ECTU Central Office SOP_HE_01:
Health Economic Evaluation Considerations

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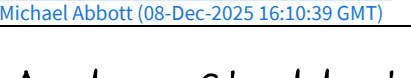
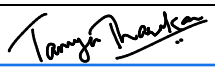
Andrew Stoddart Health Economics Team Lead	Approver	04-Dec-2025	 Andrew Stoddart (04-Dec-2025 17:50:03 GMT)
Tanya Tharakan QA Manager	QA Authorisation	19-Dec-2025	 Tanya Tharakan (19-Dec-2025 14:02:12 GMT)

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1.0	19-Jan-2026	Initial creation

1.0 PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to outline the typical requirements for an economic evaluation conducted alongside a clinical trial. It is intended as guidance only as exceptions are possible depending on the design/scope of the study. In particular, pilot/feasibility or similar work may not fit this framework, and fully modelled analyses can be highly variable in nature and purpose. Exceptions in other circumstance should be noted and justified in the Health Economics Analysis Plan (HEAP).

2.0 SCOPE

This SOP is applicable to all research staff directly involved in ECTU studies which include a health economic evaluation and all Health Economists based within ECTU irrespective of current project(s) . It covers responsibilities and procedure for the health economists on the team only, though information held here is also intended to provide important context to the wider research team. In particular it is important that non-health economic staff understand the roles and responsibilities of health economists at each stage of a study and when they may be expected to consult or otherwise interact with the health economics team.

Staff who are unfamiliar with health economics, particularly those working directly on trials with a health economic component, are encouraged to speak to the senior ECTU health economists (and/or the lead economist on their trial) to arrange an overview which can be tailored to their own study.

3.0 BACKGROUND

Health economic evaluation has increasingly been used to inform the regulatory and reimbursement decisions of government agencies throughout the industrialised world. A common vehicle for the conduct of economic evaluation is the randomised controlled trial (RCT). A key goal of a trial-based economic evaluation is to estimate relative cost-effectiveness of a new intervention typically compared to the existing and/or upcoming alternatives. Given that funding any new intervention in a healthcare system such as the NHS often incurs an opportunity cost of funding other services with the same resources, such economic evaluation provides an important analytical framework and generates important evidence to inform adoption decisions by policy bodies such as NICE. In order to undertake a rigorous trial-based economic evaluation, and ensure they provide useful evidence for such decisions, access to health economics expertise is essential at each stage of the study. This includes input from health economists during the design, conduct, analysis and reporting of the study.

4.0 RESPONSIBILITIES

Lead Health Economist	• Contribute to the design of the study • Provide oversight during the running of the study as relates to the health economic evaluation, particularly prior to the appointment of analytic staff. • Supervise the junior health economist • Review the appropriateness of planned health economic analyses • Review and contribute to reports of results and publications
Junior/Analytic Health Economist	• Provide day-to-day input on health economics for the trial/study • Draft the HEAP (supervised by the senior health economist) • Access trial data to provide data completeness/quality updates to trial meetings, as agreed with the trial team • Conduct (under supervision) the health economic analysis for the trial • Draft reports of results and publications

Variations in roles described above may be appropriate. For example, junior staff may undertake some more senior activities for career development reasons (agreed by line management and lead economist for the trial (these may be the same person)). Similarly, more senior economists may be undertaking some or all analyses in place of junior staff, potentially in addition to lead economist activities.

5.0 PROCEDURE

Definitions:

Health economic evaluation	Health economics is a branch of economics concerned with issues related to efficiency, effectiveness, value and behaviour in the production and consumption of health and healthcare. A health economic evaluation typically compares the costs and outcomes of a healthcare intervention against a suitable comparator to assist decision makers in maximising benefits from limited healthcare resources.
Budget Impact Analysis (BIA)	A form of analysis used to estimate the likely change in expenditure for a specific budget holder resulting from a decision to fund a new healthcare intervention or some other alteration in policy at an aggregate population level.
Cost-Benefit Analysis (CBA)	An economic evaluation that expresses all gains/benefits/outcomes and losses in common units (usually money), allowing a judgement to be made o whether, or to what extent, an intervention should be pursued.

