheitsökonomischer Evaluation umfassen: Geltungsbereich, Komparatorwahl, Evidenzanforderungen, analytische Methoden, Perspektive, Kostenerfassung, Diskontierung, Umgang mit Unsicherheit sowie Berichtsstandards. Eine anschließende qualitative Synthese diente der Identifikation von Bereichen methodischer Konvergenz und Divergenz sowie aufkommender Trends. Die empfohlenen methodischen Entscheidungen und ihre Implikationen wurden zudem im Hinblick auf eine mögliche Umsetzung im österreichischen Kontext kritisch untersucht.

Ergebnisse

finale Analyse: 16 Leitlinien aus überwiegend EU-Länder

Sechzehn HEEGs, überwiegend aus EU-Ländern, wurden in die finale Analyse eingeschlossen: Australien, Belgien, Deutschland, England und Wales, Finnland, Frankreich, Italien, Japan, Niederlande, Norwegen, Portugal, Saudi-Arabien, Schweiz, Slowakei, Tschechien und Ungarn.

internationale Konvergenz: CUA, QALYs, EQ-5D, ICER und Modellierung als Standards

Die Analyse zeigte eine starke internationale Konvergenz in zentralen Aspekten gesundheitsökonomischer Evaluationen. Die Kosten-Nutzwert-Analyse unter Verwendung qualitätsadjustierter Lebensjahre (QALYs) ist in den meisten Ländern der bevorzugte analytische Ansatz und unterstützt die Vergleichbarkeit über Krankheitsbereiche und Interventionen hinweg. Das EQ-5D-Instrument dominiert die Messung der gesundheitsbezogenen Lebensqualität, wenngleich Präferenzen hinsichtlich der Drei- versus Fünf-Stufen-Version sowie der Verwendung nationaler versus ausländischer Wertesätze variieren. Das inkrementelle Kosteneffektivitätsverhältnis (ICER) wird weitgehend als primäres Ergebnismaß verwendet, und randomisierte kontrollierte Studien werden durchgängig als bevorzugte Evidenzquelle für Gesundheitseffekte betrachtet, wobei niedrigstufigere Evidenz bei Bedarf akzeptiert wird. Darüber hinaus besteht Konsens über die Notwendigkeit entscheidungsanalytischer Modellierung in nahezu allen Fällen gesundheitsökonomischer Evaluationen, verbunden mit Anforderungen an die Begründung des Modelltyps, die Validierung sowie die Einreichung editierbarer elektronischer Modelle. Ebenso sollte der Zeithorizont lang genug sein, um alle relevanten Unterschiede bei Kosten und Ergebnissen zwischen den verglichenen Maßnahmen zu erfassen.

methodische Kernanforderungen der HEEGs: Vergleichsgruppe, Perspektive und Sensitivitätsanalysen

Die Auswahl der Vergleichsgruppe richtet sich nach dem Stand der medizinischen Versorgung, wobei wirtschaftlich fundierte Entscheidungen zunehmend an Bedeutung gewinnen; mehrere HEEGs verlangen ausdrücklich die Einbeziehung der kosteneffektivsten Intervention sowie Vergleiche auf der Grundlage einer vollständigen inkrementellen Analyse. Richtlinien zur Budgetfolgenanalyse sind in die meisten HEEGs integriert, da die parallele Durchführung beider Analysetypen empfohlen wird, wobei die Zeithorizonte zwischen zwei und sechs Jahren liegen. Während die meisten Länder im Referenzfall die Einbeziehung der Perspektive des Kostenträgers im Gesundheitswesen vorschreiben, erweitern mehrere HEEGs die strenge Kostenträgerperspektive um bestimmte Kosten- und Ergebniskategorien, wohingegen andere HEEGs sich für die umfassendste gesellschaftliche Perspektive entscheiden. Die Anforderungen an Unsicherheitsanalysen hängen im Allgemeinen von der Art der vorliegenden Unsicherheit ab.

länderspezifische Unterschiede: Anwendungsbereich, Diskontierung, Gerechtigkeit und Entscheidungskriterien

Bedeutsame Unterschiede zeigen sich in Aspekten, die nationale politische Prioritäten, institutionelle Kapazitäten und Wertentscheidungen widerspiegeln. Während eine erkennbare Tendenz besteht, den Geltungsbereich von HEEGs auf alle Gesundheitsinterventionen auszuweiten, gelten eine Reihe von HEEGs nach wie vor nur für Arzneimittel, mit einigen Erweiterungen. Diskontraten konzentrieren sich auf 3-4 % jährlich, wobei eine Minderheit der HEEGs differenzielle und zeitlich sinkende Raten anwendet. Gerechtigkeitsaspekte werden nur von der Hälfte der HEEGs berücksichtigt und werden vorrangig durch eine qualitative Diskussion statt durch quantitative Gewichtung einfließen. Explizite Kosteneffektivitätgrenzwerte werden in einigen Leitlinien referenziert, während andere auf den Effizienzgrenze oder kontextabhängige Entscheidungsfindung zurückgreifen. Eine erhebliche Heterogenität war zudem hinsichtlich des Detaillierungsgrads der Modellierungsvorgaben sowie der inhaltlichen Tiefe der HEEGs festzustellen.

Diskussion und Implikationen für Österreich

Diskussion: Übertragbarkeit und Umsetzungsvoraussetzungen für Österreich

Die Analyse zeigt, dass zwar kein einzelner, universell bevorzugter methodischer Ansatz existiert, jedoch ein substanzieller Konsens über die Kernelemente guter Praxis in der gesundheitsökonomischen Evaluation besteht. Für Österreich bieten diese Konvergenzbereiche – insbesondere die Präferenz für Kosten-Nutzwert-Analysen, standardisierte Ergebnismessung und transparente inkrementelle Analysen – eine robuste Grundlage für die Entwicklung einer nationalen HEEG. Die Umsetzungsanforderungen der identifizierten methodischen Präferenzen im Kontext des österreichischen Gesundheitssystems wurden ebenfalls kritisch bewertet. Bestimmte Aspekte, wie der regulatorische Status und Geltungsbereich der HEEG, der akzeptable Kosteneffektivitätsschwellenwert, die bevorzugte Perspektive und die Diskontierungsrate, sind strategischer Natur. Weitere bewährte Verfahren der gesundheitsökonomischen Evaluation, wie die Auswahl geeigneter Komparatoren und die Durchführung einer vollständig inkrementellen Analyse, beruhen auf Vorabkenntnissen über die Kosten und den Nutzen der eingesetzten Interventionen. Eine solche methodische Genauigkeit ist insbesondere bei HEEGs aus etablierten HTA-Systemen zu beobachten, was wahrscheinlich auf jahrelange iterative Verfeinerung sowie Investitionen in die analytische Infrastruktur zurückzuführen ist. Die künftige österreichische HEEG wird pragmatische Lösungen für diese methodischen Herausforderungen finden müssen.

Best Practices erfordern Vorabwissen zur Kosteneffektivität – Herausforderung für Österreich

Die Ergebnisse der Übersichtsarbeit sollten unter Berücksichtigung mehrerer Limitationen interpretiert werden. Die Analyse basierte auf einer manuellen Suche anstelle einer systematischen Literaturrecherche, wenngleich dieser Ansatz der Natur der Leitliniendokumente als graue Literatur gerecht wird und keine systematische Verzerrung verursachen sollte. Wenn mehrere HEEGs innerhalb einer Jurisdiktion existierten, wurde nur die primäre verpflichtende HEEG mit dem breitesten Geltungsbereich berücksichtigt. Weitere Ungenauigkeiten können der Interpretation der Leitlinieninhalte durch die Autor:innen zugeschrieben werden, mit dem Potenzial zu Interpretationsvariationen, insbesondere bei übersetzten Dokumenten. Obwohl die Kategorisierung der HEEGs anhand der empfohlenen methodischen Präferenzen mit den Primärquellen abgeglichen wurde, können geringfügige Inkonsistenzen bestehen.

Limitationen: manuelle Suche, Leitlinienauswahl und möglichen Interpretationsspielraum, insbesondere bei Übersetzungen

Schlussfolgerung

Die Analyse zeigt, dass zwar ein weitgehender internationaler Konsens über die methodischen Kernaspekte der Durchführung von HEE besteht, jedoch Spielraum für die Anpassung einer neuen HEEG an die Gegebenheiten, Prioritäten und Kapazitäten der nationalen Gesundheitssysteme vorhanden ist. Bei der Entwicklung der österreichischen HEEG sollte der Kapazitätsaufbau in den identifizierten Bereichen, die eine bereits vorhandene Infrastruktur erfordern, Vorrang haben, während politische Entscheidungsträger in Entscheidungen über methodische Anforderungen einbezogen werden sollten, die gesellschaftliche Werte und normative Präferenzen widerspiegeln.

Planung einer österreichischen Leitlinie: strategische Entscheidungen und Kapazitätsaufbau als Prioritäten

Introduction

steigende Nachfrage belastet Gesundheitsbudgets – HTA als Entscheidungsgrundlage

The growing demand for healthcare services, driven by demographic and epidemiological transitions alongside the accelerated introduction of new drugs and technologies, has increased pressure on healthcare budgets worldwide [1]. In the context of constrained healthcare resources, evidence-based processes such as health technology assessment (HTA) play a critical role in informing allocation decisions [2].

Transparenz und Einheitlichkeit bei gesundheitsökonomischen Evaluationen als Grundlage fairer HTA-Verfahren

To ensure policy decisions are applied fairly, a uniform, transparent process for HTA evaluations carried out in accordance with rigorous best-practice standards is needed [3]. Since economic evaluation is a mainstay of HTA, several countries have developed guidelines for the design and conduct of economic evaluations. These health economic evaluation guidelines (HEEG) serve a dual purpose: they assist researchers in determining which methods to use and provide decision-makers with standards for evaluating the quality of submissions [4].

The rationale for country-specific guidelines

nationale gesundheitsökonomische Leitlinien im Kontext unterschiedlicher Gesundheitssysteme

The development of a national HEEG reflects multiple contextual factors, including the country's economic and political environment. Healthcare systems differ fundamentally in their structures, financing mechanisms, and decision-making processes. HEEGs play a pivotal role in supporting reimbursement processes, especially in the countries of the European region [4], where healthcare systems seek to provide coverage for most drugs and technologies through predominantly publicly financed mechanisms, including social health insurance and tax-based schemes [5-7].

länderspezifische Anpassung der Methodik

Beyond reimbursement mechanisms, data availability and quality vary significantly across countries, as does local researcher capacity and health economics expertise. National guidelines thus ensure that economic evaluations are conducted using approaches appropriate to local data availability, healthcare structures, and decision-making contexts [4].

bevorzugte Herangehensweise: Adaption bestehender Leitlinien statt Neuentwicklung oder Übernahme

Moreover, the complex nature of health systems limits the complete adoption of foreign approaches. Countries developing new guidelines must balance international best practices with local feasibility and relevance. Starting "de novo" is inefficient, whilst complete replication ignores important contextual factors. As Sharma et al. (2021) note, the preferable approach appears to be the middle path, which involves adapting existing national HEEG to cater to their local health system needs, current data availability, local researcher capacity, health financing system, and the nature of predominant use for HTA and how it is communicated [4].

The Austrian context: Current situation and need for HEEG

Österreich: fehlende verbindliche Leitlinien für gesundheitsökonomische Evaluationen

Austria currently has no formal publicly endorsed guideline with detailed specifications for conducting health economic evaluations [8, 9]. Although a private industry consulting institute has addressed some methodological issues in a consensus document [10], it lacks precise methodological direction, and its use remains optional, serving as a recommendation rather than a requirement [8, 9]. In addition, there is a document establishing the legal and organisational framework governing the Reimbursement Code (EKO) [11]; it also outlines the principles applied to determine whether a medication used

in the outpatient sector is eligible for public funding based on therapeutic benefit and economic efficiency. While it requires that the cost-benefit ratio be considered justifiable from a health economics perspective, taking into account the direct costs accrued from the perspective of social insurance and the cheapest comparable reimbursed alternative, it does not provide further methodological specifications of health economic evidence typically found in HEEGs internationally. The lack of a systematic approach creates a significant gap in the methodological infrastructure for health economic evaluations in Austria.

Folgen fehlender Standards: Ineffizienz, strategisches Verhalten mangelnde Vergleichbarkeit ohne einheitliche Methodik

In general, such an absence of formal guidelines creates substantial challenges across multiple dimensions. Without standardised methodological approaches, there is a risk of inconsistent economic evaluations that are difficult to compare, undermining transparency in how evidence is generated and assessed and creating barriers to fair and objective decision-making. This uncertainty affects all stakeholders. Producers of health economic evaluations, including research institutions, pharmaceutical and medical device companies, and developers of other types of health interventions (such as public health programs), lack clear guidance on methodological expectations. This may lead to inefficiencies, as resources are spent on analyses that do not meet decision-makers' needs, or to strategic behaviour, where submitters choose approaches that present their interventions most favourably rather than most appropriately. Conversely, decision-makers and researchers face challenges in evaluating the quality and comparability of economic evidence without a clear benchmark against which to assess submissions [9].

Bewertungsboard 2023: Neuer Impuls für nationale Leitlinie in Österreich

jedoch Bedarf über das Bewertungsboard hinaus gegeben

The need for national HEEG has been brought into sharp focus by the establishment in 2023 of an appraisal board ("Bewertungsboard für ausgewählte Arzneimittel") under § 62d ff of the Federal Hospitals Act. This board was established to ensure fair and rapid access to selected high-cost and specialised medicines used in hospitals and at the intersection between hospital and outpatient care, as well as to promote nationally consistent use [12]. HTA supports the board's reimbursement decisions, contributing to evidence-based decision-making and greater transparency. These HTAs evaluate multiple dimensions of new health technologies, including health economic evidence. However, the need for national HEEG should expand beyond the Appraisal Board's specific requirements. Ideally, economic evaluations would be increasingly applied across a wide range of healthcare decision-making contexts in Austria, including hospital planning, healthcare quality initiatives, public health interventions, and resource allocation at both regional and national levels. In this context, standardised guidelines would promote the consistent application of health economic evidence across diverse settings, thereby supporting evidence-based healthcare policy more broadly.

europäische Ansätze als Referenz – Anpassung an österreichische Strukturen nötig

Austria shares similar insurance-based structures with other European countries, making these European approaches particularly relevant reference points. However, Austria's specific healthcare structure, including the interface between hospital and outpatient care, the federal organisation of healthcare delivery combined with regional provision, and the particular role of social insurance, requires careful consideration beyond general European approaches. Hence, there is a clear need for nationally consistent approaches to economic evaluation that can be applied across different regions and decision-making contexts. The integration with existing Austrian healthcare decision-making structures is essential, as guidelines must fit within established processes whilst supporting their evolution [9].

