COST-EFFECTIVENESS AND BUDGET IMPACT MODELS FOR INNOVATIVE HEALTH TECHNOLOGIES

Work Package 5 (WP5), led by the **University of Oslo (UiO)**, focuses on developing **cost-effectiveness models and budget impact models for innovative health technologies (IHTs)**. These models aim to support more transparent and evidence-based decision-making by improving how the value and financial impact of innovative technologies are assessed. WP5 develops **open-access and dynamic modelling approaches** that incorporate the **entire life cycle** of a **health technology**, allowing models to be updated as new clinical and economic evidence becomes available. By enabling the integration of evolving data and policy scenarios, these models support more adaptive evaluation of IHTs. Partners from **academia**, **professional organisations**, **patient groups**, **industry**, and **payers** contribute their expertise to ensure a broad and balanced perspective on the development and application of these models.

This position paper summarises the key findings from scoping literature reviews, outlines recommendations derived from the evidence, and explains how ASCERTAIN addresses these through concrete actions.

WHAT DID WE LEARN ABOUT MODELLING METHODS FOR INNOVATIVE HEALTH TECHNOLOGIES (IHTS)?

SUMMARY OF FINDINGS FROM REVIEWS

- We conducted a **scoping review to identify state-of-the-art statistical methods** for estimating clinical effects in health technology assessments (HTA) based on evidence from **single-arm trials (SATs)** without a control arm. As SATs are increasingly used as primary evidence sources in HTA submissions and market authorisation applications, applying appropriate methods is critical to avoid biased estimates of treatment effectiveness.
- Methods recommended in the literature to analyse evidence from SATs include **propensity score approaches, network meta-analysis**, and simulated treatment comparisons, as well as **tools** to assess and minimise bias such as **RECIST**, **RoBANS**, **ROBINS-I**, **and ACROBAT-NRSI**.
- In the literature on the evaluation of IHTs, the **most commonly applied approach for estimating relative effectiveness** was the use of **historical or case controls**, while **matching methods and meta-analyses** were also applied, most often using data from other clinical trials, databases and registries or electronic health records.
- The development of dynamic, open-access, adaptable, **global cost-effectiveness models** can support more efficient and standardised decision-making and may contribute to **more equitable access to IHTs across European countries**. To inform the development of such models, we conducted a **two-part scoping review** identifying
  1. existing global cost-effectiveness models and
  2. economic evaluations of selected IHTs in Europe.
- The review identified **three cost-effectiveness models aligning with our definition of a global open access model**, with **limited description** on how they have been adapted across settings. In addition, **53 economic evaluations** were identified, predominantly cost-effectiveness analyses of **next-generation sequencing (NGS)** conducted in the Netherlands and the United Kingdom. While model structures were often consistent within interventions, key parameters such as **cost inputs and efficacy data sources varied across countries**.

Appropriate statistical methods and open, adaptable economic models are essential to generate reliable evidence for health technology assessment.

HOW CAN MODELLING APPROACHES BETTER SUPPORT HEALTH TECHNOLOGY ASSESSMENT (HTA)?

