The Cost-Effectiveness Analysis (CEA) Registry

User Manual

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# About the CEA Registry

The Cost-Effectiveness Analysis (CEA) Registry is a comprehensive database containing detailed information on thousands of cost-utility analyses published from 1976 to the present. Health-related CEAs estimate the resources used (costs) and the health benefits achieved (effects) for an intervention compared to an alternative treatment strategy. The Registry focuses on a subset of CEAs, called cost-utility analyses (CUAs) that quantify health benefits in terms of Quality-Adjusted Life Years (QALYs) and/or Disability-Adjusted Life Years (DALYs). QALYs are a measure of years gained in perfect health while DALYs are a measure of lost years in perfect health.

The objectives of the Registry are to help decision makers identify society's best opportunities for targeting resources to improve health, to assist policymakers in healthcare resource allocation decisions, and to move the field towards the use of standard methodologies. The CEA Registry has been the source of data for hundreds of peer-reviewed studies. It has been used or cited in analyses performed by the Environmental Protection Agency, the Food and Drug Administration, the Institute of Medicine, and the Medicare Payment Assessment Commission. Additionally, the National Library of Medicine lists the CEA Registry as an important health economics resource.

The Center for the Evaluation of Value and Risk in Health (CEVR) at the Institute for Clinical Research and Health Policy Studies at Tufts Medical Center in Boston developed the CEA Registry, which can be found at <https://cear.tuftsmedicalcenter.org>.

# Database Structure

The CEA Registry has three main sections:

* **Methods**: contains one record for each article.
* **Ratios**: contains one or more ratio records for each article.
* **Utility or Disability Weight**s: contains zero or more utility or disability weight records for each article.

Figure 1 illustrates the Registry’s contents for a single article that reports information for *N* ratios and *N* utility weights.

**Figure 1. CEA Registry Hierarchical Structure**

**Methods Section**

**CEA Article**

**Ratio Section(s)**

**Ratio #1**

**Ratio #2**

**Ratio #N**

**…**

**Weight Section(s)**

**Weight #11**

**…**

**Weight #2**

**Weight #N**

# Data Collection Methodology

The published articles summarized in the Registry undergo a formalized review protocol (Figure 2). The analyses address a wide variety of diseases and treatments. Additionally, all articles measure health effects in terms of quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs). The QALY is a standard measure that accounts for quality of life (morbidity) and longevity (mortality). The DALY is a global standard for measuring burden of disease and expressed as the number of years lost due to ill health, disability or early death.

The first stage of data collection includes a literature search. The CEA Registry team searches PubMed, Scopus, and Embase for English-language articles using key search terms detailed in Table 1.

Next, the CEA Registry team screens the abstracts from identified articles to determine if the study contains an original cost-utility estimate. We exclude systematic reviews, editorials, or methodological articles, as well as cost-effectiveness analyses that do not use QALYs or DALYs to quantify health benefits.

Abstracts that meet the CEA Registry’s inclusion criteria are triaged for full data collection or partial data collection. Articles selected for full data collection are either 1) articles published in an academic journal with a journal impact factor >=2, 2) articles published in a journal that frequently publishes CEAs (Table 2), or 3) articles that use DALYs to quantify health benefits. Articles selected for partial review are published in journals with an impact factor < 2 and articles not published in one of our priority journals. At this stage, data is collected for partial review articles for the following variables: country, intervention description, intervention type, disease description, and standardized disease classifications (i.e. ICD-10, Global Burden of Disease Cause Levels).

Next, two readers with training in decision analysis and cost-effectiveness analysis independently review each article accepted for full data collection and record relevant information using a standardized set of forms and instructions. The two readers convene for a consensus audit to resolve any potential discrepancies. On occasion, a third reader is recruited to help settle disputed items. Data on over 40 variables are collected for each article. Refer to the glossary for a full description of each variable collected. The glossary is organized by the three major database sections: Methods, Ratios, and Utility Weights.

Finally, the CEA Registry team quality checks the data and performs a series of data cleaning steps. These include reviewing content for accuracy, converting foreign currency ratios into USD, and inflating ratios to the most current year. Once cleaned, the data are uploaded to the CEA Registry.

**Figure 2. Review Protocol**

Data is uploaded to the CEA Registry

Multiple databases searched with pre-defined keywords

* CEA Registry team screens abstracts for an original cost-utility estimate
* Data for partial review articles are collected

**Articles Rejected:**

* Reviews & Editorials
* Methodological articles
* Non-English language articles
* Health effects not measured in QALYs or DALYs
* Trained reviewers read and collect data on methodology, cost-effectiveness ratios, and utility and disability weights
* Reviewers consensus with a partner to resolve discrepancies

