



**Inno-HTA: Adding value to comprehensive early  
assessment of health care innovations from a public  
and private perspective**

**Information leaflet for various stakeholders**

**HTA-methodology  
for innovative healthcare technologies**

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## **Inno-HTA: Adding value to comprehensive early assessment of health care innovations from a public and private perspective**

New pharmaceuticals, medical devices, and interventional procedures provide a promise to patients and consumers of improved health care, and there is a pressure on regulatory agencies to get them out to patients as soon as possible, but secure their safety and efficacy. The industry developing these health care innovations need to anticipate requirements for later evidence-based assessment already in an early stage, and internally assess the likely performance of the new technology during all stages of development and testing. Early health technology assessment is therefore an essential support to both decision-making in the public and the private domain.

The EU-funded project ***HTA-Methodology for Innovative Healthcare Technologies (Inno-HTA)*** ([www.inno-hta.eu](http://www.inno-hta.eu)) set out to identify potential gaps between the development of new technologies and their application. This was done by applying an innovation systems approach to early assessment, by scrutinizing existing approaches to early assessment, and by means of soliciting the various stakeholders involved.

This information leaflet contains the main outcome of this project: a list of indicators (criteria) for early assessment of emerging health technologies from both a public and private perspective. The project did not include application of the indicators in particular decision scenarios. Thus, it does not provide explications about how the indicators or subsets of the checklist could be used by single stakeholder groups to support specific decisions. For this reason, this list is considered by the InnoHTA consortium as work in progress, and the main recommendation is therefore to further operationalize and test the list by applying it in practice.

On a general level, however, these indicators provide guidance on how to make better assessments. The indicators can be used as a checklist for issues that should be addressed by the stakeholders to estimate if and how innovations should be guided into application. We hope that different stakeholders working with emerging health care technologies (e.g. regulators, payers, providers, HTA researchers, patients/consumers, industry) will use the list as a checklist.

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## Checklist of indicators for the assessment of healthcare innovations

The following indicators for the assessment of healthcare innovations were selected from the areas of HTA and innovation research by means of theoretical analyses, case studies, expert workshops and an online survey. The requirements for information of different stakeholder groups vary. Depending on the specific decision situation, these indicators could be useful to make better assessments.

The examples for the measurement of the indicators are only for illustration and may be adopted according to the particular perspective of the assessment and availability of data.

No.	Indicator	Example for measurement
<i>Patient-related outcomes</i>		
1.	effects on mortality caused by target disease	RR, OR, rates; mortality / morbidity avoided (RR, OR, Rates)
2.	effects on morbidity caused by target disease	
3.	effects on general health-related quality of life	utilities; HRQoL
4.	effects on disease-specific quality of life	utilities; changes in QoL
5.	effects on life expectancy	years
6.	effects on progression of disease from start/outbreak to recovery or death	valuation formulas (survival function)
7.	rate of severe treatment failure	%
<i>Broader health impacts</i>		
8.	improvement in care for patients for which no adequate treatment existed	n of patients
9.	effects on compliance: share of patients adhering to recommended use	%
10.	degree of achieved control of the disease through technology	level (percentage of patients with controlled symptoms)
11.	pharmacodynamic or pharmacokinetic improvement of existing therapeutic principle	rating (little/strong)

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No.	Indicator	Example for measurement
<b>Safety</b>		
12.	<b>frequency of severe adverse effects</b>	events/subject-month; % of adverse reactions; number of cases
13.	<b>toxicity of new technology e.g. in cell or animal studies</b>	rating (low/high)
14.	<b>probability of dosage errors</b>	%
15.	<b>risk-benefit-ratio</b>	rating (positive/negative)
16.	<b>fear of adverse effects</b>	rating (low/high)
17.	<b>risks associated with producing or applying the new technology</b>	n and rating (low/high)
<b>Economic evaluation</b>		
<b>– Costs</b>		
18.	<b>costs of technology</b> (including all relevant indirect cost aspects)	Euro per unit; Euro per year per patient
<b>– Health economic evaluation</b>		
19.	<b>incremental cost-utility ratio</b>	Euro/QALY
20.	<b>incremental cost-effectiveness ratio</b>	Euro/effectiveness unit; rating
21.	<b>cost-benefit difference</b>	Euro per treated person
22.	<b>estimations of cost effectiveness</b>	modelling; expert estimates
23.	<b>affordability of technology</b>	% of patients in need who would buy product or get reimbursement
24.	<b>consumers' willingness to pay</b>	Euro
25.	<b>technology's impact on the budget of the third-party payers</b>	Euro
<b>– Economic evaluation – Producer perspective</b>		
26.	<b>rate of return on investment with new technology</b>	rate
27.	<b>potential of the market to reward the costs of R&amp;D</b>	rating (low/high); profit on R&D investments /total R&D investments
28.	<b>duration of time in which the technology will be effective (e.g. until resistance occurs)</b>	years
29.	<b>R&amp;D investments necessary for new technology</b>	Euro
30.	<b>seed or venture capital available for R&amp;D</b>	Euro
<b>– Economic evaluation – Society perspective</b>		
31.	<b>jobs created through R&amp;D, production and application of the technology</b>	n and qualification; relative to n of jobless