Cost-Consequences Analysis (CCA)	A form of economic evaluation where the whole array of outcomes is presented alongside the costs, without any attempt to aggregate these into a single metric. This leaves decision makers to make a more subjective decision about the relative value of each intervention.
Cost-Effectiveness Analysis (CEA)	An economic evaluation where costs are measured in monetary terms and health outcomes are measured in natural units directly related to the intervention (e.g. life year saved, pain-free day).
Cost-Effectiveness Acceptability Curve (CEAC)	A graph summarising the impact of uncertainty on the result of an economic evaluation, expressed as the probability of cost-effectiveness at a range of threshold values of willingness to pay.
Consolidated Health Economic Evaluation Reporting Standards (CHEERS checklist)	A key health economic evaluation reporting standard, functioning as a checklist to ensure key methodological techniques and principals are stated.
Cost-Minimisation Analysis (CMA)	An economic evaluation where the outcomes of competing healthcare interventions are equivalent, so comparison is made on the basis of resource costs alone. The aim is to determine the lowest-cost way of achieving the same outcome.
Case Report Form (CRF)	A printed or electronic document designed to record all of the protocol required information to record for each study participant.
Cost-Utility Analysis (CUA)	A form of cost-effectiveness analysis where a health-preference measure (e.g. the EQ-5D-5L instrument) is repeatedly recorded in patients over time, to calculate a quality-adjusted life year (QALY).
Incremental Cost-Effectiveness Ratio (ICER)	Obtained by dividing the difference between the costs of the two interventions by the difference in the outcomes (i.e., the extra cost per extra unit of effect)
Willingness-to-Pay (WTP) threshold	The maximum amount that society is willing to pay for an additional quality-adjusted life-year (QALY)
Net Monetary Benefit (NMB)	A way to express measured costs and QALYs as a single monetary value at a given willingness to pay threshold (where NMB = QALY*WTP-Cost)
Health Economics Analysis Plan (HEAP)	Prospectively agreed analysis plan describing the presentation of results, base case, and secondary analysis.
Within-Trial Analysis	Analysis of the costs and effects of treatment alternatives limited to changes occurring within the duration of the follow-up time horizon of a trial.

Health Economic Modelling (aka: Decision Analytic Modelling)	A mathematical simulation of health economic outcomes used to address hypothetical scenarios typically not measurable by within-trial analyses. These are often built in MS Excel or R studio. Typical uses include: extrapolating beyond the trial follow-up, adjusting the study population, and facilitating further analyses.

5.1 Planning and Preparation of a Clinical Trial

Health economics input should be provided at each stage of the study, including during its design, conduct, analysis, and reporting.

The lead economist should provide oversight during the running of the study as relates to the health economic evaluation prior to the appointment of analytic staff. As analysis phase(s) approaches, the lead economist should identify an ECTU health economist to undertake the analysis and take over responsibility for the day-to-day running of the economic evaluation (supported and supervised by the lead economist as appropriate). The specific timing of this will vary depending on the study but should enable sufficient time to develop the HEAP prior to them becoming unblinded.

A number of important choices regarding the economic evaluation will have to be made by the lead economist (with appropriate input from the wider trial team and other ECTU colleagues) and included in the protocol including:

5.1.1 Form(s) of economic evaluation to be adopted: these typically include: Cost-Utility Analysis (CUA), Cost-Effectiveness Analysis (CEA), Cost-Consequence Analysis (CCA), Cost-Minimisation Analysis (CMA), Cost-Benefit Analysis (CBA) and/or Budget Impact Analysis (BIA). This choice will be guided by the scope and perspective of the study, the requirements of the decision maker/funder and the type of costs and outcomes data which are collected.

5.1.2 Measure(s) of any health economic outcome(s) (effect/consequence/Quality Adjusted Life Years (QALY). This decision will be made in consultation with colleagues in the wider study team. This is often different from the primary clinical outcome, with QALYs currently being preferred by NICE reference case criteria (NICE, 2022). In such cases, the choice and source of health utility scoring algorithm should be noted in the HEAP and any dissemination.