Ziel: Systematische Analyse internationaler Leitlinien als Grundlage für österreichische Leitlinienentwicklung

To date, several attempts have been made to describe and compare national HEE guidelines [4, 11, 12], with some reviews focusing on guidelines developed in European countries [13, 14]. However, in light of recent methodological advancements in health economics, most of the included HEEGs had since been updated. In addition, the breadth of information extracted and presented in these published reviews is limited, not providing the level of granularity and learning opportunities necessary for Austrian HEEG development. This scoping review systematically examines current international HEEGs to provide an overview of international reference cases in health economic assessment. It aims to inform the development of a future national HEEG for Austria, carefully balancing international best practices with local characteristics of the healthcare system to ensure both methodological rigour and practical applicability.

1 Objectives and research questions

The main aims of this project part are to…

- obtain an overview of international HEEGs from health systems comparable to the Austrian one, with the focus on methodological requirements pertaining to the key aspects of health economic evaluation.
- identify convergences and differences in methodological preferences outlined in the HEEGs, as well as emerging trends, such as increased focus on artificial intelligence and complex interventions.
- explore available methodological approaches to health economic evaluations with the foresight of adapting them to the Austrian health system's needs, and initiation of a preliminary draft of an Austrian HEEG.

Projektziele:

Übersicht internationaler Leitlinien

methodische Übereinstimmungen und Unterschiede

Übertragbarkeit für eine österreichische Leitlinie

Research questions

RQ1 What are the key components and methodological standards present in international HEEGs that are required for the development of a robust and standardised HEEG applicable across all health technologies in Austria?

RQ2 How do existing HEEGs from different countries compare, and what lessons can Austria learn from these frameworks for a nationwide HEEG?

2 Method

2.1 Comparative analysis

vergleichende Analyse nationaler gesundheitsökonomischer Leitlinien mittels PICo-Schema

This report synthesises requirements and recommendations detailed in the mandatory national HEEGs and relevant documents of HTA agencies addressing methods for the HEE. To fulfil the objectives of the report, we performed a comparative analysis of HEEGs from selected countries. The following Problem, Interest, and Context (PICo) scheme guided identification, selection, and synthesis to address the research questions.

Table 2-1: PICo scheme

Problem	Some decisions in the Austrian healthcare system, such as reimbursement decisions, are based on evidence-based recommendations from HTAs, including health economic evidence. However, no formal publicly endorsed HEEGs with detailed specifications on the methods to be applied currently exist in Austria. Furthermore, a clear, traceable development, dissemination, and implementation process for such an HEEG is crucial to ensure transparency, objectivity, and effective use by those who contribute to HEE generation (pharmaceutical industry, medical device companies, research institutions, including researchers involved in clinical study design), as well as acceptance by those who use HEE (decision-makers).
Interests	Key components, methodological standards required, and additional domains (AI, complex interventions) for a robust and standardised HEEG based on internationally used HEEGs.
Context	International healthcare context and countries with similar healthcare systems.
Language	English and the official languages of the European Union (EU)
Publication type for literature used during the process	Health economic evaluation guidelines with mandatory use in the given jurisdictions

Abbreviations: AI…artificial intelligence, HEEG…health economic evaluation guideline, HTA…health technology assessment, PICo…Problem, Interests, Context

5-stufiger methodischer Ansatz: Leitlinienauswahl, Definition der methodischen Kriterien, Datenextraktion nach den gewählten Kriterien, qualitative Analyse und Synthese

The comparative analysis was conducted in the following five steps:

1) Selection of national HEEGs that comply with the inclusion criteria (see Chapter 3.2).
2) Definition of key methodological aspects of HEE addressed by the selected HEEGs, with further distinction of aspects that concern overall HTA (including clinical and ethical domains), and aspects related specifically to the HEE of the health intervention.
3) Initial extraction of data from the included HEEGs, familiarisation with the contents and definition of auxiliary questions for each methodological aspect (presented in Table 2-2 below) that guided

subsequent extraction. The questions were formulated by the first author (DS) based on the identification of common issues that the screened HEEGs sought to address for each methodological aspect.

4) Analysis and categorisation of the extracted raw qualitative data (Categorisation tables presented in Appendix) with the support of Claude's large language models, which were employed to assist with the interpretation and identification of common themes. The synthesised results were cross-checked against the primary sources for consistency. This analysis and categorisation were also double-checked by a co-author (SW).

5) Drafting of the report. To answer research question 1, the pre-defined methodological aspects of HEEGs were analysed and presented in the results section. Research question 2 is addressed in the discussion of this report.

Table 2-2: Auxiliary questions that guided the HEEG data extraction and analysis

Methodological aspect	Auxiliary questions
Aspects concerning the overall assessment	
Scope/focus of the guideline	*To what types of interventions is the given guideline applicable?*
Comparator	*How is the comparator defined?*
Preferred sources of evidence on health effects	■ *Is a systematic literature search required?* ■ *Is the evidence hierarchy specified, and are there some notable exceptions?*
Budget impact analysis (BIA)	■ *Is it recommended to conduct BIA alongside the cost-effectiveness evaluation?* ■ *If so, are the methodological recommendations regarding BIA addressed in the same HEEG, or do they refer to a standalone guideline?* ■ *What is the recommended time horizon?*
Equity analysis	■ *Is it specified that the assessment should also cover equity aspects?* ■ *Is equity considered a quantitative modifier via equity weighting?*
Aspects specifically concerning health economic evaluation	
Preferred analytic technique	■ *What type of analysis should be applied in the base case?* ■ *Are there some alternatives provided?*
Preferred measure and valuation of health outcomes	■ *In relation to the preferred type of analysis, what is the preferred clinical effectiveness measure?* ■ *Is there a preferred tool for deriving the outcome specified?*
Preferred perspective	*What perspective should be used for the valuation of outcomes and costs in the base case and in supplementary analysis?*
Included costs	*In relation to the preferred perspective, what categories of resource shall be included in the base case analysis?*
Time horizon	*Is the time horizon of HEE specified in the HEEG? Are there multiple required time horizons?*
Discounting	*What discount rate is used to derive the present value of future costs and outcomes:* ■ *Is the same rate used for discounting both the future costs and outcomes?* ■ *Is it the universal rate per annum, or does it vary with time?* ■ *Does the HEEG specify how the discount rate was derived?* ■ *Must the discount rate be assessed in a sensitivity analysis?*
Cost-effectiveness threshold	*Is a cost-effectiveness threshold (CET) mentioned in the HEEG?*
Modelling preferences	*How do the HEEGs differ in their approach to modelling, which provides the basis for HEE:* ■ *Do they mention an alternative approach to HEE, i.e., trial-based evaluation?*

	■ *Do they provide guidance on when modelling is necessary, or implicitly assume that it is necessary?* ■ *Do they mention some principles guiding the selection of the model (e.g. parsimony principle)?*
Model details required	*Does the given HEE specifically require* *a. inclusion of model validation,* *b. justification of model type, and* *c. submission of an unlocked electronic copy of the model?*
Uncertainty analyses	*In relation to the identified model uncertainty, what types of sensitivity analysis are to be conducted on a mandatory and/or voluntary basis (e.g., presented in a supplementary analysis)?*
Reporting of results	■ *Does the guideline specify a format for reporting results? Does it refer to some reporting standards?* ■ *What are the requirements for presenting the results of incremental analysis?* ■ *What are the requirements for presenting the results of uncertainty analysis?*

Abbreviations: BIA…budget impact analysis, HEE…health economic evaluation, HEEG…health economic evaluation guideline, HTA…health technology assessment.

2.2 Literature search and inclusion criteria

Einschlusskriterien für die Literatur nach umfangreicher manueller Suche, z.B. Leitlinien mit regulatorischer Verbindlichkeit, aus Hocheinkommensländer

A comprehensive manual search was performed to identify HEEGs that met these inclusion criteria:

- national HEEGs with a mandatory regulatory status in the given jurisdiction,
- in case of multiple national HEEGs identified, include the main national HEEG, i.e. the one with the most comprehensive scope,
- published initially or updated by 01 June 2025,
- originating from a high-income country,
- available in English, with the exception of national HEEGs from European Union (EU) member states, which were not excluded based on the publication language.

26 nationale gesundheitsökonomische Leitlinie mit verpflichtendem Charakter identifiziert

Mandatory guidelines were defined as guidelines that specify standards, which are formally (by resolution or decision) or legally binding for use in conducting HEE, whether in the context of external submissions or self-initiated HEE, to support the needs of the given national healthcare system. National guidelines meeting the given definition of mandatory guidelines mostly correspond to guidelines issued by the government authorities, assisting applicants in preparing a submission for reimbursement of a new intervention. Twenty-six guidelines were deemed to be of mandatory nature (Australia, Belgium, Brazil, Colombia, Czech Republic, El Salvador, England and Wales, Finland, France, Germany, Hungary, Indonesia, Italy, Japan, Lebanon, Mexico, Norway, Philippines, Portugal, Saudi Arabia, Slovakia, South Korea, Switzerland, Thailand, The Netherlands, Turkey). Guidelines that solely provided recommendations related to a subsection of HEE, such as costing or budget impact analysis (BIA), were not considered in this review.

initiale Leitliniensuche über ISPOR, GEAR und nationale HTA-Websites

This initial HEEG identification phase was conducted by a co-author (CS) via two website repositories that store resources related to international economic evaluation: the International Society for Pharmacoeconomic and Outcomes

Research (ISPOR) guideline overview (offline since the end of August 2025) and the Guide to Economic Analysis and Research (GEAR) guideline comparison. In addition, the websites of national HTA agencies and the health ministries of individual countries were manually searched to ensure that the latest version of the guideline was included.

Ausschluss von neun Nicht-Hocheinkommensländern und nicht-englischen Leitlinien

In the next step, the first author of the present report (DS) applied the remaining inclusion criteria to the identified national mandatory HEEGs. Firstly, HEEGs from the countries not classified as 'High Income' according to the World Bank country classifications by income level for 2024 and 2025 [15] were excluded from the review to ensure comparability with the economy of Austria. This was the case for national guidelines from nine jurisdictions (Brazil, Colombia, El Salvador, Indonesia, Lebanon, Mexico, the Philippines, Thailand, and Turkey). Secondly, HEEGs from non-EU countries that were not published in English were excluded- this was the case of the South Korean HEEG. The HEEG selection process is depicted with the PRISMA flow diagram (see Figure 2-1).

2.3 Quality assurance

Qualitätssicherung durch interne und externe Begutachtung des Berichts

The quality of the included HEEGs was not assessed, e.g. by using a standardised tool, because the HEEGs have varied recommendations, and no generalised tool is available to assess their quality. However, as part of quality assurance of the HTA report, the report was reviewed by an internal reviewer (IZK) and an external reviewer (MN). The external reviewers were primarily asked to assess the following quality criteria:

- **Technical correctness:** Is the report technically correct (evidence and information used)? Does the report consider the latest findings in the research area?
- **Adequacy and transparency of method:** Is the method chosen adequate for addressing the research question, and are the methods applied transparently?
- **Logical structure and consistency of the report:** Is the report's structure consistent and comprehensible?
- **Formal features:** Does the report fulfil formal criteria of scientific writing (e.g. correct citations)?

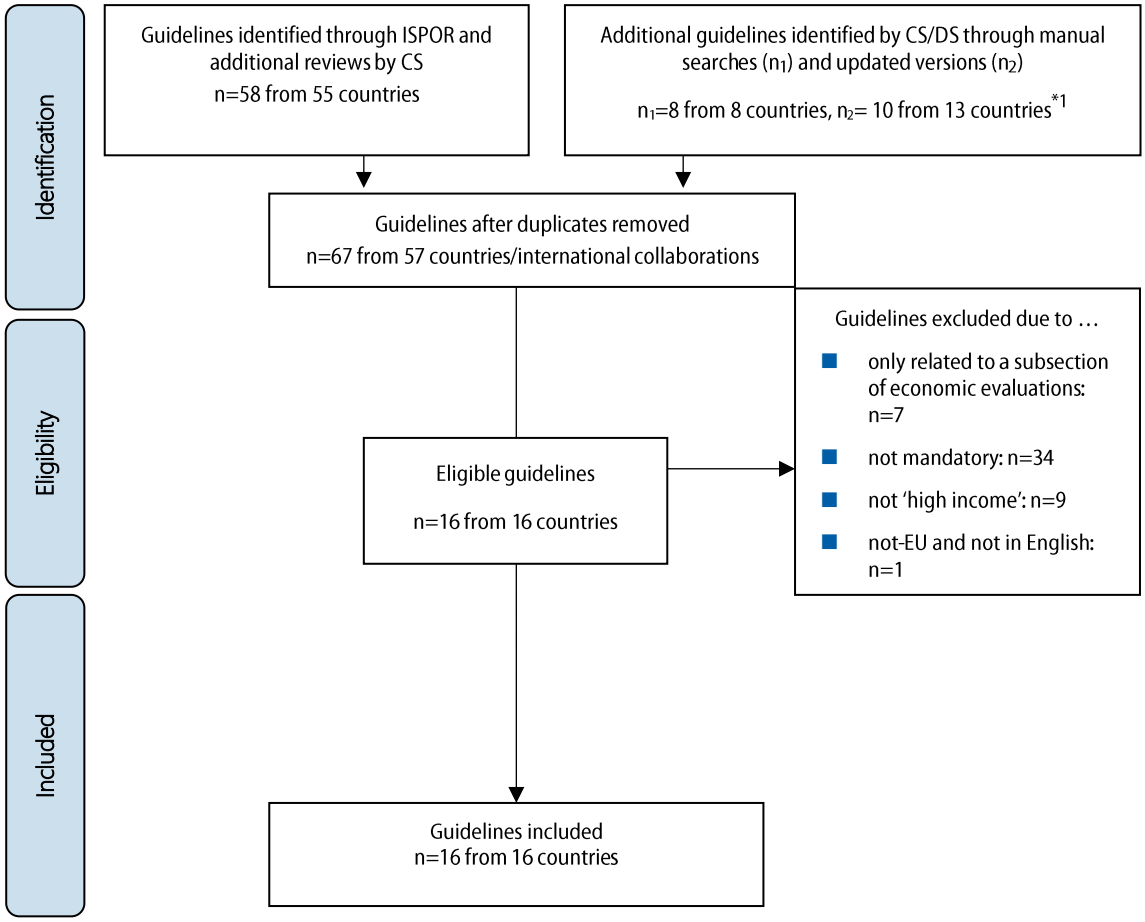

Figure 2-1: Guideline selection process using the PRISMA Flow diagram

3 Results

3.1 Guideline selection

60 Leitlinien identifiziert, davon 16 eingeschlossen

Overall, 60 national HEEGs were identified, 26 of which were deemed to be of mandatory nature[1]. The application of inclusion criteria resulted in a set of 16 national HEEGs that were included in the review (see Table 3-1).