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No.	Indicator	Example for measurement
<i>Societal aspects</i>		
32.	<b>acceptance of technology</b>	rating; qualitative (e.g. problems encountered; preferences of stakeholders) or quantitative (e. g. proportion of patients complying)
33.	<b>institutional support for translation, clinical research and HTA</b>	n of clinical trials; budget of public research funding
34.	<b>eco-efficiency of the new technology</b>	metric or rating
<i>Ethical aspects</i>		
35.	<b>factors impeding equal access to technology (e.g.: gender, age, geographical location)</b>	qualitative information; size of affected populations
36.	<b>generation of sensitive personal data during application</b>	qualitative information
37.	<b>challenge of religious, moral or cultural convictions or beliefs</b>	qualitative information
38.	<b>animals necessary for R&amp;D or production</b>	n and species
<i>Legal aspects</i>		
39.	<b>compliance with requirements of regulatory bodies</b>	yes/no; rating (low/high)
40.	<b>efforts and time necessary for compliance with regulatory requirements</b>	rating (low/high)
<i>Health problem and current use of technology</i>		
41.	<b>burden of target disease (incl. economic)</b>	prevalence; incidence; mortality; QALYs/DALYs/potential years of life lost/Euro lost due to target disease
42.	<b>current state of the art of care for the target disease</b>	qualitative information
43.	<b>current use of the new technology</b>	qualitative information
<i>Organisational aspects</i>		
44.	<b>effects of new technology on therapeutic process</b>	% of cases in which test result is judged „helpful“ in planning therapy; % of time or money saved due to new intervention
45.	<b>effects of technology use on patient satisfaction</b>	questionnaire and qualitative data
46.	<b>convenience/ease of use</b>	rating
47.	<b>costs for introduction (replacement of standard with new technology)</b>	Euro
48.	<b>effects of technology use on job satisfaction of healthcare professionals</b>	qualitative information

