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INDICATE

Deliverable D6.5

Guidance for Health Technology Assessment (HTA) of the six Use Cases

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1. Cover Page

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V0.2	21-11-2025	Lisanne van Prooyen Schuurman	Deliverable ready for review
V0.3	26-11-2025	Reviewed by Jan van den Brand & Christian Jung & Bart Haex	Add: - Glossary of Terms - Market Analysis (TAM, SAM, SOM) - Improve layout - Strengthen the explanation of DICA and more clearly articulate its relevance within the context of this deliverable
V1.0	27-11-2025	Authored by Lisanne van Prooyen Schuurman Review by Jan van den Brand	Added Glossary of Terms (Annex C), improved scope definition in 5.1 and layout. Updated 10.3.1.

[1]PU = Public; SEN = Sensitive, limited under the conditions of the Grant Agreement; CO = Confidential, only for members of the Consortium.
[2]R= Document/Report; DEC = Website; DEM = demonstrator; DATA = federated datasets

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2. Table of Content

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3.Introduction

3.1. Project context and rationale

INDICATE is a federated European data infrastructure for Intensive Care Unit (ICU) data, designed to enable secure cross-border access to routinely collected ICU information for research, analytics, and AI development. The project will federate at least 15 existing ICU datasets from 10 EU countries, harmonised to a common data model and vocabularies, following the broader European ambition for interoperable health data spaces as articulated in the *European Health Data Space (EHDS)* regulation (Commission, 2025).

To demonstrate the value of the infrastructure and ensure that it responds to real clinical needs, INDICATE includes six clinical Use Cases covering data use for research, AI model development, decision support, benchmarking, and education. These Use Cases not only drive development of the infrastructure in different ways (e.g., on both the technical and clinical side) but also are intended as early demonstrators of what the infrastructure can enable. Their success is therefore integral not only to INDICATE's scientific goals but also to its future relevance and usefulness for real-world users.

A central ambition of INDICATE is that both the infrastructure and the applications built on it are not only technically and clinically robust, but also economically viable, scalable, and attractive for real-world adoption. Achieving this requires systematic consideration of economic value from the outset, reflecting insights from broader analyses of European digital health infrastructures (DigitalHealthEurope, 2020; TEHDAS, 2023).

3.2. Why early economic thinking is essential

Experience from digital health and AI projects shows that economic questions are often addressed only after substantial investments have been made in data processing, model development, and technical validation (&Company, 2020). Only late in the process, teams begin to ask whether:

- the solution improves efficiency compared with standard practice,
- hospitals can justify the investment, or
- reimbursement pathways exist.

When these questions arise too late, it often becomes apparent that the value proposition is weak, expected efficiency gains are uncertain, or the solution does not align with existing financing mechanisms. As a result, even technically strong solutions frequently remain trapped in pilot phases with limited uptake (&Company, 2020)

Introducing economic evaluation early helps prevent these pitfalls. It enables Use Case teams to assess from the outset whether their solution is likely to be cost-effective (Elvidge et al., 2024), to understand which types of clinical and economic evidence will ultimately be required for adoption or reimbursement, and to make design and implementation choices that are feasible within real-world organisational and financial constraints.

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Robust evidence on cost-effectiveness and budget impact is increasingly expected to inform reimbursement and procurement decisions (Tarricone, Petracca, & Weller, 2024), a trend reinforced by the European HTA framework under Regulation (EU) 2021/2282, which strengthens requirements for consistent and transparent clinical and economic evidence across Member States. In addition. reimbursement pathways across Europe such as Germany's DiGA framework (BfArM, 2020) and the "Prise en charge anticipée numérique" (PECAN) in France, require credible documentation of both clinical benefit and economic value before solutions can be funded at scale (Tarricone et al., 2024).

A proactive economic perspective within INDICATE therefore increases the likelihood that the tools developed will be attractive to hospitals, payers, and other stakeholders.

3.3. Connection to the INDICATE's overall sustainability and business model

EU-level analyses also highlight the importance of economic value for health data infrastructures. The EHDS initiative stresses both the potential of secondary use of health data and the need for sustainable business models to support it. For example, the EHDS initiative estimates that enabling secondary use of health data across Europe could generate at least EUR 5.4 billion in savings over the next decade (Commission, 2025; EHTEL, 2022).

Similarly, EU studies (&Company, 2020; DigitalHealthEurope, 2020) emphasise that infrastructures and digital tools must have clear and scalable business models, not only technical or scientific excellence, to ensure long-term sustainability and to realise these expected savings.

This is directly relevant for INDICATE. Both data providers and data users must make tangible investments: data providers must establish extraction pipelines, implement governance processes, and maintain data quality, while data users must integrate INDICATE workflows into analytic or clinical processes. These investments will only be justified if the infrastructure ultimately generates demonstrable value for all actors, and a healthy Return On Investment (ROI) can hence be realised

A separate deliverable addresses the business model of the INDICATE infrastructure (Deliverable 3.2). The economic insights generated in this deliverable complement that work by assessing the value of the applications built on the infrastructure, but the broader infrastructure-level sustainability analysis remains out of scope here.

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4.Purpose of this Deliverable

The purpose of this deliverable is to provide a structured and proportionate framework for assessing the economic value of the six INDICATE Use Cases. Although the Use Cases differ in aims, maturity levels, and expected impacts, each must articulate a credible economic value proposition to progress toward real-world implementation.

This deliverable supports that process by:

- introducing a flexible economic evaluation tailored to INDICATE;
- encouraging early reflection on cost-effectiveness, budget impact, and business value;
- supporting economically feasible design and implementation choices;
- offering a structure that can be applied proportionately to tools with different characteristics and levels of maturity.

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5. Scope and positioning within INDICATE

5.1. Scope of the economic evaluation framework

The framework introduced here serves two objectives:

1. **to provide a coherent and proportionate approach for assessing the economic value of INDICATE's six Use Cases**, and
2. **to define principles that can guide future Use Cases and external users who build on INDICATE**.

The focus of this deliverable is strictly on economic evaluation, including costs, consequences, value for money and the development of credible early business cases. It does not develop the business model of the INDICATE infrastructure itself (covered in *Task 3.3, Deliverable 3.2*), nor does it assess ethical, social or organisational considerations (*Tasks 3.1–3.2 and 3.4*).

Market analysis considerations including Total Addressable Market (TAM), Serviceable Available Market (SAM) and Serviceable Obtainable Market (SOM), are relevant for SMEs and other commercial actors who may leverage INDICATE to develop products or services. These elements help determine potential commercial uptake and long-term sustainability. However, detailed market sizing falls outside the scope of this deliverable. Where helpful, Use Case teams may reference high-level market considerations when articulating their value proposition, but comprehensive TAM/SAM/SOM assessments are not required as part of the economic evaluation presented here.