Data is cleaned and quality checked

**Table 1. CEA Registry Search Terms**

|  |
| --- |
| *Filter*: *English-only** Quality-adjusted life years [MeSH]
* Quality-Adjusted Life Year [Emtree]
* Quality-Adjusted Life Year [ti,ab]
* Quality-Adjusted Life Years [ti,ab]
* Quality-adjusted life year [ti,ab]
* Quality-adjusted life years [ti,ab]
* Quality-adjusted life-year [ti,ab]
* Quality-adjusted life-years [ti,ab]
* Quality adjusted life-year [ti,ab]
* Quality adjusted life-years [ti,ab]
* QALY [ti,ab]
* QALYs [ti,ab]
* Global Burden of Disease [MeSH]
* Disability-adjusted life year [Emtree]
* Disability-Adjusted Life Year [ti,ab]
* Disability-Adjusted Life Years [ti,ab]
* Disability-adjusted life year [ti,ab]
* Disability-adjusted life years [ti,ab]
* Disability-adjusted life-year [ti,ab]
* Disability-adjusted life-years [ti,ab]
* Disability adjusted life-year [ti,ab]
* Disability adjusted life-years [ti,ab]
* DALY [ti,ab]
* DALYs [ti,ab]
 |

**Table 2. Journals that Frequently Publish Health Economic Evaluations**

|  |
| --- |
| * Applied Health Economics and Health Policy
* BMC Health Services Research
* BMJ Open
* Clinical Drug Investigation
* Clinical Therapeutics
* ClinicoEconomics and Outcomes Research
* Cost Effectiveness and Resource Allocation
* Expert Review of Pharmacoeconomic & Outcomes Research
* The European Journal of Health Economics
* Human Vaccines & Immunotherapeutic
* Journal of Medical Economics PLoS One
* Pharmacoeconomic
* Vaccine
* Value in Health
 |

# Database Glossary

## Methods Form

### Article Information

1. **Article Accepted**:

**Yes**: At least one original $/QALY or $/DALY ratio is reported.

**No**: There are no original $/QALY or $/DALY ratios reported.

**Other reasons for rejection**:

* Non-English articles
* Systematic reviews
* Opinion/perspective/editorial/commentaries
* Methodological article
* Health Technology Assessments (HTAs)
* Study protocols
* Cost benefit analysis (CBA)
* $/LY only
* $/Cases
* Cost only
* QALY, DALY, or LY only
* Cases only
* Other non-ratio
* Other non-economic analysis
1. **Health Outcomes**:

**$/QALY**: Cost ($) per Quality-Adjusted Life Year (QALY). A comparative ratio that reports the cost associated with each additional QALY gained (i.e. 1 year in perfect health) when switching from a comparator to the intervention of interest.

**$/DALY**: Cost ($) per Disability-Adjusted Life Year (DALY). A comparative ratio that reports the cost associated with the loss of one year of full health. Alternatively, reports the cost associated with each additional DALY averted a comparative ratio (i.e. 1 year in imperfect health).

**$/QALY and $/DALY**: Authors report both $/QALY and $/DALY results for the base case analysis.

1. **Affiliation of Author(s)**: The primary association or membership during time of publication for all authors.

**University/Academic Organization**:Universities, institutes/centers, research organizations, or any other academic organizations, university affiliated hospitals (i.e. teaching hospitals and medical schools) are included.

**Government Organization**: Institutes, centers, or organizations that are part of a governmental body for a single country (e.g. NIH, CDC, VA appointments, etc.).

**Intergovernmental Organization**: Organizations composed primarily of multiple sovereign states (member states) or of other intergovernmental organizations (e.g. UNAIDS, United Nations, World Bank, UNICEF, GAVI Alliance, WHO, etc.).

**Foundation/Non-profit**: Not for profit and non-governmental organizations (e.g. Robert Wood Johnson Foundation). Note that this category includes foundations belonging to pharmaceutical companies (e.g. PhRMA Foundation, Medtronic Foundation, etc.) as long as they are nonprofit.

**Health Care Organization**: Health care providers (e.g. insurance companies, hospital, HMOs). This does not include university-affiliated hospitals (i.e. teaching hospitals and medical schools).

**Pharm. /Med Device Industry**:Industrial pharmaceutical companies, biotech companies, or medical device companies (e.g. Johnson and Johnson, Pfizer, Medtronic).

**Other**:Other than the choices above. Specify the name of the organization(s) in the text field that appears.

**None**:No affiliation information provided in the article.

1. **Sponsorship/Funding**:All funding sources that supported the study. This does not include funding sources or conflict of interests reported for individual authors.

**Note**: **See categorical descriptions for author affiliation(s).**

### Intervention

1. **Intervention Description**: A concise description of the primary intervention(s) evaluated in the base case analysis.
2. **Intervention types**: This reflects the primary intervention(s) evaluated in the base case analysis. A single study can analyze intervention(s) that pertain to multiple intervention categories (i.e. categories are not mutually exclusive).

**Care Delivery**: Provision of care, the activity of supplying or providing care in a particular setting, development of facility or distribution of personnel (e.g. implementing telemedicine/telehealth methods, a policy that changes the nurse-to-patient ratio, patient self-management program).

**Diagnostic**: Measures used to determine if and what type of disease is present; diagnostic procedure assumes patients are symptomatic or are suspected of having the diagnosable disease/condition (e.g. imaging, biopsy, PET scan, x-rays, in-vitro testing).

