**Supplementary file 1: Extraction table – Procedures of HTA institutions in defining relevant outcome measures**

|  **Item****Institute** | **Source** | **Scope****a-priori** | **Involvement external groups** | **Literature search Scope** | **Public-ation Scope** | **Description of outcome selection process****+ Ranking of outcomes** | **Patient relevant outcomes** | **Surrogates** | **MD Outcome predefinition** | **Particularities** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| [AAZ](http://www.aaz.hr/) (Agency for Quality and Accredi-tation in Health Care) Zagreb, Croatia | The Croatian Guideline for Health Technology Assessment Process and Reporting (2011) | Yes | Representatives Croatian Ministry of Health and Social Welfare, Croatian Institute for Health Insurance, hospitalsHealth professionals,Patients/caregivers groups, Manufacturers of health technology  | - | - | - | All direct health effects on patients | - | - | - |
| [AHTA](http://www.adelaide.edu.au/ahta/) (Adelaide Health Techno-logy Assessment) Adelaide, Australia | Response to E-Mail request (2013) | Yes | Experts in the field (from a Health Expert Standing Panel) , applicant, Protocol Advisory Sub-Committee (PASC) of the MSAC | Yes | Yes | Assessment group draft a list of outcomes measures, based on applications received | Patient-relevant outcomes (morbidity, mortality, quality of life, pain) together with surrogatesDepending on the topic (e.g. analgesic use, length of hospital stay, rate of device removal) | - | Device failure, device breaking, device slipping, migrating, screw loosening (secondary safety outcome,unless there is no safety implications to the patient, in which case, they may be considered technical efficacy) | refer to the series of publications by the National Health and Medical Research Council (NHMRC) |
| [AHTAPol](http://www.aotm.gov.pl/) (Agency for Health Techno-logy Assessment in Poland) Warsaw, Poland | Guidelines for conducting Health Technology Assessment (2009) | Yes | - | - | - | Endpoints should: -refer to the assessed disease and its course -reflect the most important aspects of the health problem and at the same time allow to detect the possible differences between the interventions compared -be essential for reasonable decision-taking (critical points of a given health problem) | Significant endpoints playing an important role in a given disease, i.e.: deaths, cases or recoveries, quality of life, adverse effects (divided into serious and non-serious) and/or medical events | If no clinical trials with patient-oriented clinically significant endpoints, surrogates can be assessed Present the relationship between the surrogates used and the clinically significant endpoints in the analysis | - | - |
| [AHRQ](http://effectivehealthcare.ahrq.gov/)(US Agency for Healthcare Research and Quality) | Methods Guide for Effectiveness and Comparative Effectiveness Reviews (2014) | Yes | Yes, in every stepkey stakeholder informants, technical experts, and patients | Yes | Yes, 4 weeks | Follow the principle of patient-centeredness, patient-centered perspectiveEmphasize on patient relevant outcomes than on intermediate outcomes | Outcomes important to patients and consumersPatient-reported outcomes: events or conditions the patient can feel and report on, such as quality of life, functional status, or fracturesHealth outcomes: morbidity, mortality, quality of life (p.26) |  |  | Interviews with patients, as well as studies of patients’ preferences, to identify pertinent clinical concerns that even expert health professionals may overlook |
| [ASERNIP-S](http://www.surgeons.org/racs/research-and-audit/asernip-s/asernip-s-publications) (Australian Safety and Efficacy Register of New Interven-tional Procedures –Surgical) East Melbourne, Australia | Response to E-Mail request (2013) | Yes | Expert clinicians and other stakeholders | Yes, review of MD, disease, patient-related issues | - | - | Directly relevant to patient health | Not rate technical outcomes very highly (such as the results of imaging) as these may not be directly transferrable to a clinical outcome of the patient | Specific adverse events, for example implantable device infection or battery replacement, device failureSame as with other topicsExample: device for renal nerve denervation for reducing blood pressureprimary outcome: reduction in stroke or other similar patient-relevant measure,in addition: other outcomes (such as blood pressure readings) that we would also use |  |