Consequently, the scope of this deliverable remains focused on the economic dimensions most relevant for guiding Use Case development: identifying key cost drivers, understanding mechanisms of value creation, selecting proportionate evaluation methods and supporting realistic pathways toward implementation and adoption.

5.2. Positioning within the INDICATE project

As a federated European data infrastructure, INDICATE aims to enable secure cross-border access to harmonised ICU datasets. The value and long-term adoption of this infrastructure will depend on the extent to which it supports solutions that matter to clinicians, hospitals and decision-makers.

The six Use Cases developed in Work Package 6 serve as realistic demonstrations of potential INDICATE-enabled tools:

- **Use Case 1: MIMIC-EU** A European "atlas" of anonymised acute care cases to support research, benchmarking, and methodological development.
- **Use Case 2: Early detection of organ failure** An AI model designed to provide early warning of organ dysfunction, supporting clinical decision-making in critical care.
- **Use Case 3: Virtual digital twin of mechanical ventilation** Patient-specific digital twins to optimise ventilation strategies and potentially shorten ventilation duration or ICU stay.
- **Use Case 4: Prediction of neonatal and paediatric sepsis** AI-supported early detection tools aimed at improving outcomes in vulnerable neonatal and paediatric populations.

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- **Use Case 5: Quality benchmarking dashboards** Dashboard enabling hospitals to benchmark ICU performance and identify opportunities for quality improvement.
- **Use Case 6: Grand rounds workspaces** Digital environments supporting training, multidisciplinary consultation, and clinical knowledge sharing.

The economic evaluation framework helps determine whether each Use Case could deliver cost savings, productivity gains, improved outcomes or other economically meaningful benefits. Detailed mapping of all six Use Cases to evaluation tracks and expected methods is provided in Annex B.

6.Proportionality and lifecycle perspective

The economic evaluation framework is designed to be proportionate and sensitive to the lifecycle stage of each Use Case. Early-stage tools, such as initial prototypes or feasibility pilots, often lack the data and maturity to justify a full cost-effectiveness model. For these interventions, lighter approaches are more appropriate. Cost–consequence analysis, simple scenario analysis or a basic feasibility and business-case assessment can already help clarify the value proposition, identify key uncertainties and highlight critical data gaps.

As interventions mature and move closer to clinical implementation, expectations around the depth and rigour of economic evaluation increase. For more mature tools, particularly those that directly influence clinical decisions, more formal methods such as cost-effectiveness analysis or budget-impact analysis become appropriate. Recent systematic reviews show that economic evaluations of AI in healthcare are still relatively few compared to the broader AI literature and that their methodological quality and transparency vary considerably (Vithlani, Hawksworth, Elvidge, Ayiku, & Dawoud, 2023; Voets, Veltman, Slump, Siesling, & Koffijberg, 2022). This underscores the need for gradual but deliberate progression towards more robust methods as evidence accumulates.

The framework therefore does not require every Use Case to deliver a full HTA immediately. Instead, it sets minimum expectations, such as describing key costs and consequences and adopting basic ROI thinking, and outlines more ambitious “stretch” goals, such as cost-utility modelling, that Use Cases can aim for depending on their maturity, clinical impact and available data. This stepwise approach is consistent with the emerging development of AI-specific economic evaluation standards, including extensions such as CHEERS-AI (Elvidge et al., 2024), , and aligns with the principles laid out in Regulation (EU) 2021/2282 on Health Technology Assessment, which promotes transparent, comparable, and proportionate evidence generation across the technology lifecycle.

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7. Economic evaluation methods in INDICATE

This chapter outlines the main economic evaluation methods within INDICATE. The goal is to equip Use Case teams with a flexible methodological toolbox that can be applied proportionately, depending on each Use Case's maturity, intended impact and the evidence available.

The framework is not intended to impose a single uniform methodology on all Use Cases. Instead, it provides a decision-guiding structure that distinguishes between two complementary evaluation tracks:

1. **An HTA-inspired track** for Use Cases with a direct clinical or patient-level impact. These include AI tools influencing diagnosis, triage, risk stratification or treatment decisions.

2. **A business-case track** for Use Cases that primarily deliver infrastructural, workflow or operational improvements. These include for example workflows or ICU resource-optimisation tools, where value is expressed in productivity gains, reduced workload, or strategic institutional benefits.

7.1. HTA-inspired methods for clinically impactful Use Cases

Use Cases that directly support clinical decision-making, such as organ failure prediction, neonatal sepsis detection or digital twins for ventilation, are likely to require methods aligned with HTA. These interventions may influence tangible outcomes such as complications, mortality, length of ICU stay or escalation-of-care events.

7.1.1. Main forms of economic evaluation

Cost-effectiveness analysis (CEA) compares the costs and health outcomes of an intervention with those of current practice. It is suitable when INDICATE tools modify clinical trajectories in ways that can be captured in natural units, such as cases of organ failure prevented, deaths avoided or ICU days reduced.

Cost-utility analysis (CUA) is a form of CEA that expresses health outcomes in quality-adjusted life years (QALYs). It is particularly relevant when interventions have both survival and quality-of-life implications. Even when full QALY-based models are not immediately feasible, early cost-utility thinking can help clarify the potential long-term health impact and whether the intervention is likely to fall within value-for-money thresholds used by European HTA bodies.

Budget impact analysis (BIA) complements CEA and CUA by estimating the net financial consequences of adopting a technology over a defined time horizon, usually at the level of a health system, payer or hospital. BIA addresses questions of affordability and budget planning rather than pure efficiency, and is therefore especially relevant in healthcare systems with strict budget caps or regional variation.

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For interventions at lower maturity levels or with incomplete evidence, early HTA methods provide a more realistic starting point. These include:

- Cost–consequence analysis (CCA): listing all costs and consequences without aggregating them into a single ratio.
- Scenario analysis: comparing best-case, typical and worst-case assumptions.
- Headroom analysis: estimating the maximum price at which an intervention could still be considered cost-effective.
- Target product profiles (TPPs): defining minimum clinical performance thresholds required for economic viability.

Such approaches allow early exploration of economic potential before full evidence becomes available.

7.1.1. Modelling approaches typically used in HTA

Economic evaluation within an HTA framework often relies on formal decision-analytic modelling to estimate the costs and consequences of alternative strategies. These models allow evaluators to extrapolate beyond the data observed in INDICATE, represent clinical workflows, quantify uncertainty, and assess long-term value. The modelling approaches described below are widely used by European HTA agencies, and methodological guidance is available through a.o. the ISPOR-SMDM Modelling Good Research Practices (2012), NICE Guidelines, and the EUnetHTA Methods Handbook (2019)(EUnetHTA, 2019). Further details on modelling methods are described in (Andrew Briggs, 2006; Hunink MGM, 2014)

Decision trees

Description: Decision trees model a sequence of events and outcomes following a single decision point. Branches represent mutually exclusive clinical pathways (e.g., deterioration, no deterioration), with probabilities attached to each branch.