Table 3-1: Included guidelines based on pre-defined criteria

	Country	Institution	Reference
1	Australian (AU)	Pharmaceutical Benefits Advisory Committee (PBAC)	[16]
2	Belgian (BE)	Healthcare Knowledge Centre (KCE)	[17]
3	Czech (CZ)	State Institute for Drug Control (SUKL)	[18]
4	England and Wales (EW)	National Institute for Health and Care Excellence (NICE)	[19]
5	Finnish (FI)	Pharmaceuticals Pricing Board	[20]
6	French (FR)	Haute Autorité de Santé (HAS)	[21]
7	German (DE)	Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG)	[22]
8	Hungarian (HU)	Ministry of Human Resources	[23]
9	Italian (IT)	Agenzia Italiana del Farmaco (AIFA)	[24]
10	Japanese (JP)	National Institute of Public Health (C2H)	[25]
11	Dutch (NL)	Zorginstituut Nederland (ZIN)	[26]
12	Norwegian (NO)	Medical Products Agency (NOMA)	[27]
13	Portuguese (PT)	National Authority of Medicines and Health Products (INFARMED)	[28]
14	Saudi Arabian (SA)	Saudi Food & Drug Authority (SFDA)	[29]
15	Slovak (SK)	National Institute for Value and Technologies in Healthcare (NIHO)	[30]
16	Swiss (CH)	Federal Office of Public Health (FOPH)	[31]

General characteristics of the included guidelines

eingeschlossene Leitlinien: Drei außereuropäische, Publikationszeitraum 1992–2025 alle innerhalb der letzten zehn Jahre veröffentlicht oder aktualisiert

The HEEGs of Australia (AU), Japan (JP) and Saudi Arabia (SA) were the only non-European HEEGs included in this review. The earliest national HEEG included in this review was published in AU in 1992. Currently, the Pharmaceutical Benefits Advisory Committee (PBAC) uses the fifth version of the HEEG updated in 2016. The most recent HEEGs originate from Slovakia (SK) and Saudi Arabia; both were published in 2024. Overall, all included HEEGs were either published or updated in the prior ten years. The HEEGs of Belgium (BE), England and Wales (EW), Germany (DE) and Norway (NO) were updated in 2025.

All the included HEEGs had an English version available on the respective websites of the publishing institutes, except for CZ, DE, HU, IT, and SK HEEGs.

[1] See definition in the Methods section.

3.2 Aspects concerning the overall assessment

3.2.1 Scope/focus of the guideline

Arzneimittel als Kernanwendungsbereich aller eingeschlossenen Leitlinien

All included HEEGs focus on medicinal products (pharmaceuticals) as their core scope, with some extending beyond the "medicinal products only" category to include medical devices (JP, PT), nutritional products (AU, CZ), and/or vaccines (AU, NO). Most national HEEGs adopt a broad scope, covering all health technologies and interventions eligible for reimbursement under the concerned national health insurance system.

Anwendbarkeit der Leitlinie durch Erstattungsregeln des Gesundheitssystems bestimmt

In general, the HEEG's applicability is an exogenous factor determined by the health system's reimbursement rules. For example, BE distinguishes between HEEG's broad methodological applicability and the statutory economic evaluation requirements for reimbursement purposes, since the latter is specifically required only for certain health technologies, namely, Class 1 pharmaceutical products and medical devices. An overview of the HEEG classification based on the scope is presented in Table 3-2.

Table 3-2: Classification of HEEGs by their scope

Focus category	Countries
Medicinal products + limited extensions	Australia, Czech Republic, Japan, Norway, Portugal
Medicinal products only	Germany, Finland, Italy, Saudi Arabia
All types of health interventions	Belgium, England & Wales, France, Hungary, Netherlands, Slovakia, Switzerland

spezifische Anwendungsbereiche, z.B. Chirurgie, Screening, Versorgung

Below, we mention selected categories of health technologies explicitly mentioned as in the scope of the following HEEGs:

- **Surgical procedures**: explicitly included in five HEEGs (BE, CH, EW, HU, SK)
- **Screening programs**: included in four HEEGs (BE, CH, EW, HU)
- **Healthcare delivery**: included in the HEEGs of two countries (BE and EW)
- **Regenerative medicine**: JP specifically includes this emerging field
- **Digital/IT technologies**: mentioned explicitly in the HEEGs of two countries: HU (health information technology) and EW (digital products).

3.2.2 Comparator(s) selection

Länderunterschiede bei der Definition des Vergleichsstandards

Komparatorwahl: Standardtherapie vs. kosteneffektivste Alternative

Gegensätzlicher Ansatz: Fokus auf zu substituierende Behandlung

Most countries define comparator(s) as the standard or commonly used therapies for the given indication in their respective clinical practice. HEEGs of seven countries (BE, DE, EW, FR, JP, NL, PT, SA) incorporate cost-effectiveness considerations in the comparator selection, with four of them (BE, FR, NL, SA) explicitly requesting that one of the comparators is the most cost-effective intervention, even if it is not the one most used in the standard practice. If the most efficient alternative is clearly established, PT allows comparison only with this alternative, whereas BE and NL explicitly state that, in such cases, comparison with both the standard of care and the most cost-effective alternative should be conducted. Similarly, the NICE HEEG mentions the possibility of overriding clinical practice for efficiency reasons when the evaluation suggests that an established practice may not be a good use of National Health Service (NHS) resources, and thus, the committee can decide that it should not be included as a valid comparator.

By contrast, certain countries (AU, FI, HU, JP, NO, SK) highlight in their definition of the comparator the expectation of its displacement by the assessed intervention, emphasising that it should be the treatment most likely to be replaced by the assessed intervention.

unterschiedliche Anforderungen an Komparatorvollständigkeit zwischen den Ländern

Other HEEGs (CZ, FR, IT, PT) strongly emphasise in their comparator definitions the comprehensiveness and the need to identify all clinically relevant alternatives, with FR and PT HEEGs sharing the concern that ex ante restriction of comparators may exclude the most efficient technology and affect the correct determination of the cost-effectiveness frontier. On the other hand, SK is the only country with a quantitative usage requirement, establishing that an intervention must have at least 20% representation in clinical practice for the given indication to be included as a relevant comparator.

unterschiedliche Anforderungen an Erstattungsstatus des Komparators

Some countries (AU, CZ, JP, HU) specify the reimbursement status of the procedure chosen as comparator, specifying that optimally, it should be an intervention included in the benefits scheme. Notably, three HEEGs (BE, EW, PT, SK) address the possibility of choosing as a comparator an intervention that is not licenced for the target population, but its off-label use in clinical practice is well-established. BE, NICE and SK HEEGs further mention that the safety and efficacy of the off-label use need to be supported by evidence (SK HEEG additionally requires clinical data proving its clinical use is ≥20%).

Table 3-3 gives an overview of the identified primary and secondary themes in the comparator definition in the respective national HEEGs. The detailed definitions of the comparators extracted from each HEEG are available in the Appendix.

Table 3-3: Selection criteria for choosing the comparator(s) for HEE

Primary Classification	Secondary Classification	Countries
All relevant alternatives	Most cost-effective	France [21], Portugal [28]
Most commonly used/standard therapy	All relevant alternatives	Czech Republic [18], Italy [24]
	Most cost-effective	Germany [22], Netherlands [26], Saudi Arabia [29], NICE [19]
	Most likely to be replaced	Hungary [23], Slovakia [30]
	-	Switzerland [31]

Most cost-effective	Most commonly used/standard therapy	Belgium [17]
Most likely to be replaced	Most commonly used/standard therapy	Australia [16], Finland [20]
	Most cost-effective	Japan [25]
	Most commonly used/standard therapy	Norway [27]

3.2.3 Preferred sources of evidence on health effects

Evidenzhierarchie in der EBM: Systematische Reviews und RCTs als Goldstandard

In the field of evidence-based medicine (EBM), scientific evidence is hierarchically organised according to the extent to which it is free from the various biases that beset medical research. The strongest evidence for therapeutic interventions is provided by meta-analyses and systematic reviews that combine results of randomised, well-blinded, placebo-controlled trials (randomised controlled trials (RCTs)) with allocation concealment and complete follow-up, involving a homogeneous patient population and medical condition. Consequently, conducting an effective literature search to obtain the best available evidence is the basis of any evidence-based discipline, particularly EBM [32, 33]. The synthesised evidence obtained by systematic search should inform any HTA, providing input for further modelling.

RCTs als bevorzugte Evidenzquelle, indirekte Vergleiche nur subsidiär

The identified HEEGs demonstrate a unified approach to evidence requirements, reflecting broad accordance with the established principles of EBM. Unanimous preference for RCTs that directly compare the medicine with the main comparator in the proposed indication is expressed, as is acceptance of lower-level evidence, such as indirect comparisons, only when RCTs are unavailable. Nevertheless, some countries are less explicit in detailing the hierarchy of evidence (FI, IT, SA), keeping their requirements more general. By contrast, BE HEEG has the most detailed methodological framework, with a dedicated section outlining the principles for conducting a literature review.

RWE für Kontextdaten: Krankheitsverlauf, Behandlungsmuster, Pat.-Erfahrungen

The analysed HEEGs also vary in their flexibility in accepting lower-level evidence when RCTs are unavailable; for example, the HEEG of SA encourages the submission of observational data, in the form of real-world evidence (RWE), as a source of additional benefit and clinical data. Also, the NICE HEEG notes that for contextual inputs such as natural history, treatment patterns or patient experiences, RWE may be the preferred source, while the BE HEEG presents a detailed list of inputs that can be informed by RWE.

systematische Suche als methodische Voraussetzung in den Hälfte der Länder

While the systematic search is a required methodological step for evidence synthesis, further used in health economic modelling, it is not explicitly mandated by all the included national health economic HEEGs; an explicit requirement to perform a systematic search was found in HEEGs of eight countries (AU, BE, EW, FR, DE, JP, NO, NL). Most of these HEEGs also specify the inclusion of additional documentation, such as search terms and the literature selection process conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [34]; see, for instance, NO and JP.

3.2.4 Budget impact

Kosteneffektivität vs. Finanzierbarkeit: Budget-Impact-Analyse als Ergänzung

While HEE, or more precisely, cost-effectiveness analysis, aims to assess the acceptability of investing in a new intervention given the relative value for money it provides against a measure of social willingness to pay (WTP) for health improvements, it does not directly address the question of affordability. To determine whether the payer can afford a specific intervention, considering their available budget and other funding sources, it is necessary to conduct a complementary BIA [34].

Länderunterschiede: BIA verpflichtend, optional oder nicht erwähnt

The analysis of the included HEEGs reveals that most countries require BIA for healthcare decision-making, with a strong tendency to integrate BIA methodological requirements into HEEGs. Only the NL and JP HEEGs do not mention BIA at all, whereas the FR and CZ HEEGs refer readers to a separate BIA guideline. Countries that consider BIA optional include FI, SA (considered an alternative to the full HEE) and CH (although the cost impact on direct costs must be demonstrated).

Zeithorizont der BIA: 2–6 Jahre

In terms of the specified time horizon over which the BIA analyses should be conducted, it spans from a minimum of two years, applied in IT and PT, to maximum of six years, prescribed by AU and SK (with details only for three 12-month periods). In DE HEEG, the BIA time horizon is taken as one of the variables to be tested in sensitivity analyses by altering it to five years, whereas SA mentions only a wide time range of two to five years.

Table 3-4 presents an overview of the different recommendations regarding budget impact analyses and their time horizons for the selected countries.

Table 3-4: Recommendations regarding budget impact analyses

	Time horizon	Countries
BIA required and methodology specified in the same guideline	6 years	Australia [16], Slovakia [30]*(detail for three 12-month periods)*
	5 years	Norway [27]
	4 years	Hungary [23]
	3 years (base), 5 years (sensitivity)	Germany [22]
	Minimum 3 years- time needed to reach a steady state	Belgium [17]
	Minimum 2 years	Italy [24], Portugal [28]
	3 years	England & Wales [19]
	2-5 years	Saudi Arabia [29]
BIA required, reference to a separate BIA guideline	-	France [21], Czech Republic [18]
Optional or conditional requirements	Optional	Finland [20]
	Conditional	Switzerland [31](cost impact must be demonstrated; BIA can be performed with ISPOR guidance)
Not mentioned in the HEEG	-	Japan [25], Netherlands [26]

Abbreviations: BIA…budget impact analysis, ISPOR…Professional Society for Health Economics and Outcomes Research

3.2.5 Equity analysis

unterschiedliche Ansätze: von Nichterwähnung bis QALY-Gewichtung (NICE)

Equity aspects are not explicitly addressed in half of the included HEEGs (CZ, FI, FR, IT, JP, NL, NO, PT). The remainder of the HEEGs generally state that equity shall be addressed, but prefer qualitative discussion over quantitative weighting of outcomes. The only exception is noted in NICE HEEG, which states that, in exceptional circumstances and when relevant, an analysis that explores quality-adjusted life-year (QALY) weighting as a decision modifier may be accepted (e.g. disease-severity modifier [35]). A clear position is expressed in the BE HEEG, which prohibits applying equity weights to outcomes but requires disaggregated reporting of health gains by target population, enabling decision-makers to discuss equity issues such as unmet needs among disadvantaged groups.

3.3 Aspects concerning health economic evaluation

3.3.1 Preferred analytic technique

internationale Konvergenz zur Kosten-Nutzwert-Analyse (CUA) als Referenzfall

FR: leichte Präferenz für CEA, stets begleitend zur CUA gefordert

The analysis of the included HEEGs reveals a clear international convergence toward cost-utility analysis (CUA) as the preferred method for HEE in the base or reference case, with ten countries (AU, BE, CZ, FI, HU, JP, NL, NO, PT, SK) prioritising it at least implicitly. The most detailed guidance regarding the choice of analytical technique can be found in the HEEGs of AU, BE, CZ, FR, and HU. Four of these countries explicitly designate CUA as the preferred analytical method for reference (base) case analysis and require justification when cost-effectiveness analysis (CEA) is used instead, listing situations in which health outcomes cannot be appropriately translated into QALYs. However, as we report in the next subsection, some HEEGs, most notably the FR HEEG, practically require presenting results of both the CUA and CEA, with outcomes disaggregated into QALYs and life-years gained (LYGs) whenever there is an impact on life expectancy.