RECOMMENDATIONS BASED ON EVIDENCE

- **Use high-quality external data sources when evaluating evidence from single-arm trials (SATs).** When estimating clinical effectiveness based on SATs, evaluators should identify suitable external data sources—such as randomized controlled trials, disease registries, or real-world databases – that represent the current standard of care for the same indication and patient population.
- **Ensure comparability between trial data and external data sources.** External data should be selected using clearly defined eligibility criteria so that patients are comparable to those in the single-arm trial in terms of disease stage, prior treatments, and key prognostic factors. Baseline variables such as age, performance status, and biomarkers should be harmonized, and the balance of covariates after matching or weighting should be assessed using standardized differences and other diagnostics.
- **Apply structured expert elicitation (SEE) to address evidence gaps.** SEE as a systematic approach to capture experts' knowledge is increasingly used in HTA and economic evaluation to address data gaps and uncertainty where traditional evidence is limited. While several national guidelines now recommend SEE, its practical application remains limited, and further methodological work is needed to evaluate the robustness of SEE frameworks and tools.
- **Promote standardized economic evaluations through global cost-effectiveness models.** Developing shared modelling frameworks can improve consistency and comparability of economic evaluations across countries. Standardized structures and assumptions increase trust in cost-effectiveness results used for reimbursement and coverage decisions and improve transparency for policymakers and payers.
- **Develop open and transparent modelling frameworks.** Global models implemented using open-source programming (e.g., in R) allow researchers and stakeholders to review assumptions, detect errors, and propose improvements. Open models promote methodological quality, facilitate peer review, and support better handling of uncertainty, calibration, and structural modelling choices.
- **Ensure global models can be adapted to local contexts.** While global frameworks provide standardization, countries must be able to integrate local data on clinical outcomes, costs, prices, and resource use in a transparent and flexible manner. This allows countries to avoid developing completely different models for the same or comparable indications while ensuring that model results reflect national guidelines and healthcare system characteristics.
- **Enhance transparency and accountability in reimbursement decisions.** Open modelling approaches allow patient groups, clinicians, and the public to better understand how methodological choices, such as discounting, equity considerations, or outcome selection, affect decision-making, supporting fairer and more accountable priority setting.

Better use of external data, expert elicitation, and open modelling approaches can improve evidence generation and transparency in HTA decision-making.

HOW DOES ASCERTAIN TURN MODELLING EVIDENCE INTO PRACTICAL HTA TOOLS?

OUR CONTRIBUTION AND NEXT STEPS

ASCERTAIN develops **global cost-effectiveness and budget impact** models to improve evidence generation and transparency in HTA decision-making. We test the applicability of the global model concept with the help of three use cases that reflect a broad range of innovative health technologies, i.e., novel pharmaceuticals (Use Case 1), cell and gene therapies (Use Case 2) and medical devices and in-vitro diagnostics (Use Case 3). For all these **three use cases, we have designed and tested pilot models** on a specific IHT that has been selected by the ASCERTAIN consortium.

For **Use Case 1 (precision cancer medicines)** and **Use Case 2 (CAR-T cell therapies),** we are developing adaptable cost-effectiveness models built on a shared core structure, a partitioned-survival model that divides a patient cohort in mutually exclusive health states for progression-free, progressed and dead patients. Because evidence generation for HTA is often challenging, especially from single-arm trials, these models are designed to incorporate different sources of evidence for the treatment and the control arm. The model framework incorporates built-in checks of statistical diagnostics for alternative survival distributions to simplify the survival analyses required when evaluating such technologies. They can be adapted to different national contexts by updating country-specific parameters. The standardized structure and clear model code enhance transparency and facilitate critical adaptation and reuse by stakeholders.

For **Use Case 3 (next-generation sequencing (NGS) tests for precision oncology)**, we first developed a micro-costing framework that provides a detailed overview of health care resource use along the diagnostic pathway of NGS. Building on this, we are developing a global decision-tree model to assess resource use and clinical consequences of alternative genomic profiling strategies based on NGS. This model will offer decision-makers, researchers, and other stakeholders a practical starting point for economic evaluations of the complex interplay between NGS testing and precision cancer therapies.

The global models for UC 1 and 2 will interact with the pricing, reimbursement and threshold models, which enable budget impact models, based on access-based prices and inform managed entry agreements. We are currently focusing on improving the **user experience** of these cost-effectiveness models (e.g. interfaces, documentation, and guidance) before launching the platform that will host all models. In parallel, we will conduct **validation workshops** with stakeholders to ensure that the models are robust, relevant, and able to support evidence-based decisions on innovative health technologies across Europe.

ASCERTAIN develops adaptable, transparent, and user-friendly global cost-effectiveness and budget impact models, including survival-analysis, and decision-tree frameworks for diagnostics, that stakeholders can apply and validate across diverse European healthcare contexts.

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Hvordan kan prioriteringsmeldingen adressere utfordringene i persontilpasset medisin på en god måte? - Arendalsuka (political festival - Structured expert elicitation)

ISPOR - Role of Structured Expert Elicitation in Reimbursement Decisions: An Exploratory Case of Selpercatinib for Non-Small Cell Lung Cancer in Norway

Poster ISPOR 2024 - Barcelona (Yansi Wu et al)

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