When appropriate:

- Short time horizons (hours to days).
- Acute ICU decisions with no meaningful long-term cycle structure.
- Early-stage AI tools influencing single-point decisions.

Strengths:

- Simple, intuitive structure.
- Easy to communicate to clinicians.

Limitations:

- Cannot easily model recurrent events or long-term trajectories.
- Complexity grows exponentially with additional branches.

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Markov Models

Description: Markov models divide the clinical course into a set of mutually exclusive health states (e.g. “stable”, “organ failure”, “recovered”, “dead”) with probabilities of transitioning between states at each cycle (e.g. every day or every week).

When appropriate:

- Chronic or long-term conditions.
- ICU patients with multiple potential deterioration and recovery stages.
- Evaluations requiring multi-period follow-up.

Strengths:

- Handles recurrent events naturally.
- Well-suited for long-term cost and QALY estimation.

Limitations:

- Requires good estimates of transition probabilities.
- “Memoryless” assumption may be unrealistic for some ICU trajectories.

Discrete-Event Simulation (DES)

Description: DES simulates individual patients moving through a healthcare system, with events occurring at variable times (e.g., admission, deterioration, intervention, discharge). It allows stochastic modelling of queuing, resource use and patient heterogeneity.

When appropriate:

- Highly complex care pathways.
- Scenarios where timing and sequencing of events matter.
- AI tools that individualise decisions or modify resource flow (e.g., ICU bed pressure).

Strengths:

- Captures individual-level heterogeneity.
- Handles resource constraints (beds, ventilators).
- Flexible and realistic for ICU dynamics.

Limitations:

- High data requirements.
- Requires specialised modelling expertise.

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Microsimulation (Individual-Based Models)

Description: Microsimulation models individual patients with unique characteristics, allowing personalised risk profiles, treatment responses and trajectories. Each patient is simulated separately, and aggregated outcomes form the economic results.

When appropriate:

- When outcomes depend on individual risk profiles.
- When AI tools provide personalised predictions.
- Heterogeneous ICU populations with complex trajectories.

Strengths:

- Naturally aligns with AI-based personalised decision support.
- Models patient-level variability and long-term pathways.
- Flexible for complex ICU interventions.

Limitations:

- More computationally intensive.
- Requires robust individual-level data

7.2. Business-case methods for process- and infrastructure-focused Use Cases

Not all INDICATE Use Cases produce direct patient-level health outcomes. Some primarily improve workflows or support research and education. For these interventions, formal HTA may be disproportionate, and business-case-oriented approaches are more appropriate.

Return on investment (ROI) focuses on the balance between the investment required and the financial returns generated, for example through reduced staff time, less manual data work, avoided external data acquisition, or improved throughput.

Net present value (NPV) extends this by taking the time value of money into account, discounting future savings or revenues.

The **payback period** provides a simple measure of how long it takes for cost savings or productivity gains to offset the initial investment. This metric is frequently used in hospital procurement decisions, especially for digital tools that require significant integration efforts.

Finally, **cost–consequence analysis (CCA)** is a flexible method that lists all relevant costs and all relevant benefits, including non-monetary ones such as improved benchmarking capability, enhanced training capacity or strategic positioning within a European data network, without forcing them into a single metric. This can be particularly useful for infrastructural interventions whose value is multidimensional.

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8.Decision guide for selecting the economic evaluation approach

The economic evaluation framework in INDICATE is intentionally flexible, but Use Case teams still need a clear, practical way to decide which approach to use when. This chapter sets out a simple decision guide that helps teams choose between the HTA-inspired and business-case tracks, and to calibrate how "light" or "in-depth" their evaluation should be at different stages of development.

Core questions

The decision process revolves around four core questions:

1. **Does the intervention directly influence clinical decision-making or patient outcomes?**
   For example: Does it change diagnosis, monitoring, triage, escalation of care or treatment decisions?
2. **Is clinical implementation a realistic goal (within or beyond the project)?**
   Is there a credible ambition to move from research to routine use, potentially involving reimbursement or formal procurement decisions?
3. **Can the main benefits be expressed in health outcomes, or are they mainly organisational?**
   Are the key effects things like complications avoided, ICU length of stay reduced, QALYs gained, or rather time savings, streamlined workflows, improved training, etc.?
4. **What is the current maturity of the intervention and what data are available?**
   Is the Use Case at prototype or feasibility stage, in pilot implementation, or close to deployment? Is there already outcome and resource-use data, or mostly assumptions?

The answers to these questions determine whether a Use Case should follow the HTA-inspired track, the business-case track, or a stepwise combination (starting with business-case thinking and moving towards HTA as the intervention matures.

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8.1. Stepwise decision logic

8.1.1 Step 1 – Is there a direct clinical or patient-level impact?

- **Yes** – the tool is intended to change diagnosis, monitoring, triage or treatment (e.g. organ failure prediction, virtual digital twin for ventilation, neonatal sepsis early warning).
  → Proceed along the **HTA branch** (Step 2).
- **No** – the tool primarily affects dashboards, education or workflow (e.g. MIMIC-EU, benchmarking dashboards, grand rounds workspace).
  → Proceed along the **business-case branch** (Step 4).

This first step separates tools whose value is expressed mainly in health outcomes from those whose value is mainly in process improvement.

8.1.2 Step 2 – Is clinical implementation a realistic goal?

Here the team considers whether there is an explicit ambition to integrate the tool into routine care within a realistic time frame.

- **Yes – implementation is intended.**
  The tool is envisaged as decision support, part of a clinical pathway, or a monitoring / alerting system.
  → The Use Case should follow the **HTA-inspired track**, because future reimbursement or procurement decisions will depend on evidence of both clinical benefit and economic value. Proceed to Step 3.
- **No – the tool is exploratory or methodological only.**
  For example, a research model with no current plan to "productise" or deploy.
  → A **light early-HTA** approach is sufficient: basic cost–consequence analysis, simple scenarios or headroom analysis to clarify whether, in principle, there is economic potential. A full HTA would be disproportionate.

In both situations, some form of economic reflection is still useful, but the depth of analysis differs.

8.1.3 Step 3 – What kind of health-outcome and cost data are feasible?

Within the HTA-inspired branch, the type and quality of evidence guide the choice of method.

- **If health outcomes can be quantified** (e.g. reduced mortality, fewer complications, fewer organ failures, shorter ICU length of stay, improved functional recovery):
  - CEA or CUA becomes a natural target method, ideally complemented by a BIA.
  - At early stages, simple models (e.g. decision trees, short-term models) may be sufficient, with more sophisticated modelling reserved for later stages when better data become available.
- **If health outcomes are indirect or highly uncertain**, but clear changes in resource use are expected (e.g. fewer lab tests, shorter stays, fewer readmissions):
  - It may be more realistic to start with cost–consequence analysis or a partial economic evaluation that focuses on the most important cost and resource changes.