CH: keine Methodenpräferenz, nur qualitative Bewertung

Five GLs (EW, NO, NL, PT, SK) state the preference for CUA without further comparison with CEA. Two GLs express just a slight preference for CUA (FI: '*in most cases, CUA gives the best support to decision making*', JP: implicit preference given the use of QALYs). Three HEEGs (DE, IT, SA) treat CUA and CEA equivalently, allowing flexible choice between the two. Finally, the CH HEEG does not provide guidance on the preferred analytic technique, as the economic aspects are currently discussed only qualitatively. It refers to the absence of a cost-utility threshold in Switzerland, whereby the economic efficiency criterion is currently operationalised through affordability considerations and the application of the principle of proportionality to the benefit-cost ratio, taking into account the burden on the solidarity-based community.

alternative Methoden: CMA, CBA, CCA unter spezifischen Bedingungen

Alternative methods mentioned by the HEEGs include cost-minimisation analysis (CMA), cost-comparison analysis, cost-benefit analysis (CBA), and cost-consequences analysis (CCA). In principle, all HEEGs with elaborate instructions on the choice of appropriate analytic technique (AU, BE, CZ, FR, and HU) adopt a tiered approach, with CUA being the primary choice, CEA the second option in justified cases, and CMA featured as an alternative type of HEE to be performed in cases when the compared therapies exhibit

comparable effectiveness. Nevertheless, CMA is also mentioned as a possible alternative by other HEEGs (FI, JP, NO, SA, SK), provided that the claim of equivalence or non-inferiority of the efficacy and safety profiles between the intervention and the comparator is supported by evidence. Some HEEGs present further specifications, e.g. SA HEEG permits the use of CMA only for generics and biosimilars, AU and BE HEEG consider CMA insufficient if adverse effect profiles are different in nature, while FR HEEG allows the use of CMA in the reference case analysis only if there is a demonstrated equivalence in the length of life criterion.

Analysetypen nicht gegenseitig ausschließend – Kombination möglich

None of the analysed HEEGs overtly promotes the use of CBA, although the FI HEEG mentions CBA as one of the alternative methods of analysis that can be chosen. AU and FR HEEGs permit the presentation of CBA results as supplementary analysis, emphasising that the various types of economic evaluations are not mutually exclusive and that more than one analysis can be presented to strengthen the case for cost-effectiveness. CCA can be presented as an additional analysis according to BE HEEG; in very rare cases, when it is not possible to link outcomes to either QALYs or life years, it can be used as the reference (base) case analysis. Finally, the NICE HEEG uniquely mentions cost-comparison analysis as an alternative to CUA, with a fully incremental analysis, for technologies that are likely to provide similar or greater health benefits at a similar or lower cost than that of the relevant comparator(s).

3.3.2 Preferred measure and valuation of health outcomes

Gesundheitseffekte: QALYs bei CUA, klinische Endpunkte bei CEA

The measure of health effects used to quantify health benefits in HEE depends on the chosen analytic technique. CUA expresses health outcomes as a generic measure of health gain encompassing the major elements of changes in both the length and quality of life, namely, QALYs. In CEA, outcomes are expressed in clinical units, most typically, life-years gained (LYG). Consequently, all identified HEEGs that prefer CUA (see Table A- 6 in the Appendix) request that the health effects be expressed in QALYs. At the same time, some of them (BE, CZ, FR, NO, PT) request a disaggregated presentation of QALYs gained and LYG if the survival is affected.

CEA: gewonnene Lebensjahre bevorzugt, alternative Endpunkte teils zulässig

Conversely, when a CEA is presented as the primary economic evaluation, LYG is the preferred outcome measure. Two HEEGs (FI, SA) allow the outcome to be expressed in other patient-relevant natural units or surrogate endpoints without mentioning further details. Nevertheless, "Guidance on outcomes for joint clinical assessments," prepared under the European HTA regulation, specifies that intermediate or surrogate outcomes are acceptable only if there is evidence of a strong association or correlation (at least 0.85) between the effects on the surrogate or intermediate outcome and the effect on the long-term or final outcome [36]. In addition, AU HEEG includes a list of requirements for translating comparative treatment effects of proposed surrogate measures to target clinical outcomes in Appendix 5.

QALY-Berechnung: Präferenzbasierte Nutzwerte zur Lebensqualitätsgewichtung

The use of QALYs requires utility scores to adjust life-years for quality, reflecting the preference-based valuation of health states, also referred to as health-related quality of life (HRQoL) weights. These utilities should ideally be derived from patients' descriptions of their health status using validated, generic preference-based scoring systems, which are preferred over disease-specific ones as they encompass general aspects of health and facilitate comparisons across different disease areas [37].

EQ-5D als bevorzugtes Instrument – Länderunterschiede bei Version und Value-Sets

britische Werte als Ersatzlösung

The most commonly used multi-attribute utility instrument (MAUI) is the EuroQol 5 Dimensions Questionnaire (EQ-5D), which includes five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Its five-level version, EQ-5D-5L, is explicitly prioritised in the adult population over other instruments by six HEEGs (BE, FR, HU, JP, NL, PT). It should be valued using national value sets (tariffs). The three-level version, EQ-5D-3L, is mentioned as the second preferred option, mainly during the transitional phase before national value sets for 5L become available. By contrast, the NICE and SK HEEGs discourage the use of the 5L version, favouring the older 3L version. The NICE HEEG specifies that for data gathered using the EQ-5D-5L descriptive system, utility values in reference case analyses should be calculated by mapping the 5L descriptive system data onto the 3L value set[2]. Similarly, NO prefers converting 5L data to 3L to ensure consistency. In addition, the CZ HEEG states a preference for the EQ-5D without specifying the version, and both the CZ and SK HEEGs clarify that, given the unavailability of validated scoring tables with national values, utilities from Great Britain should be used as a fallback; this is also the case for NO HEEG, which recommends the use of Norwegian 15D tariff only in scenario analyses.

alternative Instrumente: HUI, SF-6D, AQoL – meist nur bei ungeeignetem EQ-5D zulässig

In addition to the EQ-5D, other multi-attribute health status classification systems have been developed, including the Health Utilities Index (HUI), the Short Form 6D (SF-6D), and the Assessment of Quality of Life (AQoL). The AU HEEG is the only one that names MAUIs across all these systems and allows their interchangeable use, without a detailed discussion of the validity or reliability of the chosen instrument. Other GLs that state a preference for the EQ-5D measurement system permit the use of alternatives only in justified cases when evidence indicates that EQ-5D is unavailable or inappropriate. Notably, the JP and NICE HEEGs provide detailed hierarchies of preferred HRQoL methods to guide selection when the most favoured option (EQ-5D data collected directly in clinical studies and valued using UK population preferences, or EQ-5D-5L with the JP value set) is unavailable.

3.3.3 The preferred perspective

meist Gesundheitssystem/ Kostenträger, breitere Perspektive teils ergänzend

gesellschaftliche Perspektive meist nur in Zusatzanalysen zulässig

The chosen perspective of a HEE determines which costs and, to some extent, which health-related outcomes ought to be included in the analysis. Nine HEEGs (AU, BE, DE, HU, CH, IT, PT, SK) require the application of a 'healthcare system' or 'payer' perspective on costs in the reference (base) case analysis, with most of them (AU, BE, CZ, HU, IT, PT, SK) allowing the application of a broader perspective in the supplementary or scenario analysis; especially in justified cases where the proposed intervention has significant societal implications extending beyond the health care system. There are some notable exceptions to the rule: CZ HEEG permits the application of societal and governmental perspectives even in the primary analysis for orphan drugs, while requiring the parallel submission of the analysis from the payer's (insurance company) perspective. NICE HEEG, while requesting the adoption of an NHS and PSS (payer) perspective, considers it appropriate to consider the cost of the caretakers' time if the given care might otherwise have been provided by the NHS or PSS; in addition, it allows the inclusion of costs

[2] However, on the 1st of December 2025, it was announced that following peer review and publication, NICE will introduce the new value set for use alongside EQ-5D-5L.

to government bodies in the non-reference-case analyses if specifically agreed with the Department of Health and Social Care.

gegensätzlicher Ansatz: NL fordert strikt gesellschaftliche Perspektive

At the other end of the spectrum is the NL HEEG, which strictly adheres to the societal perspective in the reference case analysis, explaining that this comprehensive approach is enabled by extensive research on measuring and evaluating societal costs and effects; conversely, it allows a healthcare perspective in the scenario analysis.

weitere Perspektiven: FR kollektiv, NO/FI erweitert, JP/SA weniger präskriptiv

Besides, the FR approach is distinct for its focus on production costs and the adoption of a collective perspective, which encompasses the people or institutions affected (in terms of health effects or costs) by the production of an intervention within the scope of overall patient care. Furthermore, the NO HEEG explicitly and the FI HEEG implicitly adopt an extended health-service perspective, with precise delineation of health costs and benefits to be included, slightly expanding the scope beyond the strict healthcare system perspective. Finally, the HEEGs of JP and SA are less prescriptive on the choice of perspective. JP, however, requires the parallel submission of analysis conducted from the "public healthcare payer's perspective" when a broader perspective is adopted in the reference case analysis.

A few HEEGs (AU, BE, EW, FR, PT, SK) explicitly distinguish the perspective on outcomes from the perspective on costs. While the perspective on outcomes, or health effects, corresponds by default to that of the relevant patient population (specified by AU, BE, PT), there are some notable specifications:

- FR reference-case collective perspective requires evaluation of health outcomes identified by patients, healthcare system users and informal caregivers;
- NICE HEEG requires the inclusion of all relevant health effects, both for patients and other people (mainly carers);
- If applicable, NO HEEG also accepts the inclusion of the carer's health-related quality of life.

By contrast, the BE and SK HEEGs consider the inclusion of 'effects on the carers' admissible only in the complementary or scenario analysis.

3.3.4 Included costs

Perspektive bestimmt einzubeziehende Kosten

Whether a given cost related to the intervention should be included in the HEE depends on the selected perspective (see Chapter 3.3.3). There are different cost classification systems that can be applied to categorise cost items. For an illustration, the BE HEEG organises cost categories along two dimensions — whether costs are direct or indirect, and whether they fall within or outside the healthcare sector, as summarised in Table 3-5.

Table 3-5: Overview of possible cost categories

	Healthcare costs	Non-healthcare costs
Direct costs	Health services, medicines, devices, hospitalisations, outpatient care, examinations, consultations, etc.	Travel expenses to and from the hospital, informal care, invalidity/incapacity allowances, social services, etc.
Indirect costs	E.g., health care costs in life years gained (unrelated healthcare costs)	E.g., productivity losses in a patient or an informal caregiver

Table based on [17]

In general, the strict healthcare payer perspective requires only the inclusion of direct healthcare costs (the upper-left quadrant of the matrix), whereas the broadest societal perspective, such as the one endorsed by NL HEEG, spans through all four quadrants of the matrix, including even costs incurred in non-healthcare sectors, or by volunteers.

gesellschaftliche Perspektive umfasst auch nicht-gesundheitsbezogene Kosten

A detailed overview of all possible cost categories, including an alternative cost categorisation, and cost valuation methods is presented in the complementary AIHTA report "Measures to Improve Cost Data Use for Health Economic Studies and Decision-Making" [35, 38]. In the Table 3-6 below, we adopted the cost categorisation used in the given report to synthesise the reference (base) case analysis requirements of the included HEEGs.

Table 3-6: Overview of costs that need to be included in the reference (base) case analysis

Country	Direct healthcare costs	Direct non-healthcare costs	Indirect costs (Productivity)	Unrelated future medical/ disease costs	Note
Australia	✓	X*	X*	X*	*can be presented in supplementary analysis under societal perspective; appropriate when implications extend beyond the health outcomes of the treated patient and healthcare system (e.g. education, housing or justice)
Belgium	✓	X*	X*	X	*presentation of these costs is encouraged in the complementary non-reference case analysis
Czech Republic	✓	X*	X*	X	*relevant in reference case for orphan drugs under the societal perspective
England & Wales	✓	X*	X	X**	*time spent by family members can be included, if it might have been provided by NHS or PSS instead. **costs related to the condition of interest and incurred in additional years of life gained because of technology included in the reference-case analysis
Finland	✓	✓*	✓**	X	*travel expenses and patient/caregiver time **if productivity losses are included, should be reported also separately
France	✓	✓*	X	X	*included under the recommended collective perspective
Germany	✓	✓*	✓*	X	*includes patient co-payments, transportation costs, patient/caregiver's time; productivity losses from work incapacity, but not from premature death
Hungary	✓	X*	X*	X	*can be included under optional societal perspective supplement
Italy	✓	X*	X*	X	*can be included under optional societal perspective supplement
Japan	✓	✓*	X	X	*if long-term care payer's perspective is relevant for the product, publicly funded long-term care costs can be included
Netherlands	✓	✓	✓	✓	includes costs in other sectors (e.g., education, criminal justice etc.)
Norway	✓	✓*	X	X	*transport costs related to treatment, irrespective of payer; patient/caregivers' time
Portugal	✓	✓*	X**	X	*social care costs, such as long-term care or palliative care, when financed by the NHS, should be considered in the reference case **may be presented in the scenario analysis

Saudi Arabia	✓	X*	X*	X	*long-term care and productivity costs are encouraged to be included
Slovakia	✓	X*	X*	X	*may be presented in the scenario analysis under societal perspective
Switzerland	✓	Unclear*	Unclear*	X	*'wider economic costs' are not included in the assessment of economic efficiency, but are assessed as part of the appropriateness criterion

3.3.5 Time horizon

Zeithorizont der gesundheitsökonomischen Evaluation: Grundsätze, Lebenszeitperspektive und Anforderungen an die Modellierung

All HEEGs with the exception of CH specify the time horizon of the HEE, that is, the period over which the costs and outcomes associated with the intervention are evaluated. The appropriate time horizon is universally defined as long enough to capture all relevant differences in costs and outcomes between the compared interventions. A lifetime horizon is needed whenever interventions lead to differential mortality. This generally creates a need to apply modelling techniques to extrapolate data beyond the duration of the clinical trials or other applied observed evidence. In addition, costs and outcomes must always be measured over the same time horizon for the evaluated intervention and its comparators.

Sensitivitätsanalysen zum Zeithorizont: Länderspezifische Anforderungen zur Darstellung kürzerer Zeiträume

Because extrapolated estimates are associated with increased uncertainty, it is a good practice to present results for shorter time horizons in the sensitivity analyses. It is required by AU, BE, FI (with examples of one, five and ten years, and duration of clinical trial), HU, IT (five and ten years), JP (at least the duration of clinical trial), NL (at least duration of clinical trial and halfway of the extrapolated time horizon) and PT. PT is the only HEEG that mentions the possibility of presenting scenario analysis with a time horizon longer than the lifetime for some conditions, such as infectious diseases.

3.3.6 Discounting

Diskontierung in allen HEEG gefordert – unterschiedliche Methoden

Diskontierungsraten: 2–5 %, Modalwert 3 %

Discounting future costs and benefits to convert them into present value is an established step in HEE, and it is promoted by all the included HEEGs. Differential discounting, i.e., applying different annual rates to discount healthcare costs and health effects, is endorsed by only two HEEGs (BE and NL). Their discount rate for effects is lower than that for costs, based on the idea that the value of health grows over time [26] and to avoid "too strong penalisation of interventions that generate most of their outcomes in the future (e.g., screening and vaccination programmes)" [17]. A time-varying declining discount rate with preset temporal thresholds, also known as tiered discounting, is used in FR and NO. The remaining HEEGs employ fixed, uniform annual discount rates ranging from 2% to 5% and with a mode of 3% (see Table 3-7).