| [CADTH](http://www.cadth.ca/) (Canadian Agency for Drugs and Technologies in Health) Ottawa, Canada | Guidelines for the Economic Evaluation of Health Technologies: Canada (2006) | Yes | Clinical experts or health service managers | - | - | Outcome indicator that is most appropriate for the relevant condition, and most feasibleusing the relevant and valid outcomes of the highest importance for the health of patientsOutcomes are ranked in order ofimportance and relevance for the health of patients | Preferred that the outcome measure be a final outcome (e.g., life-years)Emphasis on using the relevant and valid outcomes of the highest importance for the health of patientsOr if final outcome is impossible, an important clinical outcome | Surrogate outcome should be validated, well established link with an important patient outcome | Diagnostic device: assessing the impacts that the sensitivity and specificity of the device have on follow-up care and health outcomes Evaluation of medical devices should focus on the entire episode of care rather than on only the technical performance of the device  | Outcome should be accurately measured and common to the alternatives being compared |
| [CDE](http://www.cde.org.tw/English/Pages/e-default.aspx) (Center for Drug Evaluation) Taipei, China | Response to E-Mail request (2013) | - | clinical experts | - | - | Always clinical relevant endpoints (not functional or structural improvements) | - | - | - | - |
| [CRD](http://www.york.ac.uk/inst/crd/) (Centre for Reviews and Disse-mination, part of the NIHR) York, England | CRD’s guidance for undertaking reviews in health care (2009) | Yes | Health care professionals,patient representatives,service users experts in research methods | - | - | Clearly defined set of relevant outcomesJustify each outcomeOften necessary to assess a number of different outcomes (or groups of outcomes), and also unintended outcomes, long-term outcomes and follow-up assessment is important | Success or failure of a therapeutic intervention assessed in terms of differences in mortality or morbidity Other outcomes of importance: quality of life and participants’ subjective experiences of pain or physical functioning | Only use interim or surrogate outcomes when no other outcomes availablePay attention to the validity and reliability of surrogate measures, and extent to which they can actually predict the primary outcome(s) of interest | - | Input from the advisory group and the findings from initial scoping searches and qualitative research may be helpful in deciding which outcomes to include |
| Response to E-Mail request (2013) | Yes | Clinical experts, patient representatives and statisticians | - | - | Never accept all the outcomesSpecification in a whole team of reviewersOutcomes with relevance to the decision problem | - | - | No difference in the process | - |
| [Danish Health and Medicines AuthorityCopenhagen, Denmark](http://sundhedsstyrelsen.dk/en)Before:[DACEHTA](http://sundhedsstyrelsen.dk/en/health/quality-and-guidelines/centre-for-health-technology-assessment) (Danish Centre for Health Technology Assessment) | Health Technology Assessment Handbook (2007) | Yes | Professional experts | Yes | - | Besides assessment of patient outcome, it may be relevant: intervention’s consequences for the patient’s family and/or caregiversCompound endpoints can be used in studies with fewer patientsRisk and safety side effects and adverse events must be identifiedRanking: primary + secondary endpoints | Mortality and/or morbidity, e.g. as survival rates, risk reductions, or elimination or reduction of symptomspatients’ physical and mental well-being, often designated as “health-related quality of life” (HRQOL)Clinical outcomes are complemented by endpoints that focus on changes in the patient’s self-assessed health status that occur as a result of a treatment | Can be measured if relevant | - | Same as NBoH |
| DAHTA@[DIMDI](http://www.dimdi.de/static/de/index.html) (Deutsche Agentur für Health Technology Assess-ment - Bewertung gesundheitsrelevanter Verfahren – Deutsches Institut für medizinische Dokumentation und Information) Cologne, Germany | Methodenmanual für „HTA Schnellverfahren“ UND Exemplarisches „Kurz-HTA“: Die Rolle der quantitativen Ultraschallverfahren zur Ermittlung des Risikos für osteoporotische Frakturen (2003) | Yes | Technological and Methodological experts (p. XI) | - | - | Qualitative analysis: Type and robustness of outcome and size of effect should be described | Considering patient-relevant outcomes | - | - | - |
| [DECIT-CGATS](http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto.cfm?idtxt=25516) – (Secretaria de Ciência, Tecnologia e Insumos Estratégicos, Departamento de Ciência e Tecnologia) Brasil | Methodological Guideline: Health Technology Assessment Appraisals (2009) | Yes | External consultant | - | - | Outcomes should be reviewed by specialist, to prove if appropriate | Consider the outcome of interest: * mortality,
* morbidity,
* adverse effects,
* incidence of complications,

quality of life, etc. | - | - | - |