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- As outcome data accumulate, the Use Case can gradually move towards a more formal CEA/BIA if needed.

In both cases, the Use Case remains on the HTA-inspired track, but the level of complexity is calibrated to maturity and data availability.

8.1.4 Step 4 – Are the main benefits organisational or research-enabling?

If the intervention does not directly guide individual patient decisions, but instead:

- provides performance or quality dashboards, or
- supports education, grand rounds or research acceleration,

then a **business-case evaluation** is usually more appropriate.

For these Use Cases, the central questions are:

- What are the upfront and recurring costs of development, integration, governance, hosting and maintenance?
- What are the main benefits in terms of time saved, reduced manual work, avoided external data purchases, faster analytics, or better support for quality improvement and training?
- Over which time horizon are these benefits expected to materialise, and for which stakeholders (e.g. individual ICUs, hospital management, research groups)?

Given this profile, methods such as ROI, NPV and payback period, complemented by a structured description of non-monetary benefits (through cost–consequence analysis), provide the most relevant information for decision-makers.

8.1.5 Step 5 – Consider evolution over time

Finally, Use Case teams should recognise that evaluation needs may evolve as tools mature.

- A Use Case may start with a business-case focus, demonstrating that a dashboard, data atlas or workspace saves staff time, reduces manual reporting or enhances quality and training.
- Once integrated into practice, the same tool may begin to influence clinical decisions or care pathways. At that point, it may be appropriate to transition into the HTA-inspired track, quantifying changes in patient outcomes and undertaking more formal CEA/CUA and BIA.

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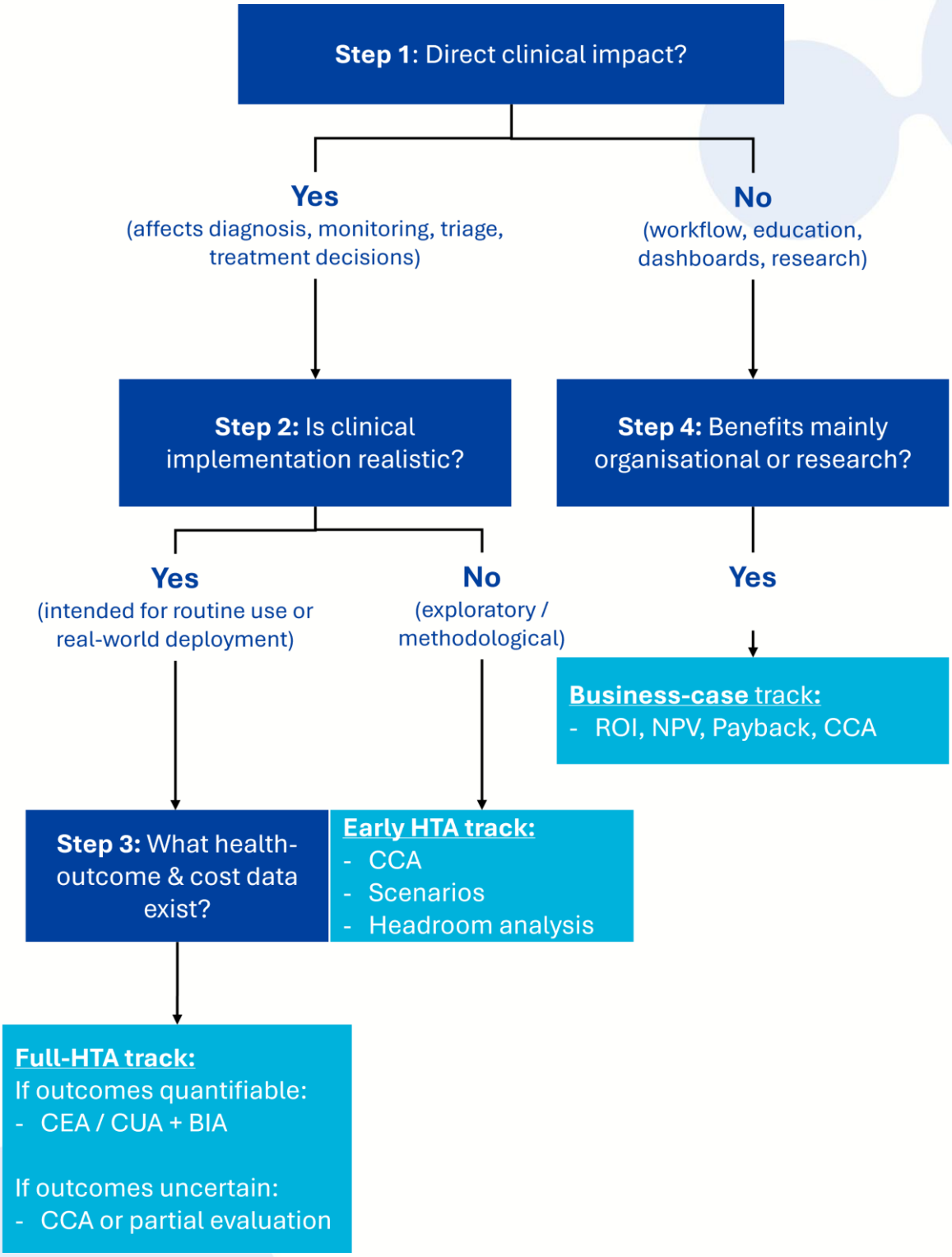

Figure 1. Overview of the stepwise decision process for economic evaluation in INDICATE
Abbreviations: HTA, health technology assessment; CEA, cost-effectiveness assessment; CUA, cost-utility analysis; BIA, budget impact analysis; CCA, cost-consequence analysis; ROI, return on investment; NPV, vet present value

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9. Data Requirements for Economic Evaluation in INDICATE (Balanced Version)

Economic evaluation depends on reliable and sufficiently detailed data. In a federated initiative such as INDICATE, where data availability differs across centres and not all variables can be extracted from routine ICU data, Use Case teams need clarity on which data are essential, which are recommended and which must be obtained externally. The aim is to support proportionate evaluation; rigorous where necessary, but realistic within the constraints of a multicentre federated project.

9.1. Core data needs across all INDICATE Use Cases

Regardless of the evaluation track, every Use Case requires a clear and structured description of the intervention. This includes what the tool does, who will use it, the intended workflow integration and the mechanism through which value is expected to be generated. Without this, it is difficult to determine the relevant cost categories or outcome pathways.

Most Use Cases will also need information on implementation and infrastructure costs. In a federated architecture, these typically involve:

- setup of local ETL pipelines and harmonisation efforts,
- governance and ethics processes,
- secure workspace compute and storage needs,
- integration with local IT systems,
- onboarding, training and maintenance,
- (for AI tools) model monitoring, recalibration and versioning.

Workflow and usability data form the final cross-cutting requirement. Even tools that do not directly affect clinical outcomes still influence staff routines. Useful information includes:

- the time required to use the tool,
- changes in workload,
- any workflow bottlenecks or improvements,
- staff acceptance and expected adoption rates.