Table 3-7: Overview of the different discount rates

Discounting approach		Rates	Countries
Differential discounting, uniform per annum		Costs: 3% Outcomes: 1.5%	Belgium [17], Netherlands [26]
Same rate for costs and outcomes	**Declining discount rates**	2.5% (<30 years), then 1.5%	France [21]
		4% (0-39 years), 3% (40-74 years), 2% (75+ years)	Norway [27]
	Uniform per annum	2%	Japan [25]
		3%	Czech Republic [18], Finland [20], Germany [22], Italy [24]
		3-5% (range)	Saudi Arabia [29]
		3.5% (1.5% in additional analysis in specific circumstances)	England and Wales [19]
		3.7%	Hungary [23]
		4%	Portugal [28]
		5%	Australia [16], Slovakia [30]

Herkunft der Diskontierungsraten: Externe Rahmenwerke und staatliche Expertengremien

Four HEEGs (FR, NL, NO, PT) provide details on the origin of the discount rate, showing a common reliance on external economic frameworks and governmental expert bodies. FR rate was defined by an expert committee as reflecting society's relative willingness to value the future. NO similarly ties its discount rate to centralised socioeconomic analysis standards set by the Ministry of Finance. NL anchors its 3% cost discount rate to the 2.25% social cost-benefit analysis (SCBA) benchmark, with upward market adjustments, while the 1.5% rate used for effects is the result of subtracting an estimated annual growth rate in the consumption value of health from the cost discount rate. Finally, PT, lacking an official national standard, pragmatically adopts the 4-5% range used for public investments and aligns with broader European practice by selecting the lower end of that range.

In some of the included HEEGs, the effect of discounting is one of the prescribed scenarios explored in sensitivity analysis:

- in AU using a discount rate of 3.5% and 0% for both costs and effects
- BE using equal discount rates for both costs and effects of 0%, 3% and 5%
- CZ and DE are using discount rates of 0% and 5% for both costs and effects
- NL illustrating the scenario with no discounting.

In addition, PT and SK HEEGs request that both discounted and undiscounted cost-effectiveness results be presented in the reference case analysis.

3.3.7 Cost-effectiveness threshold

Kosteneffektivitätsschwellenwert und ICER als Entscheidungsgrundlage

A cost-effectiveness threshold (CET) is a discrete value of the incremental cost-effectiveness ratio (ICER) below which an intervention is considered worthwhile for the given healthcare system. The ICER is regarded as the appropriate metric for meaningful comparisons of interventions, as it indicates the additional resources required to gain an additional QALY. For a detailed explanation of concepts pertaining to ICER and CETs, please refer to the complementary AIHTA report “Threshold values in health economic evaluations and decision-making” [35].

Schwellenwertfestlegung: absolut, BIP-basiert oder krankheitslastabhängig

explizite Schwellenwerte: CZ, HU, SK, EW, SA, PT, NL

CETs are explicitly mentioned by six HEEGs, either as a discrete value (CZ: 1.2 million Kč per QALY gained, HU: 1.5-3x GDP per capita depending on incremental QALYs, SK: 3-10x GDP per capita depending on incremental QALYs), or as a range (NICE: £20,000-£30,000 per QALY gained[3]; SA: SAR 50,000-75,000 per QALY gained, PT: €10,000-€100,000 per QALY gained). Furthermore, the NL HEEG refers to another methodological document, 'Kosteneffectiviteit in de praktijk' [40] for CET derivation based on the burden of disease applicable to the concerned indication.

BE und FR: Effizienzgrenze statt expliziter Schwellenwerte

As reported in the complementary report, JP and NO also have an explicit CET, although it is not directly mentioned in the analysed HEEGs [35].

By contrast, BE and FR HEEG strongly emphasise the efficiency frontier approach to their cost-effectiveness evaluations, arguing that an implicit, context-dependent threshold is better aligned with budgetary constraints [17].

[3] On 1st of December 2025, it was announced that NICE will apply new thresholds of £25,000 to £35,000 per QALY gained for cost-effective interventions [39].

3.3.8 Modelling preferences

entscheidungsanalytische Modellierung zur Überbrückung von Evidenzlücken

Economic evaluation, which aims to guide decision-makers in allocating healthcare resources efficiently by systematically comparing the expected costs and health outcomes of alternative interventions, can be conducted using data from an empirical study, such as an RCT. However, these studies rarely provide evidence that directly addresses the funding context. Therefore, decision-analytic modelling is commonly employed to generate benefit and cost estimates, compensating for gaps in available evidence. Decision models provide a coherent framework for synthesising evidence from multiple data sources, enabling, for instance, comparison of all clinically relevant options, linking intermediate endpoints to final health outcomes, and extrapolating available data to the appropriate time horizon of the evaluation [37].

unterschiedliche Detailtiefe bei Modellierungsempfehlungen

Modellierung: implizite Voraussetzung oder explizite Notwendigkeit je nach Leitlinie

The included HEEGs were assessed for how well they reflect the need for modelling and whether they provide further guidance on selecting appropriate models. Swiss HEEG does not include any recommendations on modelling. Eight HEEGs (EW, FI, FR, IT, JP, NO, SA, SK) implicitly assume modelling necessity without addressing the possibility of trial-based HEE based on the sufficiency of empirical evidence. The remaining HEEGs reflect the necessity of modelling, with the most frequently cited rationale being the need to extrapolate clinical trial results beyond their duration. In this regard, HEEGs of AU, BE, and NL offer the most comprehensive framework for distinguishing the model-based and trial-based HEE. Nevertheless, the BE HEEG downplays the importance of trial-based HEEs by stating that some modelling will almost always be necessary. Notably, CZ and DE HEEGs also include a relatively comprehensive list of situations in which modelling is necessary, e.g., for extrapolating trial results to a wider population, extending the time horizon, and combining various evidence sources.

Modellierungstechniken: Entscheidungsbäume, Markov-Modelle, Mikrosimulationen als Haupttechniken

einfachstes geeignetes Modell bevorzugt

Nine HEEGs (AU, BE, DE, EW, FI, FR, JP, NL, PT) include at least a short introduction to different modelling techniques, or model types, available for HEE, namely decision trees, cohort-based/Markov models, and individual-level/microsimulation models. While all HEEGs require justification for the chosen modelling approach, explicit guidance on selecting the most appropriate approach is provided by only a minority. The AU HEEG, for example, presents a limited number of guiding questions; the FR HEEG provides a matrix aid tool for model choice in the Annexe, while the NL and PT HEEG cite other ‘good practice’ guidelines (NL: [41-43], PT: [41, 44, 45]). Moreover, there is a notable consensus among HEEGs on the use of the parsimony principle for model selection, i.e., choosing the simplest modelling approach to address the given policy question, thereby avoiding unnecessary complexity.

3.3.9 Model details required

Modellvalidierung: weitgehend gefordert, unterschiedliche Detailtiefe der Anforderungen

z.B. AdViSHE-Checkliste: Empfohlen (AU, PT) oder verpflichtend (NL)

Model validation—demonstrating that the model produces results that accurately represent the phenomena it is intended to simulate—is widely recognised as a core element of good modelling practice [41, 46]. As such, it is a required step for HEE submission by almost all HEEGs; the only HEEGs that do not explicitly require model validation are from CH, HU, and SK, while the SA HEEG mentions it only as a recommendation. The most detailed requirements for model validation are provided by five HEEGs (AU, BE, FR, NL, and PT), with BE and FR specifically addressing model validity across various elements (i.e., internal, external, and face validity, cross-validation). The NL HEEG states that cross-validation is the one type that must be addressed at a minimum, whereas the IT HEEG refers to best practices from ISPOR [46]. Two HEEGs (AU, PT) recommend using the Assessment of the Validation Status of Health-Economic Decision Models Study Group (AdViSHE) checklist [47] to guide the validation process. By contrast, in NL, submission of a completed AdViSHE checklist is a mandatory component of the dossier.

Vorgaben zur Einreichung elektronischer Modellkopien

The submission of an unlocked, fully editable electronic copy of the model is required by eight HEEGs (AU, DE, EW, FI, IT, JP, NO, SK) to enable the respective agencies to respecify model variables. The CZ HEEG encourages the submission of editable electronic copies to facilitate the administrative procedure, while the PT HEEG only requires the annotation of 'computational code developed for the electronic model'. In contrast, the BE HEEG does not mandate routine model submission but states that the model should be made available upon request.

3.3.10 Uncertainty analyses

Umgang mit Unsicherheit in der ökonomischen Evaluation

Cost-effectiveness estimates derived from HEE are always subject to some degree of uncertainty or imprecision, arising from the data used or the methodological assumptions applied. In trial-based economic evaluations, data are subject to stochastic uncertainty due to variability in outcomes among identical patients. The NL HEEG is the only included HEEG that specifically addresses uncertainty in empirical economic evaluations and prescribes methods for quantifying it: bootstrapping and deterministic sensitivity analysis (DSA) that varies parameter values within the standard error range.

Unterscheidung zwischen Parameter- und Strukturunsicherheit

DSA, PSA und Szenarioanalyse zur Unsicherheits-quantifizierung

By contrast, HEE, based on decision-analytic modelling, entails additional sources of uncertainty, necessitating several types of sensitivity analysis to quantify them. The two primary categories of uncertainty are parameter and structural uncertainty, and the three main types of sensitivity analysis employed to explore them are: deterministic sensitivity analysis (DSA), with its subtypes one-way (OWSA) and multiway, probabilistic sensitivity analysis (PSA), and scenario analysis. Parameter uncertainty is generally assessed using PSA and DSA, whereas structural uncertainty is primarily examined through scenario analysis, although PSA can also be used to characterise structural uncertainty when parameterised [37]. Notably, the majority of HEEGs organise their requirements and recommendations addressing uncertainty by referring to the uncertainty type, highlighting the distinction between parameter and structural uncertainty, although some exceptions conflate types of sensitivity analysis (CZ, HU, JP, NO, SK).

länderspezifische Präferenzen bei Pflicht- und optionalen Sensitivitätsanalysen

While methods for quantifying uncertainty are largely dictated by the type of uncertainty identified in the HEE, national HEEGs differ slightly in their methodological preferences and in which types of sensitivity analysis should be undertaken as mandatory or voluntary in relation to the base-case economic evaluation. HEEGs opting for the most comprehensive approach, which requires DSA (either subtype), PSA, and scenario analysis (depending on the presence of the respective uncertainty types), include BE, CZ, FR, HU, IT, NL, and PT. They emphasise that the DSA and PSA represent complementary approaches to addressing uncertainty.

umfassender Ansatz in CZ, FR, HU, IT, NL, PT gefordert

gegensätzliche Präferenzen: PSA als Pflicht oder nur ergänzend

PSA-Priorisierung (BE, EW) vs. DSA-Fokus (AU, FI, JP, NO, SA, SK)

Two HEEGs (BE, EW) prioritise PSA, treating DSA as a supplementary approach and highlighting PSA's superiority in capturing joint uncertainty across multiple parameters. Conversely, six countries (AU, FI, JP, NO, SA, SK) require the uncertainty to be addressed by DSA, with PSA presented only voluntarily. The SK HEEG is the only one to provide a rationale for this preference, stating the intent to limit the additional burden on both the analysts and submitting bodies that arises from PSA preparation, while anticipating future PSA prescription in the planned HEEG update (see Table 3-8).

Diskontierungsrate als einzige unbedingt zu testende Variable

Frequently, the HEEGs also include a set of prescribed scenarios or structural assumptions to be tested in the sensitivity analysis, albeit these are almost exclusively conditional on the presence of uncertainty surrounding a given assumption or the availability of concurrent equally plausible sources of data; the only truly mandatory variable to be tested, irrespective of the presence of uncertainty, is the discounting rate. The summary of mandatory scenarios, as well as a more detailed breakdown of uncertainty analysis prescriptions, is presented in Table A- 9 in the Appendix.

Table 3-8: Overview of sensitivity analysis in health economic evaluations

	PSA...	Countries
Mandatory	Voluntary	Australia [16], Finland [20], Japan [25], Norway [27], Saudi Arabia [29], Slovakia [30]
Mandatory	Mandatory	Belgium [17], Czech Republic [18], France [21], Germany [22], Hungary [23], Italy [24], Netherlands [26], Portugal [28]
Voluntary[4]	Mandatory	England and Wales [19]

Value-of-Information-Analyse: Bewertung zusätzlicher Forschung bei Unsicherheit

Another dominant typology of analysis providing additional insight into the effect of uncertainty on decision-making is the 'Value of Information' (VOI) analysis, with subtypes: the 'Expected Value of Perfect Information' (EVPI) and the 'Expected Value of Partial Perfect Information' (EVPPI). It is an extension of probabilistic analysis that aims to estimate the added value of conducting additional research, or, equivalently, the expected costs of uncertainty associated with making the decision based on current imperfect evidence [37, 48]. This approach is mentioned by the BE, NL and PT HEEGs, with the NL HEEG including VOI as an obligatory element.

[4] Note that NICE HEEG prescribes that scenario analyses should be probabilistic as well.

3.3.11 Results reporting

variierender Detailgrad bei Vorgaben zur Ergebnispräsentation in den Leitlinien

All HEEGs specify how HEE results should be presented, though they differ in the level of detail provided. Most HEEGs include template tables for presenting results, either interspersed throughout relevant chapters (AU, BE, CZ, HU, IT) or gathered in a dedicated chapter/part/appendix (CH, FI, SA, SK). Four HEEGs (FR, NL, NO, PT) include only a verbal description of table contents without the inclusion of specific formatting directly in the HEEG, with the FR HEEG referring to a dedicated document 'Formatting a technical report. Supporting document for the drafting of technical reports filed with the CEESP' [49].

PRISMA und EUnetHTA als Referenzstandards für Berichterstattung in einigen Leitlinien

Six HEEGs mention some external reporting standards, such as the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flowcharts for literature search outcomes [50, 51], the PRISMA guidelines and its specific checklist for the description of adverse effects [52], or the EUnetHTA Core Model [53] for reporting additional domains (AU, BE, FR, HU, JP, SK).

Checklisten für gesundheitsökonomische Evaluationen: CHEERS am weitesten verbreitet, länderspezifische Varianten

Of particular importance for assessing the completeness of the submitted HEE are various reporting checklists. BE HEEG names multiple checklists available, comprising the 36-item Drummond and Jefferson checklist [54], the Drummond Ten Point checklist [55], the Consensus on Health Economic Criteria (CHEC)-list [56], the Philips checklist [57], the Quality of Health Economic Studies (QHES) checklist [58], the NICE appraisal checklist [59], and the CHEERS checklist [60]. The latter checklist is the most widely used, and its use for reporting completeness verification is explicitly recommended by the IT HEEG and referenced by the SA. The HEEG from NL requires the use of the previously mentioned AdVishe checklist for reporting validation, while two other GLs, AU and FI, have their own checklists to aid in preparing a submission.