**Environmental (Available for DALY studies only until 2021)**: Interventions aimed at removal of contamination from water bodies, soil or other areas to improve human health (e.g. measures to address pollution or to protect water supplies). Interventions to inhibit or limit environmental threats to health (e.g. provision of bed nets to reduce the risk of arthropod-vector infections).

**Health Education or Behavior**: Interventions designed to educate individuals on behaviors that promote, maintain or restore health (e.g. smoking cessation and prevention program, cognitive behavioral therapy). Interventions to treat an individual’s psychological development in and interaction with their social environment (e.g. structured counseling, motivational enhancement, psychotherapy, cognitive behavioral therapy).

**Immunization**:Vaccinations intended to prevent infectious disease (e.g. flu vaccine, HPV vaccine)

**Legislation/Regulation**: Taxes and regulatory measures that influence access to certain foods and other consumed substances (e.g. alcohol taxation, taxation of soft drinks, and controls on the use of tobacco).

**Maternal/Neonatal/Reproductive Care (Available for DALY studies only until 2021)**: Interventions to address maternal care received at antenatal visits, at delivery, and for neonates (e.g. skilled attendance at birth, screening for pre-eclampsia, care during childbirth, and screening for congenital diseases). This includes interventions such as family planning and contraceptives.

**Medical Device**: Instrument, apparatus, implant, in vitro reagent, or similar article used to diagnose, prevent, or treat diseases or other conditions. This can range from simple tongue depressors and bedpans to complex programmable pacemakers and laser surgical devices.

**Medical Procedure**: Non-surgical, non-diagnostic procedures; an activity directed at or performed on an individual with the object of improving health, or treating disease or injury (e.g. angiogram, blood donation, mole removal, casting or splinting of broken bones).

**Pharmaceutical**: Drug or biotech products used for medical treatment or prevention that is not an immunization (e.g. Lovastatin, Herceptin)

**Screening**: Measures that detect disease, or test for risk factors, before it is symptomatic (e.g. breast cancer screening – mammogram).

**Surgical**:Treatments or procedures characterized by incision or cutting intended to investigate and/or treat a pathological condition, disease, or injury, or to help improve bodily function or appearance (e.g. transplantation, appendectomy).

**None**: Do-nothing strategies. This does not indicate that the study did not specify an intervention.

**Other**: Any intervention not described above (e.g. injury prevention, food safety).

1. **Data Source for Intervention’s Efficacy/Effectiveness**: This indicates the type of data source(s) utilized in the study to measure the primary intervention(s) effectiveness of efficacy (i.e. health metrics).

**Randomized clinical trial(s)**: Quantitative, comparative, controlled experiments in which investigators study two or more interventions in a series of individuals who receive them in random order. This indicates that data was retrieved from a single source.

**Meta-analysis/systemic review of clinical trials**: This indicates that data was retrieved from multiple clinical trials.

**Observational study**: Experiments in which the investigator cannot control the assignment of treatment to subjects (e.g. case control studies, cohort studies). Investigators examine predetermined treatments/interventions/policies to assess health outcomes in groups or participants according to a research plan or protocol. This indicates that data was retrieved from a single source.

**Meta-analysis/systematic review of observational studies**: This indicates that data was retrieved from multiple observation studies.

**Expert Opinion**: This indicates that data was retrieved from experts in the field (e.g. clinicians) and not from a specific study of participants.

**Other**: Any data sources not described above.

**Not Stated/None:** The study does not provide sufficient information to determine the data sources used to measure the primary intervention's efficacy or effectiveness.

1. **Prevention Stage**:This reflects the prevention type of the primary intervention(s) evaluated in the study. Prevention stage definitions are retrieved from the Encyclopedia of Public Health.

**Primary**: Interventions aimed at altering behavioral and/or clinical risk factors *before* a targeted condition has evolved among persons who are asymptomatic (e.g. immunizations/vaccines, promotion of safety equipment to avoid car injury, anti-smoking campaigns to prevent lung cancer, and to reduce the risk of acquiring a pathogen).

**Secondary**:Interventions aimed at identifying persons who may have begun, but have not shown apparent clinical signs and symptoms of the illness (for screening purpose) or have not formally diagnosed (for diagnostic purpose) (e.g. population-level screening to identify disease or diagnostic procedures). This does not include diagnostic procedures used for cancer staging where the patient has already been diagnosed and the intervention is used to determine severity.

**Tertiary**:Interventions aimed at preventing progression of a targeted disease among persons with a clinical diagnosis to alleviate symptoms and reduce complications after initial clinical diagnosis (e.g. chemotherapy, rehabilitation, screening for further complications of a diagnosed disease).

### Study Context

1. **Country of Study**:The geographical perspective of the economic evaluation or the country to which the study’s results are applied. The perspective of the study relates to practice patterns and unit costs for medical care/interventions/other societal costs that are included in the economic evaluation. For example, if the country is UK, then the CE ratio represents the expected costs and QALYs or DALYs if the intervention were adopted in UK. This is irrespective of what country individual data (e.g. clinical trial data) are derived from. This does not include the author’s country origin, which may or may not be the country study context.
2. **Region**: World Bank defined regions that correspond with the country.
3. **Scope of the Intervention**: Defined as the population aggregation level at which the intervention is targeted. The intervention can target the local, regional/provincial, or national level.