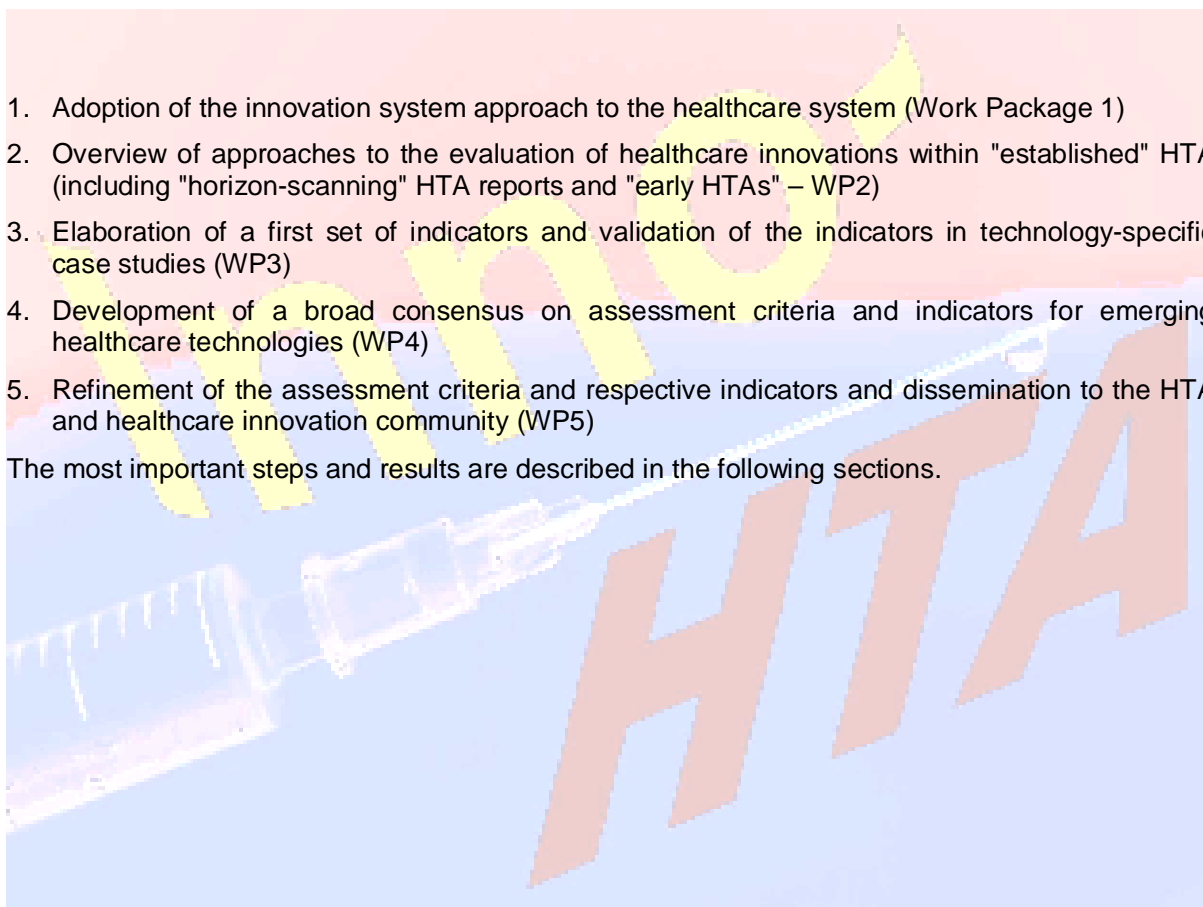
No.	Indicator	Example for measurement
<b>Knowledge/education</b>		
49.	<b>familiarity with new technology</b>	rating (low/high)
50.	<b>information/training needs of healthcare professionals for correct treatment</b>	rating of quality and quantity (low/high)
51.	<b>information/training needs of patients</b>	rating of quality and quantity (low/high)
<b>– Innovativeness</b>		
52.	<b>relevance of differences to already marketed product</b>	rating
53.	<b>alternative technology currently in development</b>	n and stage of development
<b>– Status of development</b>		
54.	<b>marketing authorisation status of technology</b>	granted yes/no; qualitative information
55.	<b>new technology is in clinical testing</b>	yes/no
56.	<b>new technology is available for clinical application or in use</b>	yes/no
57.	<b>new technology is available on prescription</b>	yes/no
58.	<b>reimbursement status of technology</b>	granted yes/no; qualitative information
59.	<b>sales of new technology</b>	Euro; n of doses sold
60.	<b>good evidence on costs, benefits, cost-effectiveness etc. available</b>	yes/no
61.	<b>intellectual property (patents, licences) or products to be used/sold/transferred</b>	n of collaborations; n of patents granted/sold/bought, n of licenses sold/bought
<b>Research activities</b>		
62.	<b>funding of R&amp;D available from public or other non-profit source</b>	Euro

## Approach of the project

The approach for the development of the list of indicators for assessment of emerging technologies for the healthcare sector included the following steps:

1. Adoption of the innovation system approach to the healthcare system (Work Package 1)
2. Overview of approaches to the evaluation of healthcare innovations within "established" HTA (including "horizon-scanning" HTA reports and "early HTAs" – WP2)
3. Elaboration of a first set of indicators and validation of the indicators in technology-specific case studies (WP3)
4. Development of a broad consensus on assessment criteria and indicators for emerging healthcare technologies (WP4)
5. Refinement of the assessment criteria and respective indicators and dissemination to the HTA and healthcare innovation community (WP5)

The most important steps and results are described in the following sections.



## Healthcare innovation system (WP1)

The healthcare innovation system was analysed.

An innovation is understood in our project as a new technology or product (pharmaceutical, "advanced therapy", diagnostic test, or medical device), but not service, process or structure. "New" means that the application (indication) is already determined as use for human health, i.e. when human studies have started. Technologies should be predominantly in clinical trials phases I or II, but without a clear end.