These aspects matter both for business-case evaluations (where time savings are central) and for HTA-inspired analyses (where workflow changes influence cost and resource use).

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9.2. Additional data for HTA-inspired evaluations

Use Cases that directly influence clinical decisions or patient trajectories require more detailed clinical and resource-use information. Such evaluations need to understand how the tool affects risk, outcomes and resource consumption.

Clinical effectiveness data are particularly important. This includes:

- baseline event rates (e.g., organ failure, sepsis),
- expected changes in complications or deterioration,
- ICU length of stay,
- mortality and morbidity,
- readmission or escalation-of-care patterns,
- adverse events related to delayed or incorrect decisions.

Although INDICATE's harmonised data model provides much of this information, completeness may vary across centres.

HTA methods such as cost-utility analysis require health-related quality of life (HRQoL) estimates(Andrew Briggs, 2006; EUnetHTA, 2019; Hunink MGM, 2014). ICU datasets rarely include direct HRQoL measures, but approximate values can be obtained from published studies in comparable clinical populations (e.g., ARDS, sepsis survivors) or national registries.

Economic models also require resource-use and cost data, including ICU bed-day costs, ventilation days, laboratory and imaging costs, staff time and treatment changes triggered by earlier or more accurate decision-making. These data usually come from hospital finance departments, national tariffs or the literature.

Finally, HTA in AI must explicitly acknowledge uncertainty and heterogeneity, especially where model performance varies across centres or drifts over time. This requires sensitivity analyses and transparent reporting of assumptions.

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9.3. Additional data for business-case evaluations

For Use Cases that primarily deliver organisational, process or infrastructural benefits, business-case evaluations rely on operational and financial data rather than patient-level outcomes.

Development, integration and maintenance costs form an important foundation. These include:

- development time of engineers, clinicians and analysts,
- hosting and workspace costs,
- licensing or subscription fees where applicable,
- governance and coordination efforts,
- ongoing maintenance and (for AI tools) periodic updates or monitoring.

Operational efficiency and productivity data are essential for ROI, NPV and payback calculations. These may include:

- time saved through automation or simplified workflows,
- reduced manual reporting or data extraction,
- faster analytics or clinical review processes,
- avoided external data purchases or consultancy.

Business-case evaluations often incorporate strategic or organisational benefits that are not easily monetised. Examples include improved benchmarking capability, enhanced training and educational opportunities, higher audit readiness or strengthened collaboration across sites. These can be captured through qualitative cost–consequence analysis even when not expressed in euros.

Finally, business-case modelling requires assumptions about adoption and scalability, such as how many users or centres are likely to adopt the tool, how often it will be used, and which barriers may limit uptake. These assumptions directly shape medium- and long-term sustainability projections.

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9.4. Data availability and expected gaps within INDICATE

The INDICATE infrastructure aims to provide rich clinical data including demographic variables, severity scores, organ dysfunction markers, interventions, outcomes, specialised neonatal and paediatric variables, and physiological time series. These datasets form a solid foundation for many HTA-oriented analyses.

However, federated clinical data do not capture everything required for economic evaluation. Missing elements typically include:

- unit cost data (e.g., ICU day cost, staff time),
- Health Related Quality of Life estimates,
- workflow and usability information,
- local integration and governance costs.

Use Case teams should therefore map their data needs early, distinguishing what can be sourced from INDICATE from what must be collected externally.

9.5. Perspectives, time horizons and treatment of implementation costs

Beyond identifying required data, Use Case teams must also decide how to interpret them. Specifically, which analytical perspective to adopt, what time horizon to use and whether to include or exclude implementation and infrastructure costs(Andrew Briggs, 2006; EUnetHTA, 2019; Hunink MGM, 2014). These choices shape the structure and conclusions of any economic evaluation.

9.5.1 Analytical perspective

Different Use Cases may legitimately choose different analytical perspectives:

- A hospital or ICU perspective focuses on operational efficiency, workflow changes and costs borne by the institution. Implementation costs are usually included.
- A payer or health system perspective emphasises clinical outcomes, cost-effectiveness and budget impact. Implementation costs may be excluded if not borne by the payer.
- A societal perspective includes the broadest range of costs, such as productivity losses and informal care.
- A research-user perspective may assume INDICATE's infrastructure as a given and exclude most setup costs.

The chosen perspective must match the intended decision context and should be clearly justified.

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9.5.2 Time horizon

The time horizon must be long enough to capture all relevant costs and effects:

- clinical evaluations may require short-term (ICU), medium-term (hospitalisation) or long-term (survival, QALYs) horizons;
- business-case evaluations may focus on operational 1–5 year periods where integration costs and productivity gains occur;
- infrastructure-heavy tools may benefit from multi-year horizons that reflect gradual adoption.

The time horizon should reflect the natural lifecycle of the intervention.

9.5.3 When to include implementation and infrastructure costs

Implementation and infrastructure costs should be included only if they are relevant to the chosen decision-maker:

- Hospitals: usually included.
- Payers: often excluded unless directly incurred.
- Societal perspective: included.
- Research-user perspective: often excluded.

In cases of uncertainty, presenting multiple perspectives can be useful.

9.5.4 Discounting

Where costs or outcomes occur over multiple years, discounting may apply. HTA typically requires standard discount rates for costs and QALYs, while business-case analyses incorporate discounting through NPV. Discounting assumptions should follow relevant national or organisational guidelines.

9.6. Principles for future Use Cases and external users

Future Use Cases developed on or alongside INDICATE should adopt this structured approach: define the intended impact, choose an appropriate evaluation track, identify essential data based on that track and select a suitable analytical perspective and time horizon. They should also plan early for data gaps, particularly where local cost data or HRQoL estimates are missing, and should document all assumptions transparently to enable reproducibility.

By following these principles, future projects will help INDICATE build a coherent, credible and scalable body of economic evidence that supports long-term adoption, sustainability and value creation across Europe.

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10. European reimbursement and policy context

Economic evaluation within INDICATE does not take place in isolation. Digital health and AI-enabled tools operate in a policy landscape that increasingly expects structured evidence of clinical benefit, economic value and real-world feasibility before adoption or reimbursement. Understanding this context is important for two reasons. First, it clarifies why early economic thinking is necessary even during research and development. Second, it helps Use Case teams anticipate the types of evidence that may eventually be required if their tools evolve from a research demonstrator to a clinically implemented service.

European policy trends show a clear movement towards more coordinated evaluation of digital health technologies (*Regulation (EU) 2021/2282 on Health Technology Assessment)*, with specific pathways emerging at both EU and national levels (Tarricone et al., 2024). While INDICATE does not aim to commercialise the Use Cases during the project, the tools developed, particularly those involving clinical decision support, may eventually progress towards implementation. This chapter summarises the key frameworks shaping expectations for economic evaluation in Europe.