### Costs and Health Effects

1. **Time horizon(s)**: The time horizon is the length of time by which resource use and health effects are measured. Only base-case time horizons are captured.
2. **Base case time horizon**:The primary time horizon in the main/base case analysis.
* **Lifetime**: Costs and health effects are measured/persists for the remainder of the population cohort’s life.
* **Years**:Time horizon was explicitly reported in years as the unit.
* **Months**:Time horizon was explicitly reported in months as the unit.
* **Weeks**: Time horizon was explicitly reported in weeks as the unit.
* **Not Stated/None**: The main/base case time horizon was unclear and unable to be determined by the reviewer.
1. **Additional base case time horizon(s)**: The study conducted the base case analysis from multiple time horizons (e.g. both 5 years analysis and lifetime analysis).
2. **Spillover**:Spillover effects measure informal caregiving by family, friends, or volunteers in terms of time devoted to caring for the patient, time lost that could be spent doing other activities, and associated costs.
3. **Costs included**

**Health care costs**: All costs associated directly with treatment (e.g., vaccine costs, drug cost, physician visit cost, follow-up visit cost, hospitalization cost, outpatient cost). These include:

* **Treatment costs/direct medical costs**: Direct cost of treatment
* **Out-of-pocket medical costs**: Costs incurred by the patient

**Implementation costs**: All costs associated with setting up of the intervention. These include:

* **Personnel salaries**: Salaries associated with staff involved in the intervention
* **Infrastructure**:Costs associated with setup of the intervention and its infrastructure
* **Administrative costs**: Expenses incurred in controlling, directing and managing an organization/intervention
* **Other**: Other costs related to the implementation of the intervention (e.g. training, surveillance, and advertising).

**Non-health care costs**: All costs that are unrelated to treatment and not incurred by or specific to the health care sector. These include:

* **Patient time**: Patient time lost due to illness or travel
* **Caregiver time**:Costs associated withtime and care provided by caregiver
* **Transportation**: Costs associated with travel to health care facility
* **Productivity gains**: Costs associated with on-job productivity losses or presentism (i.e. illnesses and medical problems that undermine job performance in the workforce).
* **Income loss**: Income lost due tolost days of work
* **Consumption costs**: Costs associated with average annual expenditures that each person is expected to spend on food, alcoholic beverages, housing, transportation, entertainment, education, personal insurance, etc., excluding annual health care expenditures.
* **Other**:Other costs unrelated to treatment.

**Other Costs/Sectors**: All social opportunity costs, costs incurred by the community as a whole. These include:

* **Public health**: Costs related to public health resources (e.g., shelters, public services, wellness programs, and food provisions).
* **Legal/criminal justice**: Costs related to arrests, convictions, days in jail/prison
* **Education**: Costs related to primary, secondary and higher education school
* **Housing**: Costs related to public and private housing, property value
* **Environment**: Costs related to environmental impact of the intervention
* **Other**:Other societal costs not listed above.

**Cost components were not reported**: The study does not provide sufficient information to determine the type of costs included.

1. **Discounting**:Money available or spent now is more valuable than money available or spent in the future because of opportunity costs. Discounting quantifies this time preference and places all economic costs in terms of the present value of money. When health effects can be valued in monetary terms over a period of time, then both health effects and associated costs can be discounted. The following discounting options are given:

**Yes**: The study explicitly reported the discount rate for costs and/or QALYs/DALYs.

**No**: The study explicitly stated that they did not discount costs and/or QALYs/DALYs.

**Not Applicable**: Discounting for costs and/or QALYs/DALYs was not appropriate to the study (i.e. the time horizon was too short to apply discounting). Discounting is not applicable if and only if the time horizon is equal to or less than one year.

**Could not be determined**: The study does not provide sufficient information to determine if discounting for costs and/or QALYs/DALYs was done.

1. **Currency of the CE Ratio**: The currency the authors adopted or converted to in the study. If the currency and year are not given, we assume the currency used in the analysis is denominated in currency of the country in which the analysis represents and valued 2 years prior to article publication.
2. **Cost-effectiveness** **threshold**:The incremental cost-effectiveness ratio (ICER) that the study authors used to assess whether the intervention is cost-effective.

**$US**:The threshold was valued in US dollars.

* **US $50K**: $50,000/QALY or $50,000/DALY
* **US $100K**: $100,000/QALY or $100,000/DALY
* **US $150**: $150,000/QALY or $150,000/DALY
* **Range**: A range in US$ is provided as the threshold.
* **Other US Value**: The study reported a single value threshold in US dollars that is not listed above.

**Other Non-US**: The threshold was valued in any currency other than US dollars.

**GDP-Based**: The per capita domestic product (GDP) of the study country was used to assess the intervention’s cost-effectiveness.