The most important actor groups which should be covered by indicators are

- health policy
- research policy
- economics policy
- labour policy
- environmental policy
- regulatory agency
- health insurance
- public, media
- patients (and insurees, citizens)
- healthcare professionals, providers
- developer/producer (industry)
- researchers, academic (incl. applied research, HTA)

Some healthcare innovation indicators may be relevant for more than one group or even for all groups together. Differentiations within some of the actor groups might still be necessary for certain purposes, e.g. separate public from private health insurance.

## HTA methods for emerging healthcare technologies (WP2)

To make best use of the internationally available knowledge base in HTA methodology for healthcare innovations Working Package 2 aimed at:

1. Compiling and assessing relevant assessment schemes including international, EU as well as nationally funded and private initiatives.
2. Integration of all actually EU-funded and most important Member States' projects into the research process.
3. To elaborate an overview of the methods actually used in HTAs for emerging healthcare technologies including their respective scope, strengths and weaknesses and to identify experts for methodological questions to be included the further steps of the project.

In order to achieve these objectives, the work was divided into four subtasks:

### Inventory of existing projects on HTA methods for emerging technologies and List of experts in the field of HTA methods

**Objective:** For health technology assessment it is a major challenge how to support evidence-based decision-making on the grounds of the limited information available during early stages of technology development. Furthermore innovative technologies are often “moving targets” meaning that they undergo changes during the early phases of application. These problems led to development and institutionalisation of units that specifically deal with the challenges of assessment of new and emerging technologies and it is still subject of multiple research activities.

**Methods:** Websites of HTA organisations as well as the scientific literature were searched in order to establish an inventory of HTA projects assessing new and emerging technologies. The targeted search for experts in the field set out from well known HTA networks, institutions and cooperative projects as well as from methodological publications on the assessment of new and emerging technologies from the scientific literature.

**Results:** Among the institutions the EuroScan Network with its member organisations of Horizon Scanning Units is most prominent. But there are also private non-for-profit and for-profit institutions offering assessments of new and emerging technologies. Two examples from the United States include the ECRI institute and Hayes Inc.. Among the research projects, Working Group 7 of the ongoing EUNetHTA project and the MATCH project specifically address HTA of innovative technologies. Furthermore there are a number of single research projects dealing with specific aspects of new and emerging technologies. These concern participatory methods of HTA, probabilistic analyses and Ethical, Legal, Social Implications.

**Conclusions:** Identified experts as well as the projects EUROScan, EUNetHTA (WP7) and MATCH were contacted and invited to join the Board of Advisors for the Inno-HTA project.

## Overview of methods that are currently used to assess emerging technologies

**Objective:** For health technology assessment it is a major challenge of how to support evidence-based decision-making on the grounds of the limited and inaccurate information available during early stages of technology development. This led to development of a number of strategies and methodologies to deal with this particular problem. Purpose of the overview over HTA methods was to identify indicators used in Health Technology Assessment to characterize technologies properties in the domains of safety, efficacy / effectiveness, ethical, social, organisational and legal impact. Economic evaluation is dealt with in another work package of this project.

**Methods:** The search for methodological literature used two different approaches: The “expert approach” set out from well known HTA networks, institutions and cooperative projects to identify further institutions, projects and working groups which are explicitly engaged in the assessment of new and emerging technologies. The literature approach set out to retrieve methodological publications on the assessment of new and emerging technologies from the scientific literature.

**Results:** The following table gives an account of Aims, HTA-Elements and Methods found in Health Technology Assessments of new and emerging technologies.

Aims	HTA-Element	Methods
Finding „emerging“ technologies	„Scanning“	Literature searches Expert consultations Searching: research programs, press releases, gathering input from stakeholders
Identifying technologies with high probability of relevant impact	„Filtering / Prioritising“	Criteria based approaches upon information from: clinical literature, epidemiology, bench research, preclinical and clinical research results, cost compilations, health system analysis, stakeholders preferences consensus methods, quantitative methods
Estimation of probable impact	„Early Assessment“	„Straightforward“ HTA “Component approach“ “Modelling, Prediction rules“ “Casuistry“
Generating Evidence	„Monitoring“ ELSI-Information	Clinical Trials Registries Postmarketing Surveillance Interactive / participatory assessments
Integrating social shaping perspective	“New HTA”	Constructive HTA Participatory HTA Interactive HTA