10.1. The EU Health Technology Assessment Regulation (HTA Regulation 2021/2282)

From January 2025 onwards, the EU HTA Regulation introduces a Joint Clinical Assessment (JCA) process for selected health technologies. While the initial scope is limited to oncology medicines and advanced therapy medicinal products, the Regulation establishes harmonised methodological requirements that will also be highly relevant for AI- and data-driven health technologies as they advance towards formal assessment.

The Regulation emphasises:

- comparative clinical effectiveness as the core of evaluation;
- non-clinical domains, including economic, organisational and ethical considerations, to inform national decision-making;
- increased methodological alignment across Member States;
- the expectation that evidence supporting digital and AI tools should be transparent, reproducible and robust, consistent with the methodological principles set out in the Regulation.

While each Member State retains autonomy over reimbursement and procurement, the Regulation sets a direction of travel: health technologies with clinical impact including, over time, AI-driven tools, will be expected to provide comparative evidence on patient outcomes and resource use. For INDICATE Use Cases concerned with prediction, early detection or treatment optimisation, this underscores the relevance of HTA-informed methods and the importance of early planning for outcome and cost data.

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10.2. The European Health Data Space (EHDS) and implications for value

The EHDS initiative illustrates the European Union's recognition of the substantial economic potential of the secondary use of health data. Regulatory documentation emphasises the need for large-scale, high-quality data infrastructures that support research, innovation, public-health monitoring and personalised care. Importantly, EHDS documents also highlight:

- the importance of sustainable business models for health-data infrastructures;
- the need for infrastructures to demonstrate clear value to both data providers and data users;
- the expectation that enhanced secondary use will generate significant efficiency gains, with the Commission's Impact Assessment estimating net benefits of around EUR 5.4 billion over a decade (EHTEL, 2022).

For INDICATE, this European orientation reinforces the relevance of assessing economic value at the level of individual Use Cases. Although infrastructure-level sustainability is addressed in a separate business model deliverable, the economic insights generated here feed into understanding how INDICATE-enabled tools may create value for hospitals, regions and health systems.

10.3. National reimbursement frameworks for digital health and AI

Several Member States have introduced specific reimbursement pathways for digital health technologies, many of which explicitly apply or are being extended to AI-enabled tools. These frameworks provide practical insight into the types of evidence that may be required for mature INDICATE Use Cases.

10.3.1 Germany: DiGA and DiPA

Germany's DiGA (Digitale Gesundheitsanwendungen) framework provides a structured pathway for reimbursing for low-risk digital health applications (medical devices class I or IIa). Key requirements include:

- evidence of positive healthcare effects, either clinical benefits or patient-relevant organisational improvements;
- compliance with MDR and robust fulfilment of requirements on data protection, information security, interoperability and usability;
- the option of provisional listing for 12 months (extendable), during which additional evidence can be generated.

Several DiGA solutions now incorporate AI components, and discussions are underway to adapt the framework for more complex, higher-risk decision-support systems. DiPA applies similar principles to digital tools used in long-term care.

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10.3.2 France: PECAN, Forfait Innovation and ETAPES

France has taken a multi-pathway approach to evaluating and adopting digital and AI-enabled health technologies:

- PECAN provides a dedicated pathway for AI-driven clinical decision-support tools. It requires robust demonstration of clinical benefit, validated technical performance and reliability, as well as an assessment of organisational and where relevant, medico-economic impact.
- Forfait Innovation supports promising technologies that require real-world evidence before wider adoption. The scheme enables early deployment under controlled conditions and explicitly allows the generation of clinical and economic evidence.
- ETAPES focuses on remote monitoring technologies but provides an instructive template: tools must demonstrate clinical benefit, safety, and cost-effectiveness to receive structured reimbursement.

These frameworks illustrate the importance of combining clinical and economic evidence at an early stage for AI-enabled tools.

10.3.3 The Netherlands: Zorgvalidering and value-based adoption initiatives

The Netherlands increasingly emphasises outcome-based and HTA-informed evaluation for digital innovation.

- Emerging validation of digital health interventions initiatives promote structured validation of digital and AI-enabled tools, including evidence of effectiveness, data protection, usability and organisational fit.
- The Dutch National Health Care Institute (Zorginstituut Nederland) advises that digital and AI interventions should demonstrate effectiveness, appropriate use, affordability and organisational feasibility, in line with HTA principles(Nederland, 2024, 2025).
- Local and regional pilots as well as national innovation programmes typically require a preliminary business case and a clear pathway toward demonstrating economic value or cost-effectiveness as a condition for scaling.

This policy direction aligns closely with INDICATE's two-track evaluation framework, combining clinical outcomes with economic and organisation

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10.4. Implications for INDICATE Use Cases

The European landscape shows increasing alignment around several core principles:

1. **Clinical impact requires comparative evidence.**
   Prediction models, early-warning systems and digital twins will be expected to demonstrate improvements over current practice.
2. **Economic value is mandatory.**
   Across Europe, reimbursement and procurement bodies expect evidence on cost-effectiveness, affordability or organisational value.
3. **Early modelling is increasingly encouraged**.
   Frameworks such as DiGA, PECAN and Forfait Innovation support provisional or early evaluation based on reasonable assumptions, provided they are transparent and well-designed.
4. **Organisational and workflow benefits count.**
   Many pathways recognise efficiency gains, reduced workload and improved process quality alongside patient outcomes.
5. **Integration and implementation costs matter.**
   Infrastructural complexity and IT integration burden are increasingly considered part of economic evaluation.

For INDICATE, this means that Use Case teams, especially those pursuing clinically impactful tools, should begin aligning their economic evaluation with these policies even during development. Tools that primarily deliver organisational or infrastructural benefits should consider how hospitals, researchers and health systems assess ROI, payback and strategic value. The landscape also reinforces the value of INDICATE's proportional approach. Early Use Cases cannot yet provide full cost-effectiveness models, but they can still:

- articulate a clear mechanism of impact,
- report preliminary resource-use changes,
- model early scenarios,
- identify key evidence gaps, and
- describe value in terms meaningful for hospitals or payers.

This positions them well for subsequent development, implementation or real-world evidence generation should they mature into deployable tools.

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11. Discussion

This deliverable provides a structured, proportional and adaptable framework for assessing the economic value of INDICATE Use Cases. It addresses recognised gaps in digital health and AI evaluation by encouraging early economic thinking, clarifying methodological expectations and providing a practical decision-making structure for selecting appropriate approaches.

The framework's strength lies in its flexibility. It accommodates use cases at different maturity levels and allows teams to scale their economic evaluation as evidence becomes available. This is essential in a project where several tools are early prototypes but may later evolve into clinically impactful applications. It also aligns INDICATE with emerging EU-level expectations for AI and digital health technologies, ensuring that future evaluation and adoption pathways remain realistic.