* **1-3xGDP**: 1 to 3 times the GDP per capita
* **>3xGDP**: Greater than 3 times the GDP per capita

**Threshold was not reported**:The study does not provide a threshold in which they compared their results to.

1. **Impact Inventory Table**:An Impact Inventory is intended to identify and enumerate all of the consequences relating to the choice of intervention or strategy, both within the healthcare sector and in other sectors. The following options are given:

**Yes**: The study includes an impact inventory table.

**No**: The study does not include an impact inventory table.

### Parameter Uncertainty

1. **Parameter/Uncertainty**:There can be considerable uncertainty regarding the parameters used to measure costs and health effects in a CEA. Different types of sensitivity analyses evaluate the impact of parameter uncertainty on the cost-effectiveness ratio. These analyses can help identify the parameters that are most likely to influence the cost-effectiveness results when varied across reasonable ranges. Studies may perform deterministic and/or probabilistic sensitivity analyses:

**Deterministic**:There are two types of deterministic sensitivity analyses:

1. **One-way (univariate)**: refers to varying input parameters one at a time, usually from high to low values relative to their base-case values. ICERs corresponding to these (high/low) ranges are reported, and often displayed with a tornado diagram.
2. **Multi-way (multivariate)**: refers to varying more than one parameter at the same time and then reporting the range in resulting ICER values.

**Probabilistic**:Characterizes uncertainty in ALL parameters simultaneously, explicating reflecting the likelihood that parameters take on particular values. When models are used for the CEA, then this is done by assigning probability distributions around the mean input values. For CEAs conducted along RCTs, bootstrapping methods are commonly used to estimate probabilistic uncertainty. These analyses show the probability that the intervention will be cost-effective at a range of willingness to pay thresholds.

**Performed but type not specified**:Authors mentioned that sensitivity analysis was conducted but did not state the type of analysis.

**None/Not stated**: No information provided; cannot determine if a sensitivity analysis was conducted; authors explicitly stated that they did not conduct sensitivity analyses.

1. **Subgroup Analyses (Heterogeneity)**:Cost-effectiveness results can differ by “subgroups.” Subgroups are created using observable factors to stratify the results of a CEA. These are most commonly characteristics of a target patient population (e.g., whether patients have co-morbid conditions, treatment or outcome preferences, individual outcome risks, etc.). However, they can also be characteristics of study factors unrelated to the patient’s characteristics (geographical location, type of hospital where treatment is delivered, characteristics of the provider who delivers an intervention.)
	1. **Was subgroup analysis based on observable clinical or socio-demographic characteristics?**
* **Yes**: Examples include age, gender, race, severity of disease, etc.
* **No**: Intervention or setting specific characteristics are ***not*** considered to be clinical or socio-demographic characteristics. Examples include country, urban/rural hospital, and surgeon with greater than or less than 10 years of experience.
1. **Graphical Representation of Uncertainty**:Graphs related to the sensitivity analyses that were provided in either the main article or any supplementary materials.

**Tornado diagram**: A sensitivity analysis that provides a graphical representation of the degree to which the result is sensitive to the specified independent variables.

**Cost-Effectiveness plane/scatterplot**: A sensitivity analysis that consists of a scatter plot of simulated ICERs on the CEA plane to illustrate uncertainty by mapping out the location and spread of the points around the expected results.

**Cost-Effectiveness acceptability curve**: The cost-effectiveness acceptability curve (CEAC) is a method for summarizing the uncertainty in estimates of cost-effectiveness. The CEAC, derived from the joint distribution of costs and effects, illustrates the (Bayesian) probability that the data are consistent with a true cost-effectiveness ratio falling below a specified ceiling ratio.

### Disease Classification

**The disease was not specified**: This generally indicates that the target population(s) are healthy individuals and the primary intervention(s) do not target a specific disease (e.g. policies to enact network of bike lanes).

**Primary Disease**: The primary disease or condition the intervention is targeting.

* **ICD Chapter and Sub-Chapter**
* **GBD Tiers**
* **Disease Description**: Concise disease name.

**Secondary Disease(s)**: Other diseases or conditions the primary intervention is targeting. This also includes diseases or conditions the target population has been diagnosed with if it differs from the intervention's targeted disease.

### Equity & Ethical Considerations

Health equity includes removing obstacles to good health such as poverty, discrimination, environment, access to housing/transportation, etc. Traditional CEAs are generally focused on maximizing population health benefits. However, when designing and prioritizing interventions, decision makers are often concerned about reducing unfair health inequality, improving total population health, and or the nature and size of any tradeoffs between the two.

Note: A retrospective study was completed in 2022 to identify articles published from 2016-2020 that included a novel element of value. The study used article text searches to find words/phrases that indicated the use of a novel element and was confirmed by an individual review (find more here). This data was added to the registry in 2022. See descriptions below for more details.

1. **Did the authors discuss ethical issues or distributional effects related to the implementation of the intervention(s)?**

**Yes**: Article discusses healthy equity issues surrounding the implementation of the primary intervention

**No**: Articles makes no mention of health equity.

Note: This data are available for articles published in 2021 and onward. For articles published from 2016-2020, an article text search was used using phrases “equity weight”, “extended cost effectiveness”, and “distributional cost effectiveness” to identify articles that discuss equity.