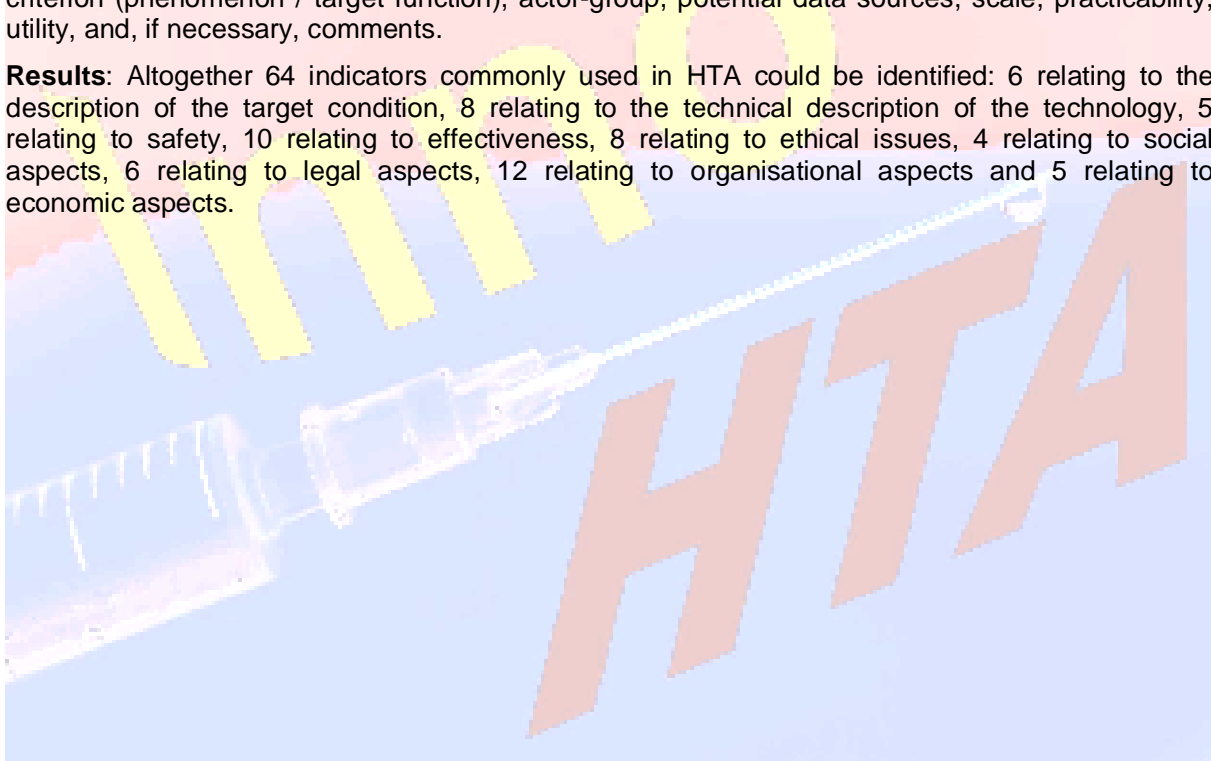
**Discussion + Conclusion:** The approach had some limitations. First of all, searches and literature analysis were limited to English or German language publications. Although we assume that major methodological progress would have been published in English language scientific journals we can't exclude that we have missed some potentially relevant developments. Furthermore, our searches did not thoroughly investigate the industry sector, which means that approaches applied within industry may well be missed.

## List of healthcare innovation indicators used in the reviewed existing HTA approaches

**Objective:** During the process of health technology assessment the properties of a technology (or the interaction of a technology with its context of application) are assessed in multiple dimensions. These measurable characteristics of a health care technology may be described as „indicators“. The Working Package aimed at compiling a list of indicators currently used in Health Technology Assessment to describe the properties of health technologies. This list was to be taken as the basis for the indicator list, specifically designed for the assessment of technologies in development.

**Methods:** Three documents from collaborative working groups on Health Technology Assessment (1-3) were searched for characteristics of health care technologies and their context which are recommended to be assessed within an comprehensive HTA. These characteristics were specified as “indicators”. The indicators are tabulated, ordered by HTA-dimension with description of criterion (phenomenon / target function), actor-group, potential data sources, scale, practicability, utility, and, if necessary, comments.