Incremental analysis

fast alle HEEG verlangen explizite ICER-Darstellung

FR: Nettonutzen (NMB/NHB) als Alternativmetrik zum ICER

In terms of the results of an HEE that shall be reported, all included GLs except those from CH and FR require explicit ICER reporting. FR is unique in offering an alternative incremental cost-effectiveness estimation metric: a net benefit (NB), expressed in monetary units (net monetary benefit – NMB) or in health units (net health benefit – NHB), which can be presented instead of an ICER. The NB metric is defended on the grounds that it resolves some issues posed by ICER; specifically, it can simplify the interpretation of the PSA, particularly when multiple comparators are used [61]. To calculate NHB and NMB, it is necessary to enter a predefined reference value (the cost-effectiveness threshold).

NL: ICER und NMB komplementär gefordert; NICE: NHB situationsabhängig

By contrast, the NL HEEG considers the ICER and NMB complementary metrics and requires reporting both, underscoring NMB's usefulness for ranking interventions to identify the most cost-effective option. Furthermore, the NICE HEEG prescribes presenting the NHB when appropriate, and lists situations in which it may be particularly informative.

vollständig inkrementelle Analyse mit Effizienzgrenze bei mehreren Komparatoren

Ausnahmen von der ICER-Berichterstattung: Dominanz, CMA, Sonderfälle

A salient feature of the BE, EW, FR, NL and PT HEEGs is their emphasis on conducting a fully incremental analysis when multiple comparators exist, comparing all relevant interventions simultaneously, rather than presenting multiple independent pairwise comparisons. This approach inherently requires constructing a cost-effectiveness efficiency frontier, as it entails identifying all appropriate comparators, ranking them by costs and QALYs with removal of dominated or extensively dominated interventions, and sequential calculation of ICERs for the remaining relevant alternatives, where each non-dominated intervention is compared against the next most effective alternative. These HEEGs also automatically allow for one scenario when an ICER need not be calculated: some dominated or extensively dominated interventions can be ruled out narratively and are thus removed from the fully incremental analysis, without detailed cost and QALY calculations. In addition, an ICER is generally not calculated when CMA is chosen as the appropriate analytic technique. Other explicit exemptions when an ICER need not be presented are found in the HU HEEG (e.g., superior effectiveness and no scenario with higher costs) and the JP HEEG (when the incremental effectiveness is only slightly positive and the incremental cost is almost zero).

disaggregierte Darstellung: ICER-Komponenten, Kostenkategorien, Gesundheitszustände

Most included HEEGs require a separate presentation of ICER components: incremental costs and incremental effects (not explicitly required only by JP, NO, SA). Similarly, most countries require disaggregated presentation, breaking down results across multiple categories, e.g. by cost categories (AU, BE, CZ, EW, FI, FR, HU, IT, JP, NL, PT, SK), health states (AU, CZ, EW, FI, FR, HU, IT, NL, PT, SK), health outcome (QALY and LY: BE, EW, FR, NL), payers (BE, CZ, PT) and/or time periods (IT: 5 and 10-year results mandatory). The presentation of both the discounted and undiscounted incremental results for evaluations exceeding one year is also a stable requirement present in most GLs.

Uncertainty analysis

tabellarische Darstellung deterministischer Unsicherheitsanalysen

Tornado-Diagramm: explizit gefordert oder empfohlen in mehreren Leitlinien

Results of deterministic uncertainty analyses and scenario analyses should be presented in a tabular format, listing the tested variables and assumptions with their distributional characteristics (e.g. range, 95% confidence interval) alongside their effects on the ICER and its incremental components. This is the typical recommendation present in all HEEGs requiring DSA. An appropriate graphic tool for summarising uncertainty in one-way (or univariate) sensitivity analysis is the tornado diagram, which is explicitly required by the HEEGs of AU, CZ, IT, NL, and SA, and recommended by the BE and NICE HEEG.

Darstellungsanforderungen für probabilistische Sensitivitätsanalysen:

Streudiagramme auf der Kosteneffektivitätsebene und Kosteneffektivitäts-Akzeptanzkurven

On the other hand, PSA results should be graphically visualised as scatter plots on the cost-effectiveness plane (CE plane). Complementary representation consists of cost-effectiveness acceptability curves (CEAC), plotting a range of possible ICERs (or cost-effectiveness threshold values) on the horizontal axis against the probability that the intervention is cost-effective at that threshold on the vertical axis. The shape of this curve depends on the location and proportions of incremental costs and effects over the four quadrants of the CE plane; examples of the CE plane and the CEA curve are available in the Appendix. Three countries specify the threshold values for which the cost-effectiveness probability must be indicated on the CEA curve: CZ reveals the actual willingness-to-pay threshold, corresponding to 1.2 million Kč per QALY gained, while the PT and NICE HEEGs mention threshold ranges of

€10,000 to €100,000 per QALY gained and £20,000 to £30,000 per QALY, respectively. For a more detailed discussion of cost-effectiveness thresholds, please see Chapter 3.3.7.

4 Discussion and learnings for Austria

Analyse von 16 gesundheitsökonomische n Leitlinien: umfassendes Bild übereinstimmender und abweichender Ansätze

This review analysed methodological recommendations contained in 16 mandatory national HEEGs from high-income countries, predominantly corresponding to submission guidelines published by European HTA or medicines agencies [17-19, 21-24, 26-28, 30]. Given the in-depth extraction of information from these HEEGs, this review provides a highly comprehensive picture of the methodological preferences of healthcare systems similar to Austria's, presenting a range of possible standpoints that Austria may adopt in developing its own national HEEG. By summarising the methodological preferences across the crucial principles of HEE, it was possible to identify both convergent and divergent approaches to key domains of HEE.

Vorteile verbindlicher Leitlinien: Einheitlichkeit für Einreicher und Entscheider → steigert Transparenz und Fairness

The first commonality of the considered guidelines directly reflects the inclusion criterion: the HEEG's mandatory status in the given jurisdiction, rendering adherence to the presented mandatory requirements compulsory for submissions to national reimbursement or pricing authorities. Clarifying the legal or regulatory status of the upcoming Austrian HEEGs is a prerequisite for establishing boundaries for evidence-submitting bodies, such as pharmaceutical companies. It also ensures that decision-makers appraise submissions according to standardised criteria, which ultimately guarantees a fair and transparent process. A stronger mandate for standardised guidelines may also improve the work of HTA bodies, as standardised submissions reduce uncertainty about both evidence quality and procedural expectations.

Unterschied in Form und Detailtiefe:

z.B. BE, EW, NL: umfassende Leitlinien; CZ, IT, SK: kürzere Politikdokumente

Überlegung für Österreich: Umfang vs. Klarheit der Leitlinie

The primary overarching distinction—emerging not from any single methodological domain but from the aggregate of all domains examined—is the overall methodological sophistication of the guideline. HEEGs offering more comprehensive, explanatory guidance and promoting comparatively more advanced approaches to HEE tend to originate from jurisdictions with well-established HTA traditions. This is particularly evident in Belgium, England and Wales, and the Netherlands, followed by Australia, France and Portugal. In contrast, the HEEGs of other countries allow greater methodological flexibility or refrain from adopting such an explanatory, almost textbook-like approach. From a formal standpoint, these documents are visibly shorter and more concise, often framed as complementary policy papers that support compliance with a specific governmental regulation governing reimbursement (e.g., Czech Republic, Italy, Slovakia). This distinction—concerning both the form and comprehensiveness of the HEEG—represents an important consideration for the authors and decision-makers preparing the upcoming Austrian HEEG, as developing a longer, more detailed guideline requires substantially more time and coordination. Nonetheless, a longer guideline does not necessarily guarantee greater methodological clarity.

vom Arzneimittelfokus zur umfassenden HTA-Perspektive: Implikationen für österreichische gesundheitsökonomische Leitlinie

breiterer Geltungsbereich erfordert differenziertere methodische Vorgaben

The analysis revealed an evolution in how countries approach the scope of their pharmacoeconomic guidelines. There's a notable shift from traditional pharmaceutical-focused evaluations toward comprehensive HTA that encompasses all types of healthcare interventions. This progression most likely reflects the adaptation of national reimbursement schemes to rapid technological advancement in healthcare; consequently, some jurisdictions extend HEEG's scope to cover, for instance, digital products, screening programmes or regenerative medicine products. From the perspective of preparing the Austrian HEEG, a clear distinction of its scope is crucial for understanding the transferability of evidence across diseases and the comparability of

different types of interventions. A pharmaceuticals-only HEEG can focus on well-established evaluation standards. In contrast, guidelines covering the full spectrum of health technologies, such as medical devices or complex public health interventions, must provide broader and more nuanced methodological guidance. For instance, guidance on aspects such as usability, learning curves, and capital costs is often more relevant for medical devices than for pharmaceuticals. Similarly, complex public health interventions may require guidance on more complex evaluation approaches, such as realist reviews. [62].

Integration der Bugetfolgenanalyse: Effizienz und Finanzierbarkeit gemeinsam bewerten

The analysis reveals that most countries integrate BIA GLs within their HEEGs, reflecting growing emphasis on comprehensive economic evaluation that considers both efficiency and affordability dimensions [34]. Simultaneously, parallel conduct of these two types of economic analyses may avoid duplication of effort, as the BIA can partly rely on the data used for the cost-effectiveness evaluation [17].

stark variierender Detailgrad bei Modellierungsvorgaben

Konsens zum Sparsamkeitsprinzip bei der Modellwahl

Potenzial für österreichische Leitlinie: explizite Modellierungsempfehlungen

Decision-analytic modelling is a widely acknowledged vehicle for conducting HEE [37], with national HEEGs either treating modelling as almost always necessary or implicitly assuming it. The alternative non-modelling approach, i.e., trial-based HEE, receives limited recognition, although more comprehensive HEEGs, such as those of AU and NL, recognise this possibility and provide guidance on when modelling is necessary. It reflects the overall methodological comprehensiveness of the included HEEGs, which varies considerably: from very detailed frameworks that provide nearly textbook guidance with rationales to those that limit themselves to minimalistic specifications. Consequently, seven HEEGs [18, 23, 24, 27, 29-31] fail to mention the different modelling techniques or model types available for HEE. Nonetheless, there is a broad consensus on applying the parsimony principle in model selection: choosing the simplest viable modelling approach to address the given policy question while avoiding unnecessary complexity. The gap between universal modelling practice and limited explicit guidance on modelling selection criteria presents an opportunity for methodological harmonisation. A new Austrian HEEG could opt for a more explanatory approach to ensure compliance with modelling best practices, including model justification, validation, and, preferably, the submission of an unlocked electronic copy.

Komparatorwahl: klinische Praxis und Kosteneffektivität – unabhängiger Referenzkomparator als Option für Österreich

When defining the comparator against which the intervention under evaluation should be assessed, all HEEGs converge on the idea that selection should be guided by local clinical practice; however, a notable number incorporate cost-effectiveness considerations into the comparator selection, indicating an evolution toward economically informed decision-making. The identification of cost-effective alternatives to include, or, conversely, potential cost-ineffective alternatives to exclude from the comparator selection, is closely related to the broader trend of explicitly requiring a comprehensive evaluation of the assessed intervention in a fully incremental analysis, replacing multiple pairwise comparisons [19, 28]. However, countries starting with CEA risk choosing an inappropriate comparator, because the standard of care has never been assessed for efficiency. Comparator is one of the aspects with the highest effect on the results of cost-effectiveness analyses; if it is not cost-effective, the whole analysis results in being biased [63, 64]. An alternative approach to using potentially ineffective disease-specific comparators has been proposed in the literature, consisting of the use of an independent reference comparator-a highly efficient public health intervention to which new healthcare interventions would be compared [64]. It might represent an option for the new Austrian HEEG.

fehlende Suchanforderungen beeinträchtigen Vergleichbarkeit der Einreichungen

In addressing the preferred source of effectiveness evidence, there is a gap between evidence hierarchy specification (not specified by only two HEEGs) and systematic search requirements (not explicitly required by seven HEEGs), suggesting that many countries expect rigorous evidence evaluation without explicitly mandating the search process. This could potentially impact evaluation quality and comparability across HEE submissions or HTA-institutions' evaluations. Given that the requirement to base the effectiveness inputs on the results of a systematic retrieval process is already imposed on health technology developers in the context of EU Joint Clinical Assessments (JCA) established by HTA Regulation [65], from 2030 applicable to all new centrally authorised medicinal products [66], the new Austrian HEEG can leverage the same requirement. Equally, the hierarchy of evidence, with its implications for the internal validity of studies, is referenced in the Guidance on the validity of clinical studies applicable throughout the EU in the context of JCA [67].

EU-HTA-Verordnung und Joint Clinical Assessments als Referenz für österreichische Anforderungen

nahezu universelle Präferenz für Kosten-Nutzwert-Analyse

The near-universal adoption of CUA exists, driven by a strong preference for expressing benefits in QALYs, which facilitates cross-intervention comparability and the assessment of opportunity costs [37, 68]. HEEG recommendations in CUA-preference countries exhibit a hierarchical structure, with CUA as the primary analytic method to be used for the reference case, CEA used only in justified cases (essentially, when health outcomes are not translatable to QALYs) or as a complement when life expectancy is affected, and CMA for proven therapeutic equivalence. Nevertheless, for transparent reporting of results, the disaggregated presentation of outcomes in terms of life years gained (LYG) alongside QALYs is a standard requirement whenever survival is affected.

QALYs für interventionsübergreifende Vergleichbarkeit bevorzugt

EQ-5D-Harmonisierung: Bedarf an österreichischem EQ-5D-Wertesatz oder Nutzung von Proxy-Werten

The international comparability of outcome measurement is enhanced by strong harmonisation around a single multi-attribute health status classification system, the EQ-5D from the EuroQoL group, ideally valued using country-specific tariffs [69]. This highlights the need for developing an Austrian value set for the EQ-5D- either for the newer EQ-5D-5L version or EQ-5D-3L, previously preferred by NICE [30]. Alternatively, it is possible to use proxy value sets from other countries, often those geographically or culturally similar, or from countries with well-established sets. This is the case for Czech and Slovak HEEGs, which, given the unavailability of validated scoring tables with national values, use the UK population-based EQ-5D-3L tariff to value health states. In this regard, it is important to mention 'Pan-European' and 'Supra-National' value sets that were developed by combining the existing value sets from different countries in Europe to address the issue of the lack of value sets in some countries and explore the heterogeneity that might stem from cultural and contextual factors [70, 71]. Researchers from the PECUNIA project, coordinated by the Medical University of Vienna, build upon these harmonisation efforts by developing standardised, cross-country methods for outcome measurement [72].

