A Data Visualisation Example: HiSCR clinical trial

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In a phase III study with patients suffering from hidradenitis suppurativa, an active drug was compared to placebo. There were 200 subjects in each group and the endpoint was the hidradenitis suppurativa clinical response (HiSCR) which is a binary endpoint. This endpoint is based on three continuous components:

* number of abscess
* number of draining fistulae
* number of inflammatory nodules

A patient reaches a HiSCR response, if all of the following three conditions are met, when the baseline data are compared to the follow-up data (at week 16):

* at least a 50% decrease in (AN) count; AN count is defined as the sum of the number of abscess and the number of inflammatory nodules
* no increase in the number of abscesses
* no increase in the number of draining fistulae

The aim of the study was to compare the two treatment arms in regards to HiSCR response.

## **Question**

Since there is still some debate around the HiSCR definition, the challenge is to **visualise the impact of changing the definition of HiSCR** on the results.

## **Approach to answer the question**

I focused on classical endpoints for binary outcomes such as the Risk Ratio (RR) and the Odds Ratio (OR) and looked at how those might change for varying HiSCR definitions.

In **Figure 1** I show this for the inverse RR (1/RR), which measures the RR of active drug vs placebo for not developing a HiSCR.

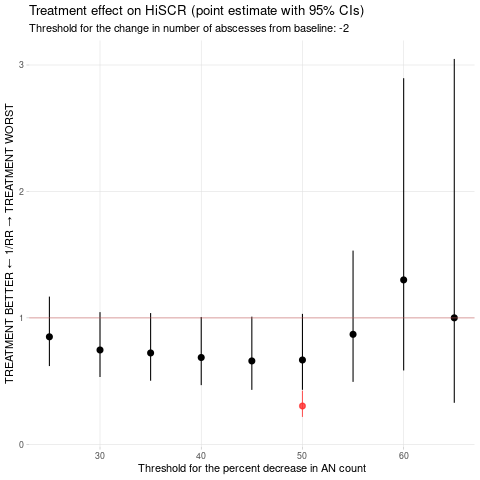
## **Impact of the analysis**

By requiring a negative threshold for the change in number of abscesses from baseline we observe a general loss of effect (**Figure 1**), which also tends to worsen for thresholds for percent decreases in AN count below 50%, or above 60%, with a dramatical increase in uncertainty (95% CIs) in the latter case due to increasing data sparsity.

As the threshold for change in number of abscesses approaches zero (the standard definition) the treatment effect increases (becomes more beneficial) with no additional improvement for further positive threshold values.

Basically, the optimal result in terms of 1/RR point estimation, and width of 95% CIs, is obtained exactly by application of the standard HiSCR definition which is further validation of this score.

Similar results are obtained for the OR and by varying other HiSCR definitions. Explore the accompanying [**web-app**](https://bonorico.shinyapps.io/HiSCR/?_ga=2.91645274.1120831357.1651571388-1024467400.1644592220) for further inspection, also providing contingency tabulation for every scenario.



**Figure 1**: Change in 1/RR by varying percent decrease in AN count and number of abscesses from baseline. The horizontal line at y = 1 is the null treatment effect. The red dot is the result under the standard HiSCR definition.

## **Reproducibility**

Find the code to reproduce the web-app and the HiSCR data [here](https://github.com/bonorico/HiSCR).