| [G-BA](http://www.g-ba.de/) (Gemein-samer Bundes-ausschuss), Berlin, Germany | Response to E-Mail request (2013) | Yes | Yes | Yes, sources: recommendations from international level (i.e. guidance documents from regulatory agencies, scientific societies and patients representatives etc.) | - | - | Relevant endpoints such as mortality,morbidity, quality of life | - | No difference in the process on definition of outcome measures for MD | work in collaboration with IQWIGPredefinition primarily when assessments made in the case of „Erprobungsregelung 137e SGB V” |
| [GÖG/BIQG](http://www.goeg.at/) (Gesundheit Österreich GmbH) Vienna, Austria | Methodenhandbuch für Health Technology Assessment Version 1.2012 (2012) | Yes | Client and experts in this filed | Yes, pre-existing guidelines, systematic reviews, for adaption answers related to the question.  | - | Adverse events from interventions should be assessedClassify the outcomes into primary and secondary outcomes. The primary outcome is the parameter on which the result of a study is assessed | Outcomes with relevance for the patients, as mortality, morbidity and quality of life | Do not have a direct relevance for the patient, but are associated with patient relevant outcomes.Are physiological or biochemical measurements, which can be obtained easily | Examples:blood pressure cuffOutcome: measurement accuracy (mmHg), reliability of measurement chronic obstructive pulmonary disease (COPD) Screening with SpirometryOutcome: process of COPD (lung function, rate of exacerbation, mortality) | - |
| [HAS](http://www.has-sante.fr/portail/jcms/c_5443/english?cid=c_5443) (Haute Autorité de Santé), Saint-Denis La Plaine Cedex, France | Rapid Assessment Method for Assessing Medical and Surgical Procedures (2007) | - | - | - | - | Diagnostic or therapeutic benefit, based on safety, efficacy, contribution to the treatment strategy | Public health benefit, based on impact on the morbidity and mortality related to the disorder treated, on patients' quality of life, on the care system, on public health policies and programmes | - | - |  |
| [HIS](http://www.healthcareimprovementscotland.org/home.aspx) (Health Care Improvement Scotland) Edinburgh, Scotland | Process for the production of Health Technology Assessments (HTAs) (2011) | Yes | Experts: relevant methodological, clinical and patient/voluntary group(s) | Yes | - | Efficacy/Effectiveness: Change in overall/ condition-specific mortality, change in morbidity, change in quality of life Safety: Mortality directly related to the use of the intervention, morbidity directly related to the use of the interventionPatient issues: Compliance, acceptance, satisfaction, preferences  |  |  |  | Contribute to Cochrane Handbook |
| [HIQA](http://www.hiqa.ie/) (Health Information and Quality Authority) Cork, Irland | Guidelines for Evaluating the Clinical Effectiveness of Health Technologies in Ireland (2011) | Yes | - | - | - | Should be clearly defined and measurable, reliable and valid, relevant to the condition being treated and sensitive to changemeasures of effect, clearly relevant to the disease, condition, complaint or process of interestAdverse effects that are of clinical or economic importance must be reported. Both the severity and frequency of harms should be reported  | Measure changes in health and functional status that are of direct relevance to the patient and sensitive to changes in health statusClinical endpoints must be justified on the basis of a clear link between the disease process, technology and endpoint | Must have clear biological or medical rationale or have a strong or validated link to a final endpoint of interest | Diagnostic or screening test: sensitivity and specificity, should be measured in relation to a recognised reference test. The threshold for a positive test result should be clearly defined | Composite endpoints: should be clinically meaningful. All of the individual components of a composite must be reliable and valid endpoints |
| Guidelines for the EconomicEvaluation of Health Technologies in Ireland (2010) | Yes | - | - | - | - | - | If surrogate or intermediate outcome, there must be a well-established, validated link between this marker and an important patient outcome, extrapolation of changes in surrogate markers to clinically relevant effects | - | - |
| Response to E-Mail request (2013) | - | - | - | - | - | - | - | No difference in the process | Follow the Cochrane methodology |
| [IHE](http://www.ihe.ca/) (Institute of Health Economics) Edmonton, Canada | Response to E-Mail request (2013) | Yes | Expert advisory group: committee of clinical content experts and other stakeholders | Yes | - | - | - | - | Same procedure with outcomes specifically for MD | HTA team to agree on a final list of outcomes measures of interest to be assessed in the systematic review  |