**Results:** Altogether 64 indicators commonly used in HTA could be identified: 6 relating to the description of the target condition, 8 relating to the technical description of the technology, 5 relating to safety, 10 relating to effectiveness, 8 relating to ethical issues, 4 relating to social aspects, 6 relating to legal aspects, 12 relating to organisational aspects and 5 relating to economic aspects.



## Validity and feasibility of the indicators based on case studies (WP4)

**Background:** The aim of WP 4 was to test the extensive set of indicators for their feasibility and validity in case studies and – if necessary to identify new/ more indicators.

The main research question was: Is there an added value for reducing uncertainty and adding to robust decision-making?

**Methods:** The indicator-set, extracted from HTA-methodology analyses (UL-IfSM, WP2) and deduced from earlier empirical research and early assessments (Fraunhofer WP3) was developed in the preceding work packages. Seventy/70 indicators were identified and listed. Subsequently 5 case studies were carried out to apply the indicators. The topics for the case studies were chosen on three criteria of a. broad spectrum of different types of technologies, b. in different fields of medicine, c. in different stages of development:

In each case-study, the feasibility of 70 indicators was judged independently by 2 reviewers according to

1. Data validity defined by property of fact-based/ credibility/ prone to bias source: interest-group independent or data of transparent origin – high validity, interest group source or expert estimations – low validity
2. The concept of validity is based on the method of “critical appraisal” developed by the Cochrane Collaboration and other initiatives of Evidence Based Medicine (hierarchy of evidence): transparency in the origin of data, in the generation of results, in the naming of confounders and possible biases.
3. Data availability defined by existence and public access of data: yes/no
4. Although some confidential information/ data might not be publicly available but existent and protected by property rights, availability might therefore not be a criterion for the quality of indicators, but displays the usability/ applicability/ feasibility of indicators at least in the public sector. The concept of availability has 2 dimensions (public vs. protected/confidential; public-access thru written material vs. public access thru personal communication).
5. Relevance for actor groups defined by necessity for decision-making for broad range of actors (6 actor-groups)

**Results:** Evaluating the feasibility of the 70 indicators showed that there is low availability and validity of many data (e.g. cost data), but they would be of high relevance to a broad range of actors. The indicators most feasible (because of highest scores in data availability/ high data validity) are in the area of epidemiology and number of patients with indication, status of technology, efficacy and guidelines (but not effectiveness), alternatives, some cost factors (expenditures, length of stay).

- > Least feasible (because of lowest scores in data availability/ low data validity) are in the area of effectiveness, compliance, some cost factors (cost-effectiveness, etc.) and macroeconomics.

Indicators that turned out to be unreliable, because data are missing were proposed to be candidates for deletion, since they make no contribution to the reduction of uncertainty.

The following case studies have been systematically analysed along the criteria validity, availability and relevance.

Table 1 Case studies

	Type of Technology	Field of Medicine	Technology	Stage of Development
1	Drug	Oncology	Aflibercept for advanced ovarian cancer	Phase II/III
2	Diagnostics	Psychiatry	Biomarker for testing of alcohol therapy adherence	Early diffusion
3	Medical device	Orthopaedics/surgery	Cervical Artificial Disc Replacement	Clinical testing
4	Tissue Engineering/advanced therapy	Dermatology	Tissue Engineering for care of chronic wounds	Early diffusion
5	Predictive diagnostics	Genetics	Testing for TMPT for adverse events with AZA	Early diffusion

**Discussion:** An assessment at early stages of development requires performance data (efficacy and efficiency) embedded in the data on the real world environment (cultural values and regulatory setting). Early assessment can be descriptive only along defined criteria/indicators (as Horizon Scanning products use to be), with limited influence on future performance or in the form of decision analytical scenarios; modelling different options of performance and setting data and possible influence on shaping the technology's performance. Thus, the essential elements for indicators for a constructive early assessment still open to shaping the technology are the

6. Identification of outcome measures and economic performance and
7. Identification of main drivers of product performance and related critical outcome measures.

**Conclusion:** Uncertainty might be reduced by enforced data analyses and data generation at an early stage, but a certain degree will stay uncertain because of the complex interplay between practice and understanding the variables influencing innovation, because of complex environments and last but not least the heterogeneity of human population and their reactions to medical interventions.

