MCDA.drugis.org tutorials

# Background

The Multicriteria Decision Analysis (MCDA) process is a quantitative approach to benefit-risk analysis which is useful whenever consensus needs to be reached about the comparative value of several alternatives, e.g. medical treatments. Without such an approach reaching consensus is often difficult, because different people may attach different importance to treatments' effects. Such preferential differences become an obstacle to meaningful and constructive discussion if they are left unquantified. In contrast, if someone has reached a different conclusion than you but has quantified their preferences, you can immediately see what underlies their conclusion, and how large the difference to your preferences is. This yields common, concrete grounds for discussion and makes clear where disagreements originate.

Examples of situations where MCDA can be of great value are the regulatory process, HTA agencies and even doctors and patients that have specific requirements for a treatment.

For more theoretical background on MCDA benefit-risk analysis, see https://mcda.drugis.org/manual.html#mcda-benefit-risk-analysis

Actions to perform are indicated with **👉**

Tips and reminders are indicated with **💡**

Theoretical background and explanations are indicated with **🎓**

# Tutorial: Manual data entry

This tutorial guides you through the process of creating a workspace with data from an existing report, so that you can use it to create an effects table and perform benefit-risk analyses. Performing these analyses is covered in later tutorials.

Our example (Table 1) is a simplified version of the effects table for lixisenatide as shown in the [EMA Guidance document for critical assessment reports](https://www.ema.europa.eu/documents/template-form/day-80-assessment-report-overview-d120-loq-template-guidance-rev-0718_en.doc) (see page 72). Since lixisenatide is a treatment for type 2 diabetes we choose the common primary endpoint (HbA1c change) and a common adverse event (Nausea) as our criteria.

Table 1 - Simplified effects table for lixisenatide

| **Effect** | **Description** | **U** | **LIX** | **PBO** | **Uncertainties /**  **Strength of evidence** | **Reference** |
| --- | --- | --- | --- | --- | --- | --- |
| ***Favourable Effects*** | | | | | | |
| HbA1c | Mean change in HbA1c from baseline | % | -0.83  (-0.91, -0.75) | -0.39  (-0.51, -0.28) | **Unc:** The effect of lixisenatide was more pronounced in Asian patients compared to Caucasian patients. The lower effect in Caucasians is partly explained by a large placebo effect especially in some geographical regions. | Pooled data from EFC6014 and EFC10743 |
| -0.82  (-0.91, -0.73) | -0.10  (-0.24, 0.04) |  | EFC6015 |
| ***Unfavourable Effects*** | | | | | | |
| Nausea | Incidence of nausea | % | 26.9 | 7.3 |  | pooled data from all phase 2/3 controlled studies |

## Sign in to MCDA.drugis.org

**👉** Open your browser and navigate to [https://mcda.drugis.org](https://mcda.drugis.org/). Use your Google account to sign in. You will be redirected to your personal homepage, containing your previously created workspaces, both finished and unfinished (if any).

**💡** At any stage during the data entry process you can press the ‘Save’ button at the bottom of the page to store the current state so that you can continue later. You can navigate to your home page by pressing the mcda.drugis.org link on the menu bar at the top-left of the screen.

## Create a new workspace

**👉** Press the ‘Create workspace’ button, select the option ‘Manual input’ and press the ‘Create button’. This leads to the first step of the manual entry process.

**🎓** A workspace contains the clinical efficacy and safety data that you have entered for a particular benefit-risk assessment. Within a workspace you can build effect tables and perform quantitative benefit-risk analyses. From your homepage, workspaces are created through a dialog opened by clicking the ‘Create workspace’ button. Existing workspaces are opened by clicking on the name of that workspace, or navigating to their URL directly via a link or bookmark.

## Enter general information

**👉** Enter a descriptive title, for example “lixisenatide data entry tutorial” in the ‘Workspace title’ field at the top of the page. In the ‘Therapeutic context’ field enter sufficient information to give context for your effects table, e.g.: “Assessment of lixisenatide for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in patients not adequately controlled on oral antidiabetics.”

