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Big Data & Economy's project

Sulfonylureas and sitagliptin for the treatment of type 2 diabetes (T2DM) in terms of number of discontinuations

Master 2 EBDS « Econométrie Big Data et Statistiques »

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INTRODUCTION

T2DM is a serious and common chronic disease resulting from a complex inheritance-environment interaction along with other risk factors such as obesity and sedentary lifestyle. T2DM and its complications constitute a major worldwide public health problem, affecting almost all populations in both developed and developing countries with high rates of diabetes-related morbidity and mortality. Several treatment options are available for T2DM, among them: **Sulfonylureas and Sitagliptin.**

Sulfonylureas are second line agents widely used in the treatment of T2DM patients who are not severely obese. The major acute adverse reaction of sulfonylureas is higher rate of hypoglycaemia, especially in older adults with impaired renal function, hepatic dysfunction, and those with poor oral intake, or alcohol abuse, or caloric restriction and so on.

Sitagliptin is a Dipeptidyl peptidase-4 (DPP-4) inhibitor available for use in Japan for the past few years, and now used in many T2DM patients with low insulin secretory capacity, whose efficacy and safety have been confirmed in many clinical practices.

We want then to evaluate sulfonylureas and sitagliptin for the treatment of T2DM in terms of number of discontinuations.

1- What should we conduct and why?

In order to evaluate sulfonylureas and sitagliptin for the treatment of T2DM in terms of number of discontinuations, we should combine a systematic literature review and meta analysis. Systematic literature review aims to identify, select and do a critical review studies on sulfonylureas and sitagliptin. Meta-analysis is a statistical analysis that combines the results of multiple scientific studies.

This combination is beneficial in several ways, it aims:

- To combine results from different studies in one unique analysis
  - To improve the statistical power
  - To improve the precision of the estimation
  - To conduct subgroup analyses
  - To increase the generalisability of the results
  - To identify the studies to conduct to answer a question
- To compare treatments not already compared in a clinical trial

2- Study question

To evaluate sulfonylureas and sitagliptin for the treatment of T2DM in terms of number of discontinuations, we will use the « PICOS » to formulate our study question :

Population : Type 2 diabetes (T2DM)

Intervention : Sulfonylureas and sitagliptin

Comparator : Placebo

Outcome : Number of treatment discontinuations

Study Design : Randomised controlled trials

3- Search strategy using Pubmed

According to the National Library of Medicine, PubMed is a service of the US National Library of Medicine® that: Provides free access to MEDLINE®, the NLM® database of indexed citations and abstracts to medical, nursing, dental, veterinary, health care, and preclinical sciences journal articles. Includes additional selected life sciences journals not in MEDLINE.

The search strategy is the follow :

#	Topic	Search Terms	Hits
#1	Disease	**(type 2 diabetes mellitus[Text Word]) OR (Diabetes Mellitus, Type II[MeSH Terms]) OR (type 2 diabetes mellitus[Text Word]) OR (diabetes mellitus, type 2[MeSH Terms])**	167 827
#2		**(sulfonylureas[Text Word]) OR (sulfonylureas[Text Word])**	3 627

#3	Study	**randomized controlled trial[PT]) OR (randomized[TiAB]) OR (placebo[TiAB]) OR (randomly[TiAB]) OR (trial[TiAB])(randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract]) OR (placebo[Title/Abstract]) OR (randomly[Title/Abstract]) OR (trial[Title/Abstract])**	1 449 477
#4	Combination	**#1 AND #2 AND #3**	441
#5	Restictions	**(Animals[MeSH Terms]) NOT (Humans[MeSH Terms])**	4 923 609
#6	Combination	**#4 NOT #5**	441

4- Next steps

After the search strategy, the next steps are :

- Evaluating the search results
- Study selection
- Screening
- Data extraction
- Critical appraisal
- Analysis