5.1.3 The perspective of analysis. This should be chosen to match the specifics of the decision makers the study intends to inform. In most trials, a National Health Service and Personal and Social Services (NHS/PSS) perspective is the preferred choice, selected to match the specifications of the NICE Reference Case (NICE, 2022). Multiple perspectives presented as sensitivity analyses are also common.

5.1.4 Type and range of resource use items to be measured. This choice will be informed by the perspective of the analysis and consultation with the wider study team.

5.1.5 Method of measurement of resource utilisation (e.g., the number of consultations at a specific clinic). Typical options include extraction of data from patient records, prospective data capture form, or use of data from a secondary data source, (e.g., Hospital Episode Statistics records). Care pathway assessments or activity-based costing exercises are also often used to estimate direct intervention costs. This decision should be made in consultation with the wider study team. Of note, it is often necessary to strike an appropriate balance between brevity (which effects completion rates) and depth of patient surveys.

5.1.6 Source of unit costs. Choice of price weights (e.g., the price applied to a given type of clinical consultation) should be informed by the perspective, In most cases this will be a UK NHS perspective, for which it is typical to use the annual PSSRU unit costs (Curtis et. al. 2023), and/or National Cost Collection (NHS England 2023) as first priority. Where possible these should be selected prior to unblinding and recorded in the HEAP. An appropriate base year for all costs should be established, recorded in the HEAP, and reported in all dissemination. This will usually be the latest financial year for which price weight reports are available at time of HEAP sign off and at least one patient provided data. Where unit costs derive from different years these should be adjusted to the using published health service inflation indices, with the associated indices noted alongside price weight reporting.

5.1.7 Method of collecting data relating to prescribed medicines. Data may be collected directly (from hospital notes and/or primary care) or through patient recall (i.e., a type of Case Report Form (CRF) that measures resource utilisation) or a similar approach. This decision will be made in consultation with the wider study team.

5.2 Analysis Approaches

5.2.1 Health Economic Analysis Plan

The study economist(s) will prepare a health economic analysis plan (HEAP) for the study This will be written and, following consultation, approved by the Lead Economist and Chief Investigator, prior to unblinding of the health economist, and ideally before database lock. The HEAP may be developed earlier than this time, particularly if sections of a model are being developed which are not reliant on trial data, however it is noted that price weights may require updating closer to analyses to account for new releases. In such circumstances, the anticipated sources of the price weights may be recorded instead, with a new version of the HEAP developed and signed off closer to final analysis.

The HEAP would usually be expected to reflect the following general principles for economic analysis:

5.2.1.1 An intention to treat approach should be used for the base case analysis.

5.2.1.2 The study health economist(s) should consistently address missing or censored data by making use of relevant statistical techniques to handle missing or censored cost and health-related quality of life data.

5.2.1.3 Uncertainty analysis should be conducted by applying the standard methods (e.g., bootstrapping for calculating cost-effectiveness acceptability curves (CEACs) and confidence intervals).

5.2.1.4 A time horizon that is appropriate to the analysis should be adopted.

5.2.1.5 Appropriate discount rates for long-term costs and benefits should be applied.

5.2.1.6 Where applied, appropriate cost-effectiveness threshold(s) should be adopted according to established guidelines (NICE, 2022).

5.3 Economic database

The study economist should request access to the database by contacting either the trial manager or the relevant Data management and programming team member. The study health economist(s) will manage the economic data in an appropriate software package (e.g., STATA, R) in accordance with University SOPs and in compliance with the UK GDPR. Where possible, the software package used for health economic analysis should also be pre-specified in the HEAP. For ECTU projects, the study health economist(s) will work in collaboration with ECTU's Data management and programming team, where applicable, to manage the data as specified above and resolve any coding issues or devise appropriate changes in response to issues arising early in each project. All the documentation, programs for analysis, and data should be stored in a separate Health Economics sub folder.