1. **Did the study explicitly quantify equity effects of health interventions?** These analyses may be the base case, or included as a sensitivity analysis.

**Yes**:If yes, select the type(s):

* **Distributional CEA**: An extension of CEAs that compares the distribution of health effects and health opportunity costs of different interventions by subgroup.
* **Extended CEA**: An extension of CEAs that assesses the distribution of both health effects and protection against illness-related impoverishment.
* **Equity weighting**: Assesses trade-offs between equity and efficacy by quantifying how much concern for equity is required to choose cost-ineffective options that improve equity and cost-effective options that harm equity. Equity weights for health benefits can be applied to people with different characteristics or using an “equity parameter” that quantifies the degree of concern for reducing health inequity versus improving total health.
* **Other:** Other methods for quantifying equity effects that are not described above.

**No**: The authors discussed health equity but did not conduct a formal analysis.

1. **Novel elements of value**: Novel elements broaden the view of what constitutes value in health care, and are generally included in the societal perspective. They address limitations related to traditional CEAs that only capture a subset of benefits generated by an intervention.

**Yes**:If yes, the following novel elements are reported:

* **Real option-value**: captures the value of future benefits generated from extended life-years due to treatment
	+ Note: This data are available for articles published in 2021 and onward. For articles published from 2016-2020, an article text search was used using the phrase “real option value” to identify real option value.
* **Value of hope**: captures a premium on therapies that offer the possibility of substantial benefit for a subset of recipients, particularly patients with a serious disease
* **Severity of disease**: captures a greater value placed by individuals for health gains when the initial state of health is inferior
	+ Note: This data are available for articles published in 2021 and onward. For articles published from 2016-2020, an article text search was used using the phrase “severity of disease” to identify severity of disease.
* **Fear of contagion and disease**: captures value of fearing the spread of disease
* **Insurance value (financial and health)**: captures the value placed by individuals of a treatment being available to them through a health plan, even if they never utilize it
* **Value of Knowing**: captures the benefit of reducing uncertainty, such as whether treatment will provide benefits or diagnosis of diseases
* **Other:** Other than the choices above.
	+ Note: This data are available for articles published in 2021 and onward. For articles published from 2016-2020, an article text search was used using the phrase “adherence improving”, “improvement in adherence”, “genericization”, “future drug price”, “life cycle pricing”, “future cohorts” to identify other novel elements of value.

**No:** The authors discussed health equity but did not conduct a formal analysis.

### Reporting Transparency and Quality

1. **CHEERS Guideline Checklist: A task force through ISPOR developed The** Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist in order to provide recommendations that optimize the reporting of health economic evaluations.

**Yes**: The authors include a completed CHEERS checklist in either the main paper or supplementary materials.

**No**: The authors did not provide a completed CHEERS checklist.

1. **Overall quality of the analysis**:A subjective rating score by reviewers from 1 (lowest quality) to 7 (highest quality). Scores should be aligned with these 7 principles of economic evaluations:

|  |  |
| --- | --- |
| **1** | Methods and results were communicated clearly and transparently to enable easy interpretation |
| **2** | Time horizon was of sufficient length & discount rate appropriate |
| **3** | Detailed disaggregated cost and QALY information was provided & recalculated ICER was correct (or did not differ by more than 10%).  |
| **4** | Comprehensive characterization of uncertainty (sensitivity analyses are present and comprehensive) |
| **5** | Explicit reporting of utility weights (includes utility weight value and estimation method) |
| **6** | Subgroup analysis performed |
| **7** | Non-health effects and/or spillover effects were quantified |

1. **Comments**: Any general, notable comments regarding the methods of analysis employed, or information that was not captured elsewhere.

## Ratios Form

### Target Population

1. **Disease classification**: Health status of the target population

**Primary Disease**: The primary disease or condition the intervention is targeting.

* **The ICD Chapter and Sub-Chapter**
* **GBD Tiers**
* **Disease Description**: Concise disease name.

**Secondary Disease(s)**: Other diseases or conditions the target population has been diagnosed.

**Disease was not specified**: This includes generally healthy population.

1. **Sex**: Sex of the target population.
2. **Age**: Age of the target population.

**At least**: Target population is greater than or equal to the age value. If no specific age was given, but reader can deduce that it was an adult population, specify the age to be at least 18 years.

**No more than**: Target population is less than or equal to the age value. If no specific age was given, but reader can deduce that it was a pediatric population, specify the age to be no more than 17 years. If the target population was infants, specify the age to be no more than 1 year. If the target population was newborns, specify the age to be no more than 2 months.

**Range**: Target population was a given range. Specify both minimum and maximum age values in the text fields that appear.

**Single age**: The target population is a singular age value.

1. **Country**: Country of the target population
2. **Other characteristics**: Other detailed characteristics of the recipients of the primary intervention and comparator (e.g. co-morbidities) not included in health status that are pertinent to intervention and/or comparator.