## Enable favorability

**👉** Because our example groups the criteria into favourable and unfavourable effects, check the ‘Use favorability’ checkbox below the ‘Criteria’ heading. Now we can proceed to define the criteria (i.e. the outcome variables used to evaluate the different treatments).

**🎓** Criteria are outcome variables used to evaluate therapeutic strategies. A criterion has a name (a short identifier) a description (defining what was measured, e.g. for “HbA1c” this could be “mean change from baseline” or “median absolute value”), and optionally the unit in which it is measured. Associated with each criterion are one or more data sources that measure this outcome for different treatments. During drug regulation assessments, criteria may also be classified as favourable or unfavourable, with favourable criteria being ones where a new treatment under consideration outperforms the status quo.

## Add the HbA1c favourable effect

**👉** Click ‘Add Criterion’ button.

**🎓** The upper section of the criterion creation dialog (title, description, unit and favorability) describes the criterion, and the following section concerns the characteristics of the data used to measure it (further explained in Box x). Creating a criterion implicitly also involves specification of a data source. Further data sources can be added later (see Step 6).

**👉** Fill out the criterion dialog as shown in Figure x (you can copy/paste the reference for the first data source and uncertainties texts from Table 1).

**🎓** Assessments often include data from multiple studies that measured a specific criterion, especially in the case of favorable effects. In the next step we will show how to add more data sources to a criterion. For more details on how data of a source are supplied see the Appendix.

## Add a second data source for HbA1c

**👉** On the HbA1c criterion, click the ‘Add data source’ button. In the dialog, specify the reference “EFC6015” and leave the other fields unchanged (the data from this study are reported in the same format as step 5). Then click ‘Add.’ Now there should be a second row in the data sources for the criterion.

## Add nausea as an unfavourable effect

**👉** Click the ‘Add criterion’ button, fill in the dialog as specified in Figure x and click ‘Add’ (note that favourability is now ‘Not favorable’ and that the units are left blank). The reference for the data source is “Pooled data from all phase 2/3 controlled studies.” There are no further data sources for this criterion.

## Add lixisenatide and placebo as alternatives

**👉** Under the ‘Alternatives’ header, fill in “lixisenatide” in the text box and click the ‘Add alternative’ button to the right, or hit the enter key. Now do the same for “placebo”.

**💡** You can press the ‘Save’ button at any time to save your work in progress.

## Proceed to data entry

**👉** Click the ‘Enter data’ button. Take a moment to inspect the effects table that the system has generated based on the information you entered. If you spot any errors or inconsistencies you can always click the ‘Back’ button to correct them.

⚠️ To prevent inconsistencies changing the characteristics of a criterion’s data source will delete any effects or distribution data you entered for that data source.

## Enter data

**👉** Click on the red text saying ‘missing or invalid input’ for the ‘Pooled data’ data source of HbA1c. Fill out the dialog as shown in Figure x, and click anywhere on the page outside of the dialog to close it.

The values you entered should now be shown in the table (Figure x).

**👉** Proceed to fill out the rest of the data for HbA1c with the values from Table 1.

**👉** Similarly, fill out the cells for Nausea, with the values from Table 1, selecting ‘Percentage’ as the input parameters.

Your final effects table should look like Figure x

## Finalize entry

You have now finished preparing your effects table for analysis.

**👉** Click ‘Done’ and you will go to the overview page of your newly-created workspace.

# Appendix: Data source characteristics

The data for a specific characteristic can be supplied in several ways, depending both on the way in which they were measured, and the interests of the supplier of the data and the analyst. The main consequence of these differences for the MCDA process is whether Stochastic Multicriteria Acceptability Analysis (SMAA) is possible, because stochastic analysis requires that the distributions for the effects are either known or can be derived.

Distributions can be entered either as source data (e.g. event rates out of a certain sample size) from which the distribution will be derived, or by entering the distribution manually (e.g. a Normal distribution with certain mean and standard deviation).

Dichotomous data concern measurements where a proportion of patients either did or did not have a certain characteristic (e.g. reported a headache).

Continuous data concern value measurements (e.g. blood sugar level).

In case of continuous data, you can choose which point estimate parameter is the one of interest: either the mean, median or cumulative probability.