# Database of treatment effects user guide

The following is a manual for how to use the database of treatment effects. The first section explains how the spreadsheet works. The second section explains some the measures of effect that the spreadsheet can display. The third section discusses one particular nuance around confidence intervals for numbers needed to treat.

1. How to use the database

Before using the database you are advised to read the introductory sheet and for more information on how the evidence in the database was generated consult the evidence review as part of NICE's multimorbidity guideline. Having read the introductory sheet, click on the database worksheet:
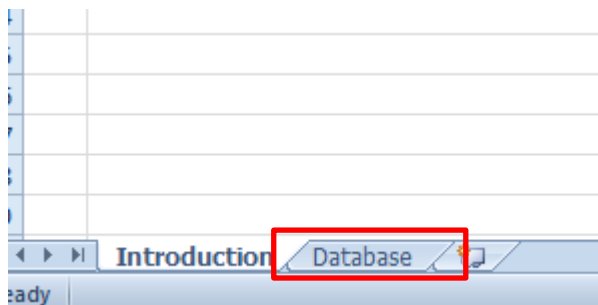
1) Click on the filter icon in cell BD2.
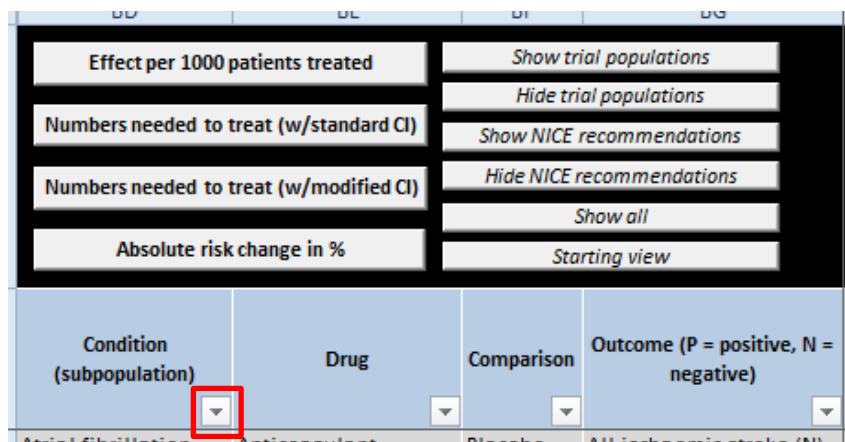
2) Uncheck select all and select the conditions you are interested in.
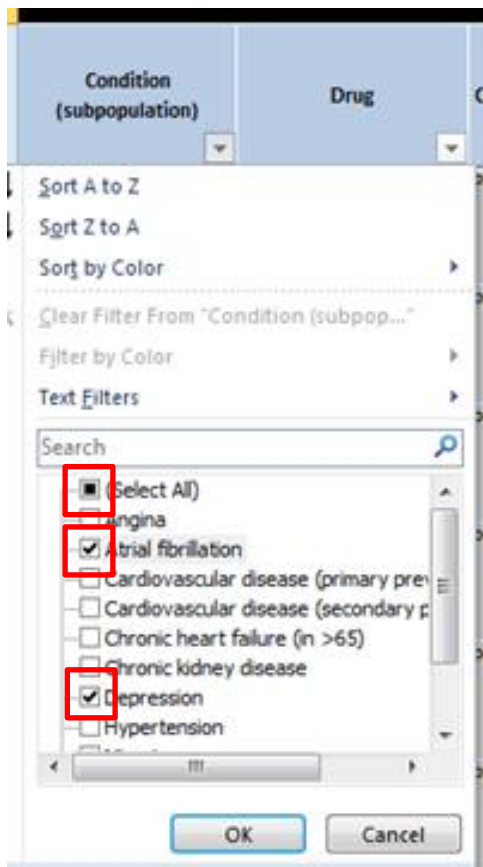
Columns BE to BG will now display the drugs and outcomes for which data is available for your selected condition.

Condition (subpopulation)	Drug	Comparison	Outcome (P = positive, N = negative)
Atrial fibrillation	Anticoagulant	Placebo	All ischaemic stroke (N)
Atrial fibrillation	Anticoagulant	Placebo	All cause mortality (N)
Depression	Antidepressants	Placebo	Relapse (N)

3) Now choose and click on one of the four options for data presentation in row 1: "effect per 1000 patients treated", "numbers needed to treat (with standard CI)", "numbers needed to treat (with modified CI)" or "absolute risk change in %".

Clicking on any one of the four options will display the basic data from clinical trials in columns BH to BK: the median duration of the clinical trials reporting that outcome, the percentage of patients in the control (placebo) group that experienced that outcome during the clinical trials, an annualised version of that risk, and the risk ratio when comparing the drug specified in column BE with placebo as well as the 95% confidence intervals for that risk ratio.

	Median duration of studies (years)	Patients experiencing outcome in control group/baseline ri	Annualised baseline risk	Relative risk with treatment vs placebo (95% CI)	
come (P = positive, N = negative)					
ischaemic stroke (N)	1	3.7%	3.70%	0.33 (0.53 to 0.21)	
cause mortality (N)	2	147/1475 (9.97%)	4.99%	0.78 (0.98 to 0.62)	
apse (N)	1	599/1222 (49.02%)	49.02%	0.46 (0.52 to 0.4)	

The next two columns after BK will depend on the option selected, section 2 below discusses these measures in detail.