### Intervention

1. **Intervention Modality**:

**Single**: Treatment was a single intervention.

**Multiple/Combined**: A treatment is given in conjunction with another treatment (e.g. physical activity *and* changes to diet to prevent obesity)

**Sequential/Step**: The treatment is given conducted one intervention after another (e.g. cancer patients' first receiving chemotherapy *before* undergoing surgery to remove a tumor).

1. **Intervention Phrase**:A concise description of the primary intervention evaluated in the study.
2. **Intervention Description**:Additional relevant details pertaining to the primary intervention evaluated in the study.
3. **Intervention Type(s)**: Classify the intervention type specific to the individual ratio you are reporting.

### Comparator

1. **Comparator Modality**:

**Note**: See categorizations and descriptions for Intervention Modality above.

1. **Comparator Type(s)**:

**Note**: See categorizations and descriptions for intervention type(s) in the Methods information section.

### Ratio

1. **Ratio Type**:

**Cost/QALY**: Ratio being reported is measured as the cost per quality-adjusted life year gained.

**Cost/DALY**: Ratio being reported is measured as the cost per disability-adjusted life year averted.

1. **$/QALY or $/DALY from article**:The incremental cost-effectiveness ratio (ICER) reported by the authors in the original article. Reports are only original, base-case $/QALYs or $/DALY.
2. **Ratio Value**:

**Per patient**: The ratio being reported represents costs and health effects at the patient level.

**Entire population**: The ratio being reported represents costs and health effects of a particular population.

1. **$/QALY or $/DALY from Reviewer**:Reviewer recalculated ratio based on the disaggregated costs and QALYs gained or DALYs averted reported within the study.
2. **Ratio Quadrant**:The quadrant describes where the ratio is located in the cost-effectiveness plane (Figure 4):

**Quadrant I**: The intervention increases costs and worsens health (i.e. costs more and provides less QALYs gained than the comparator). Ratios in this quadrant are sometimes referred to as “dominated”. ICERS should be a negative value.

**Note**: Ratios that cost more (intervention more costly) and have no impact on heath (QALYs=0) fall into quadrant I.

**Quadrant II**: The intervention increases costs and improves health (i.e. costs more and provides more QALYs gained than the comparator).

**Quadrant III**: The intervention saves money and worsens health (i.e. costs less and provides less QALYs gained than the comparator)

**Quadrant IV**: The intervention both saves money and improves health (i.e. costs less provides more QALYs gained than the comparator). Ratios in quadrant IV are sometimes referred to as "dominant" or “cost-saving”. ICERS should be a negative value.

**Note**: Ratios that save money (intervention less costly) and have no impact on health (QALYs=0) fall into quadrant IV.

|  |
| --- |
| **Figure 4**: **Four Quadrants of Cost-Effectiveness Plane****QALY****QUADRANT IV ‘Southeast’**Less costly, More QALYs(Dominant)**QUADRANT III ‘Southwest’**Less costly,Less QALYs**QUADRANT I ‘Northwest’**More costly, Less QALYs(Dominated)**QUADRANT II ‘Northeast’**More costly, More QALYs**Cost** |
|  |

1. **Extended Dominance**:Whether the reported ratios/interventions is eliminated by extended dominance (sometimes referred to as weak dominance). Extended dominance is when one intervention is ruled out from the analysis because it is less effective and is associated with a less attractive cost-effectiveness ratio than an available alternate intervention.
2. **Incremental analyses**: Indicates whether the study provided enough data (i.e. disaggregated cost and QALYs) for the reader to recalculate the ICER.

**Not Reported**: Incremental analyses were not reported (Note: does ***not*** include when author say that a ratio is cost-saving/dominant, dominated, or extendedly/weakly dominated. If authors state any of these, count the ICER as being reported by the author.)

**Correct**: The incremental analysis was conducted and calculated correctly (i.e. the percent error between the reported ICER and the recalculated ICER is <10%). This also includes ratios where the study did not report an ICER, but reported the intervention as dominated, cost-saving, or extendedly dominated, and the reader was able to recalculate the ICER to determine how to the authors came to their conclusion.

**Incorrect**: The incremental analysis was conducted but calculated incorrectly (i.e. the percent error between the reported ICER and the recalculated ICER is >=10%).

**Not enough data to recalculate**: The study did not provide sufficient data to repeat the ICER calculation.

1. **Cost per Life Year**: If available, reports corresponding $/Life-year results
2. **Other types of CEA Ratios**: If available, reports ICERs measured in other units of effectiveness (e.g. $/case saved, $/case averted).
3. **Budget Impact**: The budget impact is an estimated aggregate cost for the actual (rather than a hypothetical) population.
4. **Perspective**:The viewpoint from which costs and QALYs were calculated.