| [IQWiG](https://www.iqwig.de/) (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen) Cologne, Germany | Allgemeine Methoden, Version 4.2 (2014) | Yes | patients, patient representatives and consumer organizations  | Yes | Yes, for 4 weeks | Outcomes are assessed when direct link between outcome and health conditionInstrument to assess the quality of life should be relevant for the clinical study and validated Assessment of harm emphasis is given on relevant adverse eventsPatients and patient representatives should be considered by defining the outcome (p.31)It can be useful to rate the outcomes Outcomes are assessed when direct link between outcome and health condition. | should be related to the patient, patient-relevant outcomes should be used (how a patient feels, how he can perceive his functions and activities or whether he survives), so mortality, morbidity and health-related quality of life | Surrogates should only take into account when validated with appropriate statistical methods within a confined patient population and comparable intervention | - | - |
|  | Allgemeine Methoden zur Bewertung von Verhältnissen zwischen Nutzen und Kosten (2009) | Yes | Competent bodies of the client, possibly involving external professionals or individual clients | Yes, the report plan includes (…) collecting and assessing this information | Yes | Endpoints are considered when describe specific changes of the health status reliably and directlyEndpoints are, for example, mortality, morbidity and health-related quality of life | How a patient feels, how he perceives his functions and activities or whether he survives | - | - | - |
|  | Response to E-Mail request (2013) | - | - | - | - | - | - | - | No MD specific endpoints, Assessment of the surrounding procedure in which the MD is used | - |
| [KCE](https://kce.fgov.be/) (Belgian Federal Health Care Knowledge Centre) Brussels, Belgium | KCE Process Book (2012) | Yes | Experts and stakeholders | Yes, pilot test inclusion criteria on a sample of articles | - | - | Using clinical outcomes when high-quality evidence regarding important outcomes is lacking | If only surrogates are available, list the surrogates as their measures of outcome | - | Process is based on GRADE |
| [LBI](http://hta.lbg.ac.at/page/homepage) (Ludwig Boltzmann Institut for Health Technology Assessment) Wien, Austria | (Externes) Manual Selbstverständnis und Arbeitsweise Teil 1 (2007) | Yes | Yes | - | - | - | Perspective of benefit analysis: Patient oriented like mortality, morbidity (harms and complications), quality of life, Intervention and disease-related expenses, patient satisfaction | - | - | - |
| (Internes) Manual Abläufe und Methoden Teil 2 (2007) | Yes | Clients, and as needed clinical, economical and methodological experts | Not obligatory | - | Basically outcomes should be relevant for patients | Outcomes patients can experience and feel  | Laboratory findings are not determining in pragmatic studies, but there are significant exceptions, when there is a strong causal relationship with aPatient relevant Outcome | - | - |
| [MaHTAS](http://medicaldev.moh.gov.my/v2/) (Health Technology Assessment Section, Ministry of Health Malaysia) Malaysia | Response to E-Mail request (2013) | Yes | Expert committee members (multidisciplinary experts in the related fields) | - | - | - | - | - | Same procedure, but also include non-RCT | References HTA 10[1] and Cochrane Handbook |
| [MSAC](http://www.msac.gov.au/) (Medical Services Advisory Committee) Canberra, Australia | Guidelines for the assessment of diagnostic technologies (2005) | Yes | Yes | Yes, existing systematic reviews and health technology assessment reports | - | Diagnostic tests: clinical effectiveness of a test is determined by the extent to which incorporating the test into clinical practice improves health outcomesEffectiveness of a test depends on whether the overall accuracy of testing is improved by including the index test, its impact on therapeutic decisions, and the effectiveness of the therapies selectedTest safety, accuracy, impact on management and health outcomes are all relevant to a review of test effectiveness | - | - | - | Exception: prognostic test: the information from the test may be used to provide benefits to the patient’s quality of life that are not directly related to treatment |