Several limitations must be acknowledged. The federated clinical datasets do not include cost variables, workflow data, HRQoL measures or integration costs; these must be sourced externally and will introduce uncertainty. Differences across centres in coding, practice patterns and data completeness may affect the stability of outcome estimates. Early economic analyses will therefore depend partly on assumptions and scenario modelling. Stakeholder engagement (clinicians, managers, nurses, data engineers and, where relevant, payers) is essential to validate assumptions and ensure credible adoption scenarios.

Despite these limitations, the framework provides INDICATE Use Case teams with a clear, actionable and policy-aligned approach for demonstrating value. The accompanying templates and mapping (Annexes 1–2) further operationalise this process, helping ensure consistent and meaningful economic insights across the project.

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12. Conclusion

This deliverable establishes a proportionate and practical economic evaluation framework for the INDICATE Use Cases. It clarifies when HTA-inspired methods are required, when business-case approaches are more appropriate and how Use Case teams can navigate between these tracks as their tools mature. It also identifies the data needed for credible evaluation and aligns these requirements with European policy and reimbursement trends.

By embedding economic thinking early, INDICATE increases the likelihood that its demonstrator tools will prove not only technically and clinically valuable, but also economically attractive and sustainable for real-world users. This supports the long-term relevance of the INDICATE infrastructure and contributes to broader European ambitions for data-driven healthcare.

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13. References

EIT Health McKinsey&Company, E. H. a. M. (2020). *Transforming healthcare with AI: The impact on the workforce and organisations*. Retrieved from

Andrew Briggs, M. S., and Karl Claxton. (2006). *Decision Modelling for Health Economic Evaluation*: Oxford University Press.

BfArM. (2020). *The Fast-Track Process for Digital Health Applications (DiGA) according to Section 139e SGB V*.

Regulation (EU) 2025/327 on the European Health Data Space (EHDS) and amending Directive 2011/24/EU and Regulation (EU) 2024/2847, (2025).

DigitalHealthEurope. (2020). *Better Utilisation of Data Infrastructures to Support Secondary Uses of Health Data*.

EHTEL. (2022). European Health Data Space: Insights into savings, financing, and governance.

Elvidge, J., Hawksworth, C., Avsar, T. S., Zemplenyi, A., Chalkidou, A., Petrou, S., . . . Group, C.-A. S. (2024). Consolidated Health Economic Evaluation Reporting Standards for Interventions That Use Artificial Intelligence (CHEERS-AI). *Value Health, 27*(9), 1196-1205. doi:10.1016/j.jval.2024.05.006

EUnetHTA. (2019). *EUnetHTA Technical Review of methodological standards in comparative effectiveness & clinical HTA*. Retrieved from

Hunink MGM, W. M., Wittenberg E, et al. (2014). *Decision Making in Health and Medicine: Integrating Evidence and Values*: Cambridge University Press.

Zorginstituut Nederland. (2024). *Toetsingskader Digitale Zorg - uitgebreide versie*. Retrieved from

Zorginstituut Nederland. (2025). Handleiding beoordeling digitale en hybride zorg.

Tarricone, R., Petracca, F., & Weller, H. M. (2024). "Towards harmonizing assessment and reimbursement of digital medical devices in the EU through mutual learning". *NPJ Digit Med, 7*(1), 268. doi:10.1038/s41746-024-01263-w

TEHDAS. (2023). *TEHDAS' recommendations to EU and member states to ensure EHDS sustainability*. Retrieved from

Vithlani, J., Hawksworth, C., Elvidge, J., Ayiku, L., & Dawoud, D. (2023). Economic evaluations of artificial intelligence-based healthcare interventions: a systematic literature review of best practices in their conduct and reporting. *Front Pharmacol, 14*, 1220950. doi:10.3389/fphar.2023.1220950

Voets, M. M., Veltman, J., Slump, C. H., Siesling, S., & Koffijberg, H. (2022). Systematic Review of Health Economic Evaluations Focused on Artificial Intelligence in Healthcare: The Tortoise and the Cheetah. *Value Health, 25*(3), 340-349. doi:10.1016/j.jval.2021.11.1362

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Annex A. Use Case reporting template

1. **Use case overview**

- Use Case name:
- Lead institution(s):
- Brief description of the intervention/tool:
- Intended users (clinicians, data scientists, managers, researchers, SMEs):
- Intended setting (ICU, research workspace, quality department, training):

2. **Problem statement and current practice**

- Brief description of the clinical or organisational problem:
- Current workflow or standard of care:
- Gaps or inefficiencies that motivate this intervention:
- Evidence from literature or benchmarking (optional):

3. **Intended impact and mechanism of action**

- Clinical impact (if applicable: changes in decisions, earlier detection, improved treatment):
- Operational impact (reduced workload, faster analytics, improved benchmarking):
- Educational impact (training, simulation, grand rounds):

4. **Alignment with the INDICATE evaluation track**

- Selection of evaluation track:
  - ☐ HTA-inspired evaluation
  - ☐ Business-case evaluation
  - ☐ Hybrid (start with business-case, evolve toward HTA)

Justification based on the decision guide (Chapter 6).

5. **Description of the intervention**

- Technical description (AI model, dashboard etc.)
- Required inputs (data elements, patient parameters)
- Outputs (predictions, visualisations, alerts, reports)
- Maturity (prototype, pilot, validated model, ready for implementation)
- Dependencies on INDICATE infrastructure components

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6. Economic evaluation approach

6.1 Evaluation type

- HTA-inspired:
  - ☐ Cost-effectiveness analysis (CEA)
  - ☐ Cost-utility analysis (CUA)
  - ☐ Budget impact analysis (BIA)
  - ☐ Early HTA
  - ☐ Cost-consequence analysis
- Business-case:
  - ☐ ROI
  - ☐ Net present value (NPV)
  - ☐ Payback period
  - ☐ Cost-consequence analysis

6.2 Time horizon

- Short-term (during project)
- Medium-term (1–3 years)
- Long-term (3–10 years)

6.3 Perspective

- Hospital
- ICU department
- National payer
- Research organisation
- Societal (optional if data available)

7. Data inputs and assumptions

7.1 Clinical and operational data

- Relevant patient outcomes
- Process outcomes (e.g. LOS, complications, readmissions)
- Workflow changes (minutes saved, tasks automated)

7.2 Cost data

- Implementation costs (integration, ETL, governance)
- Operational costs (compute, staff time, licenses)
- Resource-use cost drivers (ICU day cost, test cost, treatment cost)
- Maintenance and monitoring costs (especially for AI models)

7.3 Uncertainty and variability

- Sensitivity analyses planned
- Sources of uncertainty (data heterogeneity, model drift, adoption variation)

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8. **Value proposition**

8.1 For hospitals and clinical departments

- Expected returns (cost savings, efficiency gains, improved quality)
- Strategic benefits (benchmarking, participating in a European infrastructure)

8.2 For clinicians and staff

- Reduced burden
- Improved decision support
- Training/educational benefits

9. **Results of the economic evaluation**

(Can be preliminary for early-stage Use Cases)

- Main economic outcomes (ICER, cost savings, ROI, NPV, payback period)
- Scenario results (best case, realistic case, worst case)
- Sensitivity analysis results
- Key drivers of cost and value

10. Reimbursement and sustainability implications

- Likely reimbursement pathway (if any)
- Alignment with EU HTA standards
- Potential for DiGA/PECAN/other national pathways

11. Conclusions and next steps

- Readiness level of the economic case
- Key data gaps and priorities for further evidence
- Plan for refinement during the remainder of the project

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Annex B. Mapping of the six Use Case to the evaluation tracks

The six INDICATE Use Cases differ substantially in purpose, maturity, expected users, and type of impact. To ensure proportional and appropriate economic evaluation, each Use Case is aligned with either the HTA-inspired evaluation track or the business-case evaluation track, following the decision logic outlined in Chapter 6.