Empfehlung für Österreich: zunächst qualitative Berücksichtigung von Verteilungsgerechtigkeit

While equity is addressed by half of the analysed HEEGs, none of the countries a priori allow quantitative weighting of outcomes to account for equity, indicating that equity is among the less readily quantifiable factors influencing reimbursement decisions. The approach promoted by Belgian HEEG is particularly noteworthy, as it calls for disaggregated reporting of QALYs by target population to highlight the unmet needs of certain disadvantaged groups. This allows decision makers to use quantitative information on the effects of health inequality without distorting the CEA methodology itself, thereby representing an example of distributional cost-effectiveness analysis

(DCEA). However, while DCEA has an advantage over equity weighting in terms of comparability and transparency, it is more challenging to implement due to extensive data requirements (e.g. data on baseline distribution and subgroup-specific outcomes) [73, 74]. Therefore, a new Austrian HEEG could initially require incorporating equity considerations qualitatively by describing the more salient distributional health impacts of the new technology.

Perspektivenwahl: politische Entscheidung zwischen Kostenträger- und gesellschaftlicher Sicht

nur NL befürwortet gesellschaftliche Perspektive im Referenzfall

Perspectives on the inclusion of costs in base-case analyses range from the narrow healthcare-payer perspective to a broad societal perspective. Although the societal perspective could be viewed as superior because it aims to maximise overall societal welfare, only one of the analysed HEEGs, the one from the Netherlands, explicitly endorses it; other HEEGs allow its use only in the supplementary analysis. The comprehensive approach is feasible thanks to extensive research on measuring and valuing societal costs and effects [26]. Nevertheless, most HEEGs use a healthcare payer perspective, in line with the argument that the target audience of the report is the healthcare decision maker whose primary objective is to maximise health within a constrained healthcare budget [17, 35] [38]. Consequently, analyses conducted from the healthcare payer perspective are considered to provide the most appropriate support for resource allocation decisions within their remit. Therefore, it is apparent that the choice of perspective is a policy decision underpinned by both the data availability and the political reality of segmented government budgets. In addition, the choice of perspective can affect the results of the incremental analysis (ICER), potentially altering the conclusion about the intervention's cost-effectiveness. Considering the perspective of the main evidence-submitting bodies - marketing authorisation holders - they usually have an incentive to favour the use of a societal perspective, as the inclusion of non-health benefits and societal cost offsets can enhance the assessed value of their products [75, 76].

internationale Annäherung bei Diskontierungsraten trotz früherer Divergenz

The discount rate is a methodological factor that has been found to cause the greatest divergence among HEEGs in previous reviews [13, 14]. Nevertheless, we recognised a rough international convergence around 3-4% rates among the analysed guidelines, with the same-rate application to costs and outcomes, though two more sophisticated approaches emerge as alternatives:

a) a stepwise approach with time-declining discounting that acknowledges long-term uncertainty; used in France and Norway;
b) a differential discounting of costs and outcomes underpinned by the idea that as many health interventions generate most of their outcomes in the future, effects merit being discounted at a lower rate; used in Belgium and the Netherlands.

soziale Opportunitätskosten oder Zeitpräferenz als Basis der Diskontierung

Diskontierungsgrundlagen: 3–5 % empfohlen, Sensitivitätsanalysen mit Alternativraten

Traditionally, the discount rate can be based on either the social opportunity cost or the social rate of time preference [37]. A more elaborate discussion on the implications of the chosen perspective and discounting can be found in the complementary AIHTA report on Costing [38]. Nevertheless, in the absence of a pre-set rate in the given jurisdiction, it is recommended to apply the prevalent rate of 3 – 4% p.a. for both costs and effects used internationally, since it facilitates comparability of evaluations [14, 37]. In addition, as the choice of discount rate can materially affect outcomes (especially for interventions with long-term benefits), it is a good practice to conduct sensitivity analyses using alternative discount rates, including a zero rate [14].

disaggregierte ICER-Darstellung als grundlegende Anforderung

Umsetzung erfordert korrekte Komparatorwahl und methodische Kompetenz

Regarding the presentation of cost-effectiveness results, ICER reporting with disaggregated presentation of incremental components represents a universal requirement across all specified countries (with the exception of Switzerland), serving as a fundamental metric supporting cost-effectiveness claims. Methodologically more advanced HEEGs with cost-effectiveness considerations in comparator selection require reporting results in the form of a fully incremental analysis, which involves ranking the relevant treatment options based on incremental QALY gains and costs, and removing strictly/extendedly dominated options; in other words, the interventions are identified on the cost-effectiveness frontier [37, 61, 64]. However, the implementation of fully incremental analysis hinges upon the correct identification of appropriate comparators on the cost-effectiveness frontier [64], discussed previously. In addition, an adequate interpretation of the results of incremental analysis presupposes an adequate methodological literacy among HTA researchers and decision-makers, which could be strengthened via targeted training.

Unsicherheitsanalyse: Trend zur probabilistischen Sensitivitätsanalyse

z.B. BE, EW: Nur PSA gefordert;
NL: Verpflichtende Value-of-Information-Analyse

Finally, all countries acknowledge that HEE is subject to uncertainty, which should be described through uncertainty analysis. This review evidences a transition from deterministic approaches toward PSA, recognised for its superiority in capturing joint and interactive effects when multiple uncertain parameters are varied together [19]. The most methodologically sophisticated guidelines, such as those from Belgium's KCE and NICE, mandate PSA as the primary tool for parameter uncertainty, while retaining scenario analysis as the required approach for structural and methodological uncertainty. Notably, NICE goes a step further by explicitly recommending that scenario analyses also be conducted probabilistically where feasible. In addition, the mandatory Value of Information analysis required by the Dutch HEEG, which essentially quantifies the benefits of additional research, marks a progressive shift from uncertainty exploration toward its reduction [77]. As with modelling and fully incremental analysis, a correct assessment of sensitivity analysis requirements in relation to the identified sources of uncertainty presupposes adequate analytical competencies. For example, the Slovak HEEG uniquely recognises that the PSA represents an additional burden for both the submitting body (marketing authorisation holder) preparing it and the HTA analysts interpreting it; therefore, it was not included as a requirement in the first version of the national HEEG.

Limitationen der vorliegenden Übersichtsarbeit: explorative Suche, Einschlusskriterien und Leitlinienkategorisierung

The results presented in this review should be interpreted in light of the following limitations. Firstly, the analysis was based on a comprehensive, exploratory manual search rather than on systematic literature searches commonly used to answer methodological questions in the HTA and health economics contexts. However, this approach was deemed methodologically appropriate, given that national HEEGs are typically published as official institutional documents rather than research papers and should not introduce systematic bias into our comparative findings. In addition, when multiple guidelines were identified as used in the given jurisdiction, we included only the one we considered the main mandatory guideline applicable to multiple health technologies. Additionally, the inclusion criteria were formulated to ensure comparability of the selected jurisdictions with Austria and relied on the co-author's own categorisation of identified national HEEGs as mandatory or recommendatory/voluntary. Therefore, the categorisation might differ slightly from that used in other published reviews of HEEGs.

Einschränkungen bei der Datenextraktion, z.B. Umfang, Interpretationsspielraum, Übersetzung

Secondly, the data extraction process, while comprehensive, presented a challenge for full double-checking due to the volume of qualitative information in the guidelines and the complexity of the extraction framework (which included both pre-defined and ad-hoc categories). Furthermore, the accuracy of data extraction and subsequent HEEG categorisation also depends on the precision of the extractors' interpretation of the guideline content. Additional bias may have been introduced in the case of HEEGs, which were not available in English or in a language spoken by the authors, and had to be machine-translated.

fehlende standardisierte Qualitätsbewertung als Limitation

Lastly, a quality appraisal of the included HEEGs was not undertaken because the HEEGs have varied recommendations, and no generalised tool is available to assess their quality. Consequently, the review does not take a standpoint on what is theoretically right or wrong approach; instead, we assumed that the divergence across methodological aspects is caused by inherent preferences of the decision makers, unless the guideline provided an alternative explanation for the given methodological choice.

5 Conclusion

internationale Übereinstimmung: CUA, EQ-5D, ICER als gemeinsame Grundlage Abweichungen bei Perspektive, Diskontierung und Unsicherheitsanalysen

Overall, the methodological aspects of HEE associated with the strongest international convergence comprise the preferred analytic technique, the outcome measure and measurement tool, the time horizon, the preferred sources of effectiveness evidence, and the modelling details. Specifically, at least 12 of the included national HEEGs agree on the preference for CUA, with QALYs derived from the EQ-5D instrument, and a sufficiently long time horizon to reflect all relevant incremental differences between the compared interventions. Also, if a modelling approach is chosen, nearly all guidelines require that the model be validated, the model type be justified, and, ideally, an unlocked copy of the model be submitted. On the other hand, aspects marked with the greatest divergence could be defined as those in which fewer than eight national HEEGs align in their approach. According to our analysis, these aspects are the scope of the HEEG, the approach to equity, the comprehensiveness of the guidance on modelling- especially on model selection, the instructions for reporting results (in particular, the requirement for fully incremental analysis), and the prescribed discount rate. The remaining methodological aspects analysed are characterised by a shared principle but a slightly divergent operationalisation, as eight to twelve countries endorse the same approach in their HEEGs.

Empfehlungen für Österreich: Kapazitätsaufbau bei Dateninfrastruktur und frühzeitige Einbindung der Entscheidungsträger

Generally, the convergence around methodological principles creates a strong, shared foundation that enhances the comparability and transferability of economic evaluation results and provides a common language for international discourse. In contrast, the differences negatively affect transferability of HEE; nonetheless, a previous review of EU HEEGs suggested that the exchange of results between European countries could be facilitated by sensitivity analyses that accommodate the present methodological variety [14]. Consequently, the main learning for the development of an Austrian HEEG is to build on the recognised international convergence observed across multiple HEE domains, while considering the local context. The methodological aspects can be roughly grouped into those that reflect strategic decisions and value judgements (legal status, scope, discount rate, equity approach), and those informed by the local analytical capacities (modelling and uncertainty analyses requirements) and data availability (perspective, outcome valuation). Therefore, it is vital to prioritise capacity-building in the identified areas that require pre-existing data infrastructure and analytical literacy, while involving policymakers in early discussions of methodological requirements that shall reflect their preferences.

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Appendix

Comparator definitions

Table A- 1: Extraction of comparator definitions

Countries	Comparator How is the comparator defined?
Australia	Therapy expected to be **the most replaced** with the proposed medicine by prescribers in practice. Usually a PBS-listed medicine or **standard medicinal management.**
Belgium	**Standard or usual care** (SoC) in practice, provided that it is **the most cost-effective alternative** identified on the efficiency frontier. If SoC is not the most CE, then the most cost-effective intervention should also be included as a comparator.
Czech Republic	**Therapeutic procedures recognized as common** for the respective disease in target patient group (disease stage, line of treatment). Must be reimbursed from Czech health insurance funds ideally on permanent basis. If multiple relevant comparators are identified, the comparison should be made against each one separately.
Finland	The comparator should be therapeutically the most appropriate alternative. If the medicinal product is **meant to replace the use of a certain medicinal product or a certain treatment**, the product should be compared to that medicinal product or treatment. There can be several comparators. Reasons must be given for the choice of the comparator, and the choice must be based on Finnish clinical practice.
France	**All clinically relevant interventions** in the population analysed shall be identified for the reference case. Comparators include interventions for which there is published clinical data, and health products for which there are published prices or maximum compensation amounts. The medicines under evaluation by EMA, and which meet those conditions, may be included if they are covered by a temporary usage authorisation (TUA), a post-TUA programme, or an early filing procedure with HAS. There is no a priori reason for considering that a **little-used intervention in standard practice** is not **on the cost-effectiveness frontier.**
Germany	Treatment option used in the previous benefit assessment procedure; if several alternatives for the comparator therapy are equally appropriate, the proof of additional benefit compared to one of these therapies is sufficient, e.g. with the most cost-effective alternative or usual treatment practice.
Hungary	In the case of a new drug – if **it replaces the old one** – **the current standard therapy** can be the comparator. However, the comparator can also be a placebo or minimal care if there is no suitable therapeutic option available for the given disease or if the standard therapy cannot be used for the patient. Ideally, the comparator is the reference health technology that ● has a domestic routine application supported by data/evidence and ● is defined based on modern, effective, high-quality European and international clinical practice guidelines and ● is supported by high-quality scientific evidence on efficacy, effectiveness and safety published in the international medical literature and ● is approved in the indication and treatment line under analysis and its social security support category has been previously defined.
Italy	**Italian Standard of Care**, whenever possible; exclusion of any relevant alternatives should be clearly stated and justified. SoC is defined followingly: treatments or combination of treatments most used in the Italian clinical practice for each subpopulation/indication in the question; treatment strategy recommended by national or international guidelines; Best supportive care or active surveillance or no intervention in absence of therapeutic alternatives
Japan	Product that results in the best outcome should be selected from candidate products reimbursed by public health insurance, **widely used in clinical practice and expected to be to a large extent replaced**. Non-treatment or watchful waiting can also be used as a comparator. If a single comparator cannot be determined, the selection of a comparator should be considered following the comparators in randomized controlled trials (RCTs), similar products for the official pricing and cost-effectiveness of candidate products, based on agreement in consultation.

Norway	Alternative **intervention most likely to be exclusively or partially replaced** by the intervention under assessment. In most cases, the **comparator will reflect current standard of care** (for example, according to national guidelines), or the treatment that is most extensively used in terms of number of patients treated. If there are several commonly used comparator treatments, then all relevant comparators should be included in the assessment.
The Netherlands	**Standard and/or most usual intervention** in the Netherlands (if this is not the most cost-effective intervention, a comparison must also be made with the most cost-effective intervention). The standard intervention is the intervention which is regarded as the first choice in accordance with clinical guidelines or practice. A comparison with the usual intervention is appropriate if no standard intervention exists. The usual intervention refers to the intervention which is used most frequently in conjunction with the defined patient population and with which people have the most experience in daily practice. The usual intervention may also imply that no treatment is offered, but rather a recommendation to wait and observe, possibly combined with symptom relief (supportive or palliative care). If the standard or usual intervention is not **the most cost-effective intervention**, a comparison will have to be carried out with multiple interventions, using a fully incremental analysis.
Portugal	**All other healthcare options relevant** to the disease or clinical condition in focus, as defined in the scope of the pharmacotherapeutic evaluation and considered in the pharmacotherapeutic recommendation by CATS. Relevant comparators are all therapeutic alternatives available in Portugal and may include therapeutic sequences, inactive therapeutic options, non-therapeutic active treatment options, and include alternative rules to start-stop the new technology. The economic evaluation must compare the new technology with all relevant comparators in a fully incremental analysis, where each is included individually rather than blended into a single comparator. When **the most efficient alternative** is clearly established, the comparison can be made with only this one.
Saudi Arabia	**Current standard of practice**. Must include **the least expensive and the most effective** treatments available at least. Inclusion of emerging technologies are encouraged.
Slovakia	A medicine, other medical intervention or a combination thereof shall be selected which is **standardly used in the conditions of normal therapeutic practice**, can be **fully or partially replaced** by the use of the assessed medicine and is the **most cost-effective** in relation to public health insurance (defined in Directive 422/2011 Z. z. that the HEEG cites) For the sake of clarity and predictability, in line with current NIHO practice, we consider a procedure that has at least 20% clinical practice coverage as a relevant comparator. A 10-20% coverage takes into account international and national recommendations (the stronger the position of the procedure in the recommendations, the lower the coverage is needed. With a clear position, 10% is sufficient). … It can also be a yet unreimbursed intervention used off-label or on exceptional basis, if there are clinical data from Slovakia proving its use above the given threshold.
Switzerland	Typical **standard of care** that presents the closest therapeutic equivalent ("Doing nothing" may also be an evaluable alternative)
England & Wales-NICE	Normally the **established practice in the NHS**. When the evaluation suggests that an established practice may not be **considered a good use of NHS resources** relative to another available treatment, the committee will decide whether to include it as an appropriate comparator in the evaluation, after reviewing an incremental economic analysis. The committee's overall decision on whether a cost-ineffective practice is a valid comparator will be guided by whether it is recommended in other NICE guidance, or whether its use is so embedded in clinical practice that this will continue unless a new technology replaces it

Preferred sources of evidence for effectiveness

Table A- 2: Is systematic literature search required?