5.4 Monitor collection of health economics data

5.4.1 The study health economist(s) will work closely with the study team throughout the data collection period to ensure suitable data are collected and provide updates on data completeness for trial meetings as and when agreed with the Chief Investigator and statistician. Data collection forms (e.g., CRFs) will be assessed throughout the study period to monitor the quality of data and amend any forms or procedures if necessary.

5.4.2 Where possible the health economics team will access an intermediate trial data set, e.g. as analysis approaches. This permits detailed quality checks, may help identify data issues and allows analysis code to be developed that can be used for the final analysis. The adequacy of within-trial analysis (or the need for further modelling) should be explored.

5.5 After the data collection period - Economic analysis of data

5.5.1 Final validation checks should be completed, with any data queries referred to the Trial Manager / for investigation or resolution.

5.5.2 Costs and outcomes for each study participant will be calculated. Costs and utilities should (normally) be analysed using a net monetary benefit framework (at a patient or group level) to produce incremental cost-effectiveness ratios (ICERs), cost-effectiveness planes, and CEAC.

5.5.3 The base case (prospectively planned primary analysis) should be reported.

5.5.4 Due to the composite nature of total cost and QALY variables, even small amounts of missing data can result in a low or no complete cases (for example a patient missing a single entry for nurse consultations at a single time point would technically render total costs incomplete, even if all other data were available). As such imputation methodology is common in economic evaluations even when not needed/applied for clinical outcomes. The handling of any missing data should be recorded alongside final reporting, specifying the proportion of missing data across health economic variables, assumptions regarding patterns of missingness, and any approach(s) taken to impute missing data.

5.5.5 Supportive sensitivity analyses should be carried out to assess the impact of uncertainties on the base case findings (e.g. relevant sub-groups, regression model specification, observed vs. imputed data). Prospectively planned and post hoc analysis should be clearly delineated.

5.5.6 Decision-analytic modelling should be considered where within-trial analysis may be inadequate. Reasons modelling may not be required include convergence of treatment group costs or utilities during the within trial follow-up; clear dominance of one of the treatments; or uninformative (poor quality) trial data.

5.5.7 The key economic analysis documents (e.g., HEAP, analysis programs/scripts and final analysis report referenced in this SOP) will be added to the Trial Master File (TMF), Section 9 for Full service and Section 3 for Partial service, for archiving.

5.6 Report and publish

The results will be published in accordance with standard guidelines (e.g., NICE, 2022; Husereau et al., 2022). In general:

5.6.1 The results of the analyses will be presented in a format that is appropriate for the stakeholders and incorporated into the final study report.

5.6.2 Where possible, the economic evaluation results will aim to be published alongside or in compliment to clinical results, whether in a join paper, or a separate related paper published at a similar time, ideally cross referencing each other.

5.6.3 Effort will also be made to publish secondary analyses, particularly of a methodological nature, based on economic data collected as part of the study.

List of Terms/Abbreviations

CBA	Cost-benefit analysis
CCA	Cost-consequences analysis
CEA	Cost-effectiveness analysis
CEAC	Cost-effectiveness acceptability curve
CMA	Cost-minimisation analysis
CRF	Case Report Form
CSRI	Client Service Receipt Inventory
CUA	Cost-utility analysis
EVPI	Expected value of perfect information

FRS	Functional requirement specification
HEAP	Health Economics Analysis Plan
ICER	Incremental cost-effectiveness ratio
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMB	Net monetary benefit PSS Personal and Social Services
RCT	Randomised Controlled Trial R&IS Research & Impact Services
WTP	Willingness-to-Pay

6.0 RELEVANT DOCUMENTS AND REFERENCES

References:

1. National Institute for Health and Care Excellence. NICE Health Technology Evaluations: The Manual. NICE Process and Methods.; 2022.
2. Curtis L et al. Unit Costs of Health & Social Care 2023. Kent: Personal Social Services Research Unit 2023
3. NHS England. National Cost Collection Data Publication: National Schedule 2023/24.; 2023.
4. Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008

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