**As Judged by Author**:The primary or most comprehensive perspective used in the study as stated by the author

* **Health Care Payer**: Includes only monetary costs incurred by a health care payer (e.g. Medicare/Medicaid, British National Health service, an HMO or private health care plan).
* **Health Care Sector**: Unlike the Health Care Payer perspective, Health Care Sector accounts for all monetary costs of health care regardless of who bears the cost (i.e., includes out-of-pocket costs).
* **Limited Societal**:Also known as “Modified perspective”, this analysis accounts for costs not unique or specific to the health care sector. The perspective is designated “limited societal” if at least one non-health care cost is included (e.g. unpaid caregiver time, productivity impacts, patient time). It does not include spillover costs to other sectors besides health care, such as education.
* **Societal**:The Societal perspective is broader than limited societal perspective. It represents the overall public interest by including social opportunity costs where the use of resources results in the loss of opportunity to use those funds (or resources) for other purposes.
* **Other**:Authors report a perspective other than those listed above.
* **Not Stated/Could Not Be Determined**:Authors did not provide sufficient information to determine type of costs or benefits evaluated.

**As Judged by Reviewer**:The primary or most comprehensive perspective used in the study as judged by the reviewer based on costs included. For example, a study might state ‘societal perspective’ but fail to include non-medical costs and other sector costs. In this case, the perspective as judged by the author would be “limited societal” but as judged by the reviewer would be ‘health care payer’.

* **Health Care Payer**: The analysis only included treatment costs/direct-medical costs.
* **Health Care Sector**:The analysis only included health care costs and must include out-of-pocket medical costs.
* **Limited Societal**:The analysis included any non-health care costs.
* **Societal**: The analysis included any sector costs.
* **Other**:Authors report a perspective other than those listed above.
* **Not Stated/Could Not Be Determined**:Authors did not provide sufficient information to determine type of costs or benefits evaluated.
1. **Comments**:Any general, notable comments regarding the ratio, or information that was not captured elsewhere.

## Utility or Disability Weights Form

Base utility or disability values are a value between 0 and 1 that represent a specific health state or disease. One is “perfect health” and zero is “death”. Values closer to 1 represent less severe health states, while values closer to 0 represent more severe health states.

**Utility or disability weights we do *not* collect**:

* 0 for death
* 1 for perfect health
* Age specific base utilities (no additional health characteristics specified)
* In randomized controlled trials, we are only interested in the baseline utilities (pre-treatment) that represent patients with a specific clinical condition.

### Utility or Disability Weight

1. **Health State**:Description of the utility weight for the specific health state/condition.
2. **Utility or Disability Value:**

**Utility or Disability Value**:The weight is a regular, base utility value.

**Disutility**: Small decreases to a base utility value. They are sometimes referred to as a “decrement”; these represent the loss of utility from a base utility weight.

**Incremental Gain**: Small increases to a base utility value. Positive increases to a base utility weight will often represent a treatment benefit or positive gain in patient quality of life that would increase an individual’s baseline health-related quality of life.

### Sensitivity Analyses

1. **Sensitivity Analyses**: If available, reports the confidence interval, range, standard deviation, and/or the standard error of the utility used in the sensitivity analyses

### Measurement Instrument/Estimation Methodology

1. **Measures**:If available, reports the estimation instrument/method as described in the study.

**Measurement instrument/method not stated**: The study does not describe or mention the methodology used to estimate the utility value.

**Direct Measures:** Measures participants’ preferences under conditions of uncertainty.

* **Standard Gamble**: Reflects the patient's willingness to accept a certain risk of death in order to avoid the given health state.
* **Time Trade-Off**: Reflects the remaining life expectancy that a patient may be prepared to give-up in order to avoid remaining in a sub-perfect health state.
* **Person Trade-Off:** Tradeoff is expressed as a ratio of the number of people who live in perfect health that is equivalent in value to the number of people who would live with a specified condition.
* **Visual Analog Scale (of EQ-5D VAS)**: Reflects the patient's perception of the intensity or frequency of the health state, measured on a continuing scale.
* **Other:** Other direct elicitation methods that are not described above (e.g. magnitude estimation, expert opinion).

**Indirect/Generic Measures**: Typically obtained indirectly by asking patients to fill in a quality of life questionnaire and then converting the results to a utility using population values.Performed by applying a utility algorithm to a generic preference-based measure such as EQ-5D or HUI.

* **EQ-5D-5L/3L/Y**: Developed by the EuroQoL Group, the EQ-5D is a generic questionnaire commonly used in clinical trials and economic evaluations. It assesses health status in terms of five dimensions– mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.
* **SF-6D/12D/36D**: A preference based measure similar to the EQ-5D questionnaire, but includes 8 total dimensions of health– physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health.
* **Quality of Well-Being (QWB)**: Another generic preference based questionnaire of health status that measures the patient's overall well-being over the previous 3 days using 4 domains: mobility, physical activities, social activities, and symptom/problem complexes.
* **Health Utility Index (HUI)**: A rating scale questionnaire mapped onto 2 classification systems, HUI-2 and HUI-3.
* **Other:** Other direct elicitation methods that are not described above.

### Data Source(s)

1. **Source Type**

**Primary Data**: Data are derived from author’s collection of utility weights generated specifically for this study

**Secondary/Published Source(s)**: Data are derived from another source other than this study

* **PubMed ID**
* **GBD Study Year**

**Not Stated/Could not be determined**: The study does not provide sufficient information to determine the data source of the utility weights reported.

1. **Comments**:Any general, notable comments regarding the utility weight, or information that was not captured elsewhere.