Answer	Countries
YES- explicitly required	Australia, Belgium, France, Germany, Japan, Norway, Portugal, Netherlands, England & Wales (NICE)
NO/UNCLEAR - No explicit requirement stated	Czech Republic, Finland, Hungary, Italy, Saudi Arabia, Slovakia, Switzerland

Table A- 3: Is the order of preferred evidence sources specified?

Answer	Countries
YES Clear Evidence Hierarchy Specified	Australia, Belgium, Czech Republic, Finland, France, Germany, Hungary, Japan, Norway, Netherlands, Portugal, Slovakia, Switzerland, England & Wales (NICE)
NO/MINIMAL Limited hierarchy specification	Italy, Saudi Arabia

Budget Impact Analysis

Table A- 4: Recommendations concerning BIA specified in the HEEGs

	Time Horizon	Countries
BIA required and methodology specified in the same guideline	6 years	Australia, Slovakia (detail for three 12-month periods)
	5 years	Norway
	4 years	Hungary
	3 years (base), 5 years (sensitivity)	Germany
	Minimum 3 years	Belgium
	Minimum 2 years	Italy, Portugal
	3 years	England & Wales (NICE)
	2-5 years	Saudi Arabia
BIA required, reference to a separate BIA guideline		France, Czech republic
Optional or Conditional Requirements	Optional	Finland
	Conditional	Switzerland (Cost impact must be demonstrated; BIA can be performed with ISPOR guidance)
Not Required or Not Mentioned		Japan, Netherlands

Equity analysis

Table A- 5: Recommendations concerning equity analysis specified in the HEEGs

Equity Approach	Quantifiable Modifier in CEA	Countries
Explicitly Addressed Qualitative Discussion	No weights/modifiers	Australia, Belgium, Hungary, Saudi Arabia, Slovakia, Switzerland
Explicitly Addressed Quantitative Consideration	Limited/specific circumstances	England & Wales (NICE)
Not Explicitly Stated/Addressed	N/A	Czech Republic, Finland, France, Germany, Italy, Japan, The Netherlands, Norway, Portugal

Preferred analytic technique

Table A- 6: Analytic technique to be applied in the base (reference) case and alternative methods allowed

Primary preference for reference case	Countries	Alternative methods mentioned	Countries
CUA, CEA only in justified cases if CUA not possible	Australia, Belgium, Czech Republic, Hungary	**CMA for proven equivalent interventions**	All countries with stated preference allow it (Saudi Arabia different wording- for generics and biosimilars)
CUA Clear Preference (not further comparison with CEA)	Norway, The Netherlands, Portugal, Slovakia, England & Wales	**Cost-consequences analysis (CCA)**	Belgium (for uncaptured outcomes), France
CUA slight preference	Finland, France (as CUA always accompanied by CEA if survival is affected), Japan (as QALY should be used in principle for outcomes)	**CBA also mentioned**	Finland, France, Germany, Switzerland
CUA/CEA Flexible Preference (no clear distinction between the two)	Italy, Germany, Saudi Arabia	**Cost-comparison analysis**	England & Wales (NICE)
No clear preference	Switzerland		

Preferred Perspective

Table A- 7: Perspective to be applied in the base (reference) case and in supplementary analysis

Primary Perspective	Supplementary Analysis Allowed	Countries
Healthcare System/Payer Perspective	Societal perspective supplementary	Australia, Belgium, Czech Republic (societal and governmental perspectives relevant for orphans), Hungary, England and Wales (governmental), Italy, Japan, Portugal (other costs admissible in scenario analysis), Slovakia (caretaker perspective admissible in scenario analysis)
Strict Healthcare Payer/Insurance Perspective	Limited/no supplementary options	Switzerland
Collective/Broader Perspective	Healthcare system with justification	France
Societal Perspective	Healthcare system as alternative	The Netherlands
Extended Healthcare Perspective	-	Germany, Norway, Finland
Flexible Perspective	-	Saudi Arabia

Model Details Required

Table A- 8: Requirements associated with the use of modelling

Countries	Model validation specifically required?	Justification of model type	Submission of unlocked electronic copy of the model
Australia	YES	YES	YES
Belgium	YES	YES	Upon request
Czech Republic	YES	YES	Recommended

Finland	Not in traditional sense	YES	YES
France	YES	YES	NO
Germany	YES	YES	NOT directly
Hungary	Not in traditional sense	NO	NO
Italy	YES	YES- partially	YES
Japan	YES	YES	YES
Norway	YES	YES	YES
The Netherlands	YES- AdVISHE checklist	YES	NO
Portugal	YES	YES	YES- implicitly
Saudi Arabia	Encouraged to be provided	YES	NO
Slovakia	NO	NO	YES
Switzerland	NO	NO	NO
England & Wales- NICE	YES	YES	YES

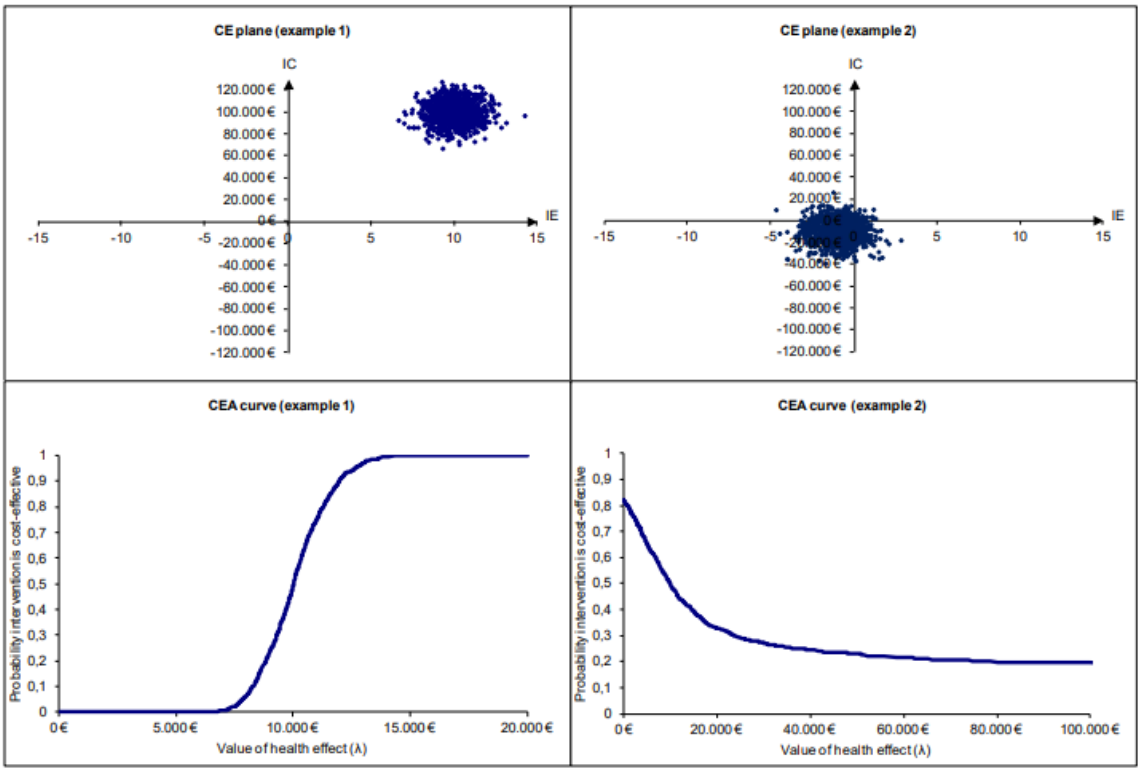
Uncertainty analysis concerning base case modelling

Table A- 9: Mandatory and voluntary uncertainty analyses

Countries	Mandatory	Voluntary
Australia	**Parameter:** DSA- Univariate, multivariate (if applicable) **Structural (and *translational*)**: scenario **Mandatory scenarios:** scenarios with discounting rate variations (3.5% and 0% p.a.), alternative time horizons, and substantial use of medicine beyond the intended population	PSA
Belgium	**Parameter:** PSA **Structural**: Scenario **Mandatory scenarios:** scenarios with discounting rate variations (0%, 3%, 5% equal p.a.) *If applicable*: shorter time horizons, extrapolation scenarios (waning of effectiveness), price discounts on comparators	• Additional univariable DSA, i.e. threshold analysis • Incremental net monetary benefit (INMB) • Expected value of perfect or partially perfect information (EVPI or EVPPI)
Czech Republic	**Parameter (*implied*)**: DSA- OWSA + PSA **Structural (*implied*)**: scenario **Suggested scenarios:** varying discounting rates (0%, 5%); different extrapolation methods; cross-over removal, disregarding certain conditions, etc. *If applicable*: discounted comparator costs; excluding temporarily reimbursed comparator; including comparator under revision; excluding caregiver QoL (for orphans with broader perspective)	NA
Finland	**Parameter:** DSA- OWSA **Structural:** alternative assumptions/scenario analyses **Mandatory scenarios:** parametric survival distribution uncertainty (partitioned survival models), comparators with conditional pricing (uncertain prices of comparators or actual hospital costs) **Other:** sub-group analysis *(if applicable)*	PSA Scenario with alternative discount rates (e.g., 0%, 5%, other)
France	**Parameter:** PSA, DSA- univariate, multivariate (if necessary) **Structural:** alternative assumptions (implicit scenario analyses) **Suggested structural elements to test:** perspective, time horizon, population analysed, comparators, discount rate (4.5% and 0%), cost valuation methods **Modelling assumptions to test (*if applicable*):** model type and structure, data sources (if multiple for key parameters), calculation methods, extrapolation methods (waning effects) **Other:** subgroup analysis *(if applicable)*	Fundamentally different scenario from the reference case
Germany	**Parameter:** Univariate and multivariate DSA; PSA **Structural:** scenario analysis	NA

	Recommended scenarios: a fixed time horizon of 5 years, discount rates between 0 and 5% and, if necessary, examining differential discounting (costs 3%, benefits 1.5%).	
Hungary	**Parameter:** DSA (specifically Two-way DSA), PSA **Structural (*if applicable*):** scenario analysis for a shorter time horizon, alternative extrapolation methods, multiple potential comparators **Other:** subgroup analysis *(if applicable)* NB: Parameters whose input value has no expected uncertainty, i.e., whose value is set by some external regulator (such as discount rates or financing tariffs), do not need to be considered in sensitivity analyses.	Additional scenario analyses beyond those required More extensive parameter variation ranges Alternative modelling approaches
Italy	**Parameter:** univariate DSA, PSA **Structural:** discount rate variations (0%, 5%); *if applicable*: surrogate endpoint scenarios (if efficacy uses surrogate endpoints); extrapolation scenarios	Additional scenario analysis addressing other structural assumptions (e.g. time horizon); Subgroup analysis
Japan	**Parameter:** DSA (one-way, confidence interval-based; *if applicable*: threshold) **Structural:** scenario analysis (if multiple scenarios identified) **Mandatory scenarios:** discount rates from 0- 4% p.a., *if applicable*: shorter time analysis	PSA
Norway	**Parameter (*implied*):** DSA (one-way, two-way, multiway), scenario (base case, "worst case", and "best case", or other alternative plausible scenarios) **Structural (*implied*):** DSA, scenario	PSA
The Netherlands	**Parameter:** DSA: univariate (based on standard error, or ±20% if no information available); PSA **Structural/methodological:** scenario, PSA (parametrised uncertainty) **Mandatory scenarios:** no discounting, healthcare perspective (without the indirect costs of life years gained), shorter time horizons (clinical trial duration and halfway extrapolated), other extrapolation distributions; *if applicable*: alternative data sources (costs, utilities), non-inclusion of unrelated future medical costs, inclusion of QoL of carers **Other:** VOI analysis- EVPI and EVPPI; *if applicable* (missing data >5%): scenarios to test 'Missing At Random' (MAR) assumptions	DSA- threshold analysis; Other relevant scenarios; Extended VOI analyses (EVSI, ENBS)
Portugal	**Parameter:** PSA, DSA- OWSA, threshold analysis with price and CET range €10.000-100.000/QALY **Structural (*non-parameterised*):** scenario, PSA within scenario (if feasible) **Suggested scenarios (*if applicable*):** alternative model structures or health state definitions, alternative assumptions on the extrapolation of treatment effects, alternative statistical distributions used to describe the course of the disease, or alternative data sources (utility) **Other:** EVPI	Other DSA: Multivariate (e.g., two-way), Best-case/worst-case analysis; EVPPI
Saudi Arabia	"Preferred": DSA- OWSA, PSA,	"If feasible": multi-way DSA, scenario
Slovakia	**Parameter:** DSA-OWSA (varying key parameters by ±30%); **Structural:** scenario	PSA
Switzerland	NA	NA
England & Wales- NICE	**Parameter:** PSA **Structural (*if applicable*):** PSA (with parametrised uncertainty), scenario **Mandatory scenarios (*if applicable*):** extrapolation assumptions, appropriate representation of care pathways, eventual economies of scale	DSA: univariate and best- or worst-case sensitivity analysis (mainly for identifying parameters for PSA) Threshold analysis (an option for highly uncertain parameters) 1.5% discount rate (in specific circumstances)

Results reporting



CE: cost-effectiveness; IC: incremental cost; IE: incremental effect

Figure A- 1: Examples of CE plane and CEAC

Source: [17]

HTA Austria
Austrian Institute for
Health Technology Assessment
GesmbH