If you wish to see all four options simultaneously click the "show all" button.

4) For more detail on the trials that this data was extracted from and the NICE recommendations regarding these drug-condition combinations, click on the "show trial populations" or "show NICE recommendations".

This additional information will appear in column BT (NICE recommendations) and BU (trial populations).

2. Measures of effect

a) Effect per 1000 patients treated

   i.   The measure of absolute effect in this option is a verbal statement about what would happen if you were to treat 1000 patients with a drug as opposed to with placebo

   ii.   For example, people on oral anticoagulation have one third the risk of ischaemic stroke compared to those on placebo. In the trials, the baseline risk of stroke was 3.7% per year.

Risk with placebo = 3.7% over one year

If 1000 patients were treated with placebo = 37 experience the outcome

Risk with drug = 1.2% over one year

If 1000 patients were treated with drug = 12 experience outcome

25 fewer people with atrial fibrillation have an ischaemic stroke if treated with oral anticoagulation instead of placebo for one year

b) **Numbers needed to treat (with standard or modified confidence intervals – see below for discussion)**

    i.   The measure of absolute effect in this option is the number of patients you would need to treat with the drug instead of the comparator in order to expect one patient to avoid a harmful or get a beneficial outcome.

    ii.   For example, people on oral anticoagulation have one third the risk of ischaemic stroke compared to those on placebo. In the trials, the baseline risk of stroke was 3.7% per year.

Risk with placebo = 3.7% over one year

If 1000 patients were treated with placebo = 37 experience the outcome

Risk with drug = 1.2% over one year

If 1000 patients were treated with drug 25 avoid the outcome. The number needed to treat with oral anticoagulation instead of placebo for one year to prevent one ischaemic stroke is therefore 1000/25 = 40

c) **Absolute risk change in %**

    i.   The measure of absolute effect in this option is the actual change in the % of people experiencing the outcome caused by the treatment compared to the comparator.

    ii.   For example, people on oral anticoagulation have one third the risk of ischaemic stroke compared to those on placebo. In the trials, the baseline risk of stroke was 3.7% per year:

Risk with placebo = 3.7% over one year

Risk with drug = 1.2% over one year

Absolute risk reduction = 3.7%-1.2% = 2.5% for one year's treatment

3. Confidence intervals for numbers needed to treat

The database has two options for numbers needed to treat, either with standard or modified confidence intervals. Confidence intervals applied to numbers needed to treat can be difficult to interpret. If the confidence intervals for the risk ratio of a treatment cross one then the concept of numbers needed to treat shifts considerably. A risk ratio lower than one suggests a drug reduces the likelihood of an outcome whereas a risk ratio of greater than one suggests a drug increases the likelihood of an outcome.

Consider the following example, a drug designed to reduce stroke has a risk ratio point estimate for drug vs placebo of 0.95 with confidence intervals from 0.85-1.05. If the control group risk is 10%, the point estimate number needed to treat would be 200 (100 per 1000 have a stroke with placebo, 95 per 1000 have a stroke with the drug, therefore with the drug 5 less people have a stroke, 1000/5=200). In other words if you treated 200 people you would expect to prevent one stroke. The lower confidence interval is still below one and therefore the lower confidence interval NNT is still

intuitive. In this case the lower confidence interval NNT would be 67, if our estimate of the risk ratio was actually as low as 0.85 we would only need to treat 67 people to prevent one stroke.

At 1.05, the upper CI is greater than one which means if we treated people with the drug, we would expect <u>more</u> people to have a stroke than if we treated people with placebo. An NNT calculation results in 200 again (100 per 1000 have a stroke with placebo, 105 per 1000 have a stroke with the drug, therefore with the drug 5 <u>more</u> people have a stroke, 1000/5=2) however the 200 now refers to the number of people we would need to "treat" with the drug to <u>cause</u> a stroke.

We have provided two options for dealing with this situation. The two options both present NNT with standard confidence intervals if the confidence intervals do not cross one. However their approach differs when the confidence intervals do cross one.

a) Standard confidence intervals
   a. Calculation and estimates are done per default calculations
   b. Information is provided qualified by verbal descriptors
   c. In the example above the measure would be "Need to treat 200 people to prevent one stroke (from treating 200 people to cause one to treating 67 people to prevent one)
   d. *Advantages = allows comparison of the degree of imprecision between two different drugs*
   e. *Disadvantages = not intuitive, requires an understanding of NNT calculations*
b) Modified confidence intervals
   a. Calculation and estimates are done per default calculations
   b. However confidence intervals are replaced by a statement that "confidence intervals crossed the line of no effect"
   c. In the example above the measure would be "Need to treat 200 people to prevent one stroke (confidence intervals crossed the line of no effect)"
   d. *Advantages = more intuitive, does not detract from main component of information, the point estimate*
   e. *Disadvantages = masks variable degrees of imprecision, some drugs will only just cross the line of no effect and others will cross it to a much greater degree and both will be marked as crossing the line of no effect*

The two options are included because there was mixed feedback from the guideline development group about which would be preferable. Including both options enables the user to access the data at the level that best suits their understanding and purpose.