Below, each Use Case is summarised and mapped accordingly.

Use Case	Brief description	Primary impact type	Evaluation track	Rationale
UC1 – MIMIC-EU	Federated "European MIMIC" data atlas for research & benchmarking	Research support	Business-case	No direct clinical decision-making; primarily reduces research time, increases data access, and enables federated analytics
UC2 – Prediction of Organ Failure	AI model predicting acute organ deterioration using ICU time-series	Clinical decision support	HTA-inspired	Direct influence on monitoring, escalation, treatment; measurable patient outcomes and cost savings
UC3 – Virtual digital twin of mechanical ventilation	Simulation-based model supporting personalised ventilation strategies	Clinical decision support	HTA-inspired	Potentially influences ventilation settings, complications, LOS; strong implications for patient outcomes
UC4 – Neonatal & paediatric sepsis prediction	Early detection model for paediatric/neonatal sepsis	Clinical decision support	HTA-inspired	High clinical stakes; potential to reduce morbidity/mortality; strong alignment with HTA requirements
UC5 – ICU Quality benchmarking dashboards	Dashboards comparing ICU performance across sites	Organisational / quality improvement	Business-case	Focused on workflow, reporting, quality management; not a patient-level intervention
UC6 – Grand rounds workspace	Federated platform for education, case discussions, and training	Educational / workflow support	Business-case	No direct clinical impact; value primarily in time savings, training capacity, and knowledge exchange

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Annex C. Glossary of terms

BIA (Budget Impact Analysis)
Economic evaluation that estimates the financial consequences of adopting a health technology for a specific budget holder (e.g. hospital, payer) over a defined time horizon.

CCA (Cost–Consequence Analysis)
Economic approach that lists all relevant costs and all relevant consequences (clinical, organisational, etc.) in a disaggregated way, without combining them into a single summary measure.

CEA (Cost-Effectiveness Analysis)
Economic evaluation that compares the costs and health outcomes of alternative interventions, expressing results in natural units (e.g. complications avoided, ICU days saved).

CHEERS-AI
Extension of the Consolidated Health Economic Evaluation Reporting Standards tailored to interventions that use artificial intelligence.

Cost–utility analysis (CUA)
Type of CEA in which health outcomes are expressed in quality-adjusted life years (QALYs), allowing comparison across different diseases and interventions.

DES (Discrete-Event Simulation)
Modelling technique that simulates individual patients and events over time, capturing queues, timing, resource use and heterogeneity in care pathways.

DiGA (Digitale Gesundheitsanwendungen)
German reimbursement pathway for low-risk digital health applications, requiring evidence of positive healthcare effects and compliance with regulatory and data-protection requirements.

DiPA (Digitale Pflegeanwendungen)
German framework for reimbursing digital applications used in long-term care, analogous to DiGA but focused on the care setting.

EHDS (European Health Data Space)
EU initiative to enable secure primary and secondary use of health data across Member States through interoperable infrastructures, governance frameworks and common rules.

EUnetHTA (European Network for Health Technology Assessment)
European collaboration that develops methodological guidance and tools for HTA across Member States.

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ETAPES
French programme for the evaluation and reimbursement of remote-monitoring solutions, emphasising evidence on clinical benefit, safety and cost-effectiveness.

Headroom analysis
Early economic method that estimates the maximum acceptable cost (or price) a new technology could have while still being considered cost-effective.

HRQoL (Health-Related Quality of Life)
Measure of how health status affects a person's overall quality of life, typically captured by standardised questionnaires and used in QALY calculations.

HTA (Health Technology Assessment)
Multidisciplinary evaluation of the clinical, economic, organisational (and in some cases ethical and social implications) of a health technology to inform policy and reimbursement decisions.

ICER (Incremental Cost-Effectiveness Ratio)
Summary measure in economic evaluation expressing the additional cost per additional unit of effect (e.g. cost per QALY gained) when comparing two interventions.

JCA (Joint Clinical Assessment)
Procedural element of the EU HTA Regulation where clinical evidence for selected technologies is jointly assessed at EU level to support national decisions.

Markov model
Decision-analytic modelling approach in which patients transition between defined health states over repeated time cycles, used to estimate long-term costs and outcomes.

Microsimulation (individual-based model)
Modelling technique that simulates individual patients with their own characteristics and trajectories, allowing detailed representation of heterogeneity and personalised risk.

MDR (Medical Device Regulation)
EU regulatory framework governing safety and performance of medical devices, including many digital and AI-based medical tools.

NPV (Net Present Value)
Financial metric that sums all future costs and benefits of an intervention after discounting them to their present value; positive NPV indicates a financially attractive investment.

Payback period
Time required for the cumulative financial benefits or savings of an intervention to equal the initial investment.

PECAN (Prise en charge anticipée numérique)
French pathway for early reimbursement of digital and AI-enabled clinical decision-support tools, requiring evidence of clinical benefit and organisational/medico-economic impact.

QALY (Quality-Adjusted Life Year)
Composite health outcome measure combining quantity and quality of life into a single metric, used in cost–utility analysis.

ROI (Return on Investment)
Ratio expressing net financial gains (or losses) from an intervention relative to the initial investment.

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Scenario analysis
Method that explores uncertainty by comparing economic results under different plausible assumptions (e.g. best case, realistic case, worst case).

TAM (Total Addressable Market)
The overall revenue opportunity available if a product or service achieved 100% market share in the relevant market.

SAM (Serviceable Available Market)
The portion of TAM targeted by a company or initiative given geography, regulatory constraints or product focus.

SOM (Serviceable Obtainable Market)
The realistic share of the SAM that can be captured, given competition, resources and adoption constraints.

TEHDAS (Towards the European Health Data Space)
EU Joint Action providing recommendations to support the design and sustainability of the European Health Data Space.

TPP (Target Product Profile)
Specification of the minimum and desired features (e.g. clinical performance, usability, economic properties) a technology should achieve to be viable for adoption.

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