5- Analysis for sitagliptin vs placebo and for sulfonylureas vs placebo

- Sitagliptin vs placebo

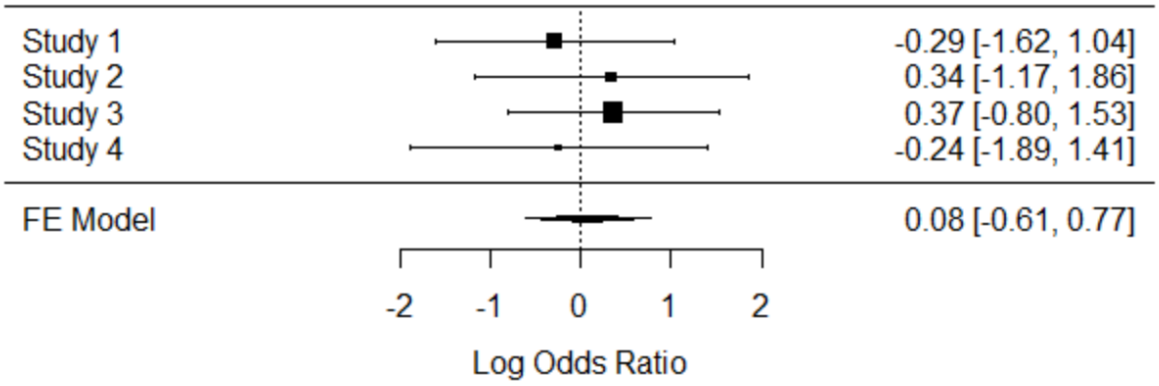
R_Code

```r
install.packages("metafor")
library(metafor)

##### Sitagliptin vs Placebo

data1 <- data.frame(n1=c(4, 3, 7, 2), n2=c(5, 4, 5, 5),
                    N1=c(253, 110, 176, 178), N2=c(238, 205, 179, 352))
mod1 <- rma.uni(ai=n1, ci=n2, n1i=N1, n2i=N2,
                measure="OR",
                data=data1,
                method = "FE",
                weighted = TRUE,
                level = 95)
forest(mod1)
```

Forest Plot



The 95% confidence interval is the range of values in which we are 95% certain of finding the true value. In the case of "Sitagliptin vs. placebo", we notice that all the confidence intervals of the studies contain the value 0, so the results of the studies did not observe a statistically significant difference between the treatment and control groups.

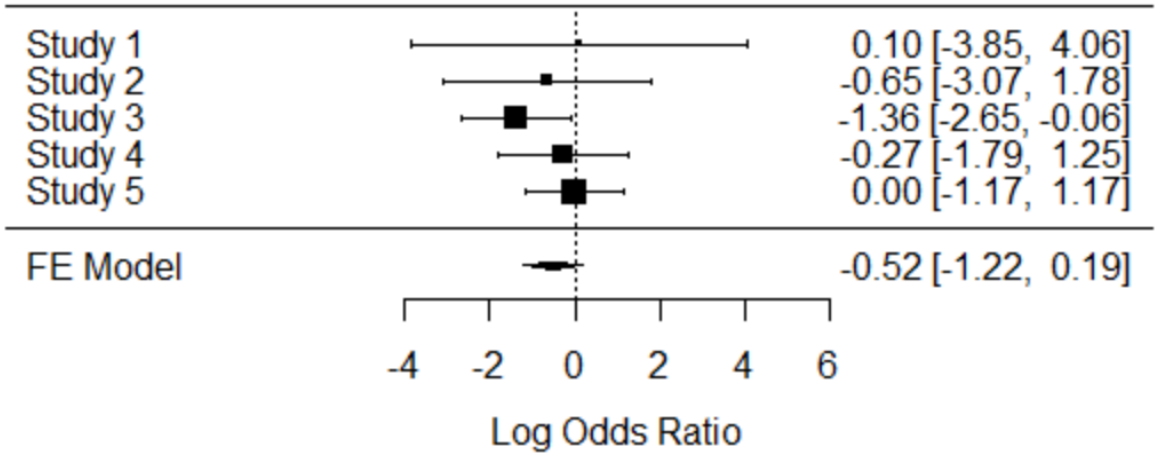
- Sulfonylureas vs placebo

R_Code

```
##### Sulfonylureas vs Placebo

data2 <- data.frame(n21=c(0, 1, 3, 3, 6), n22=c(0, 2, 11, 4, 6),
                    N21=c(27, 65, 161, 123, 92), N22=c(30, 69, 160, 126, 92))
mod2 <- rma.uni(ai=n21, ci=n22, n1i=N21, n2i=N22,
                measure="OR",
                data=data2,
                method = "FE",
                weighted = TRUE,
                level = 95)
forest(mod2)
```

Forest Plot



In this case, we notice that all the confidence intervals of the studies contain the value 0 except the one of study 3. The study therefore makes a statistically significant difference between the treatment group and the control group. An individual treated with Sulfonylureas is 1.36 times more likely to recover from the disease

6- Next step

Here, the next step would be advanced methods

7- Why do we conduct that kind of analysis?

Sometimes, in abscence of head-to-head trials of treatments, to provides evidence for the difference in treatment effects between competing interventions or in order to judiciously select the best choice of treatment.