| Funding for new medical technologies and procedures: application and assessment guidelines (2005) | - | - | - | - | Safety and adverse events as three categories:common outcomesRare and/or severe outcomesOutcomes which are the consequence of misclassification or misdiagnosis | All-cause mortality; cause-specific mortality; changes in morbidity, side effects of treatment, including adverse reactions to drug therapies; disease specific outcomes, including disease specific quality of life measuresClinical outcomes on the basis of the disease being studied | Physiological variable, there is a statistical association between the surrogate outcome and the clinical outcome of interest or there is a biological and pathophysiological basis for believing that the surrogate outcome is a major determinant of the clinical outcome in the disease being studiedPresent evidence that it is an appropriate surrogate | - | Chosen outcome is often a clinician thinks is of primary concern, and that can be measured (this approach does not capture all the relevant outcomes)Factors that relate to an improved quality of life may be more relevant to the patient, though these may be hard to measure |
| [NBoH](http://www.sst.dk/) (National Board of Health) Copenhagen, Denmark | Health Technology Assessment Handbook (2007) | Yes | Professional experts | Yes | - | Besides assessment of patient outcome, it may be relevant: intervention’s consequences for the patient’s family and/or caregiversCompound endpoints can be used in studies with fewer patientsRisk and safety side effects and adverse events must be identifiedRanking: primary + secondary endpoints | Mortality and/or morbidity, e.g. as survival rates, risk reductions, or elimination or reduction of symptomsPatients’ physical and mental well-being, often designated as “health-related quality of life” (HRQOL)Clinical outcomes are complemented by endpoints that focus on changes in the patient’s self-assessed health status that occur as a result of a treatment | Can be measured if relevant |  | Same Handbook as DACEHTA |
| [NICE](http://www.nice.org.uk/) (National Institute for Health and Care Excellence) London, England | Guide to the methods of technology appraisal 2013 | Yes | Receive evidence from independent academic group, manufacturers, sponsors of technologies, national patient or carer groups, healthcare professional organisations, clinical specialists, commissioning experts and patient experts commissioning bodies | - | - | Health outcome(s) that will be relevant for the estimation of clinical effectivenessMeasure health benefits and adverse effects important to patients and/or their carersAll direct health effects, whether for patients or other people | Quantify an impact on survival or health-related quality of life that translates into quality adjusted life years (QALYs) for the evaluation of cost effectiveness | relationshipmust be provided together with an explanation of how the relationship isquantifiedwhen the use of 'final' clinicalend points is not possible | - | - |
|  | Methods for the development of NICE public health guidance(third edition) (2012) | Yes | Yes, stakeholders | Yes | Yes | Outcomes specified in terms of health or disease; an intermediate outcome could be a behaviour leading to the disease or to health improvementMatters to the population or individual (for example, mortality, morbidity, relapse rates, physical and social functioning, costs, health status)Valid and appropriateConsider adverse or unintended outcomes | - | How valid is self-report versus biologically validated measures? | - | - |
| Diagnostics Assessment Programme manual (2011) | Yes | Yes, expert advisers, sponsor of the notified technology, Manufacturers of alternative technologies | Yes | - | Relevant outcomes include any health outcomes resulting directly or indirectly from the use of the testInformational outcomes of value to the patient for the relief (or imposition) of anxiety or for personal planningBenefits/ harms resulting directly or indirectly from the use of the diagnostic tests (true and false results, longer-term outcomes, all costs stemming from the use of the test)Always included: following testusually included: treatments and tests undertaken based on the resultsIncluded if goof accuracy: downstream outcomes | - | Diagnostic test accuracy statistics are intermediate measures | - | - |
| [NHS QIS](http://www.nhshealthquality.org/nhsqis/CCC_FirstPage.jsp) (Quality Improvement Scotland) Edinburgh, England | SIGN 50 – ‘A Guideline developer’s handbook’ (2011) | Yes | Yes | - | - | Wide range of outcomes used in the literature, and if useful comparisons are to be made across studies it must be made clear which of these outcomes are importantObjective and directly related to patient, rather focusing entirely on clinical outcomes | - | - | - | Guideline Developing document |
| [SBU](http://www.sbu.se/en/) (Swedish Council on Technology Assessment in Health Care) Stockholm, Sweden | Response to E-Mail request (2013) | - | Yes, experts within the area of interest, patient associations or patient experts | - | - | Mortality and quality of life as primary outcomes and morbidity as secondary are considered | - | Try not to use surrogate measures | - | - |