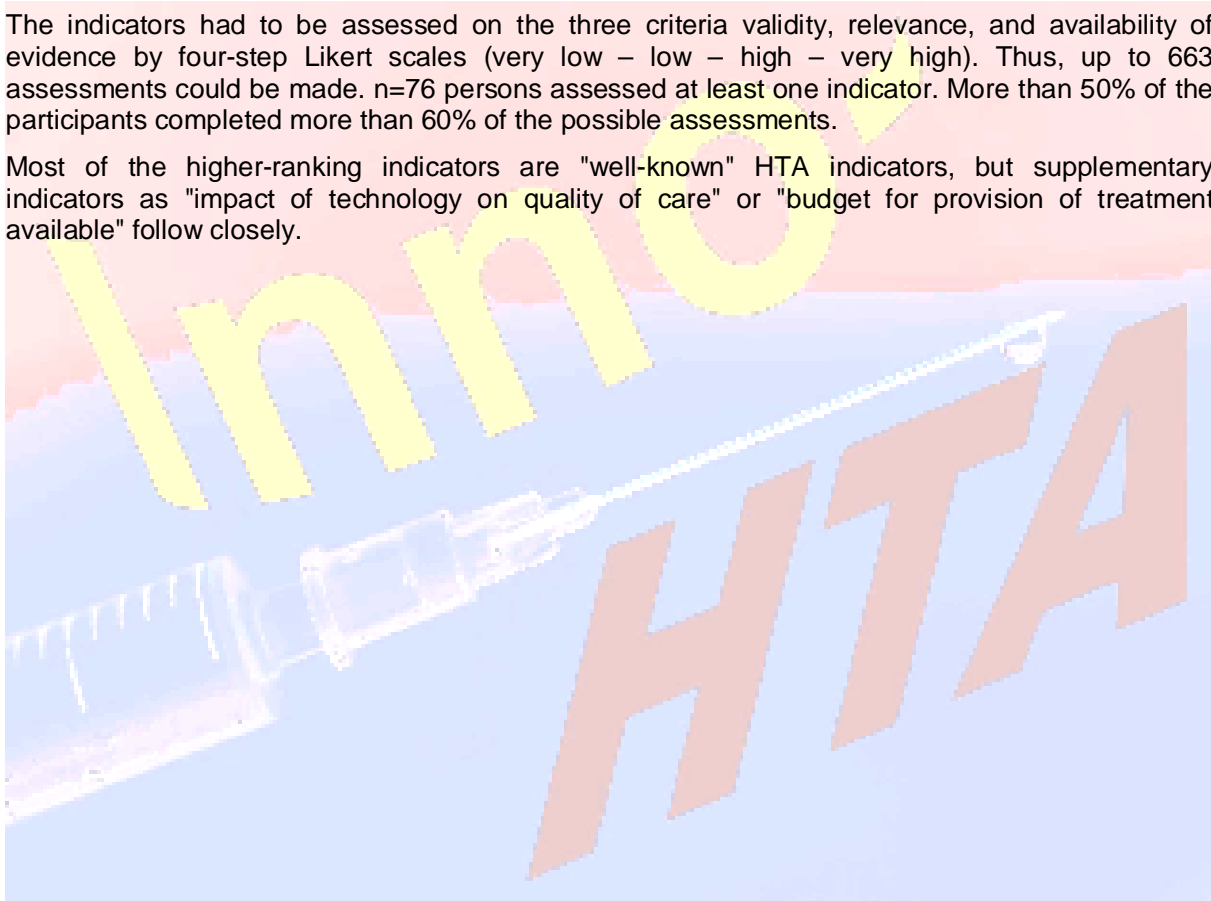
## Innovation indicators (WP3,5)

### *Online Survey*

From the earlier steps, a draft list of 221 indicators in 31 domains resulted. The invitation to participate in the online survey was individually sent to  $n_0=492$  persons or organisations, as well as the members of the EUnetHTA network (approx.  $n_E=300$ ) and the mailing list of the German Network for Evidence-based Medicine (approx.  $n_D=700$ ).

The indicators had to be assessed on the three criteria validity, relevance, and availability of evidence by four-step Likert scales (very low – low – high – very high). Thus, up to 663 assessments could be made.  $n=76$  persons assessed at least one indicator. More than 50% of the participants completed more than 60% of the possible assessments.

Most of the higher-ranking indicators are "well-known" HTA indicators, but supplementary indicators as "impact of technology on quality of care" or "budget for provision of treatment available" follow closely.



## Participants in the Inno-HTA project

### The Inno-HTA-Consortium:

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