

SHORT TERM SCIENTIFIC MISSION (STSM) – SCIENTIFIC REPORT

The STSM applicant submits this report for approval to the STSM coordinator

Action number: FA 1403

STSM title: Inter-individual variability on the effects flavanols on the cardiovascular system: systematic review and meta-analysis

STSM start and end date: 05/12/2017 to 15/12/2017

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PURPOSE OF THE STSM/

The POSITIVE research group aims to investigate the heterogeneity in individuals' responsiveness to plant food bioactives, in particular about the effects of the cardiovascular system. In this framework, a meta-analysis about inter-individual variability after consumption of flavanols from cocoa, apple and tea has been conducted. As the latest studies included are from 2015, the analysis should be updated with the most recent publications. During this STSM, the new dataset will be produced and analysed using a dedicated software licenced at the host institution.

This STSM is requested to support such work which consists in the following tasks:

- Data extraction from the new studies about cocoa, apple and tea flavanols' effects on vascular health
- Perform the analysis of the new dataset using the Comprehensive Meta-Analysis Software
- Update current results and contribute to the writing of the meta-analysis paper

The previous querying terms will be used in a systematic research analysis to retrieve new clinical trials. Data will then be extracted using the previous template. Finally, the whole dataset will be re-analysed using the dedicated software Comprehensive Meta-Analysis Software, licenced at the hosting institution.

Planning:

- Extract primary data using previous querying terms and the data extraction template
- Report extracted data in the meta-analysis software
- Meta-analysis and software tutorial

- Perform meta-analysis
- Update results of the previous analysis

DESCRIPTION OF WORK CARRIED OUT DURING THE STSMS

The first part of the work has consisted into retrieving the new papers related to the topic, published between July 2015 and December 2017, using the querying terms of the first research in Pubmed and Web Of Science, as used in the previous research.

The papers retrieved have been reviewed and the non-relevant discarded. In particular, papers related to lipid profiles, glycemia or co-interventions. A few new papers related to apple extract have been retrieved, however, not enough to include them in the analysis.

All relevant data have been extracted and filled into the Excel template as used in the previous research and then imported into the CMA software. After, a course has been given by Dr Paula Pinto. All analysis have been re-launched: Fixed or random effect meta-analysis (Placebo vs Treatment) on the difference in means, 95% confidence intervals, heterogeneity of studies was assessed by the Cochran's Q, Inconsistency index I^2 , Funnel plots and Egger's regression test to assess publication bias.

The interindividual variability was assessed by exploring effects in different subgroups defined by the variables Sex, Age, World region, Baseline BMI, Baseline BP, Health status, Smoking and use of medication. An association between the response and the Flavanol dose or duration of supplementation has been explored using random-effects meta-regression analysis. Sensitivity analyses were carried out using the leave-one-out and by excluding studies with high risk of bias.

All relevant figures have been saved for modification and later inclusion in the paper. P-values and all other relevant values such as confidence intervals have been saved to be reported in the updated draft paper.

DESCRIPTION OF THE MAIN RESULTS OBTAINED

The new extraction gave a total of 403 papers to review (period 2015-2017). This list has been reduced using the abstracts and the titles. The remaining papers have been assessed by a full-text reading.

A total of 6 studies have been extracted. All of them were with moderate risk of bias. One of them has been discarded as it was performed with an apple extract intake.

The remaining studies represent a total of 5 new interventions with FMD as outcome and 4 interventions in blood pressure as outcome.

Despite the low number of studies included, they brought sufficient power to change the amplitude and significance of the effects, in particular:

- FMD: Country and Health status are now significant variables. The source of flavanols also explains the outcome.
- SBP: Sex is now a significant variable.

FUTURE COLLABORATIONS (if applicable)

The saved figures should be improved to reach a publication grade and incorporated in the draft. The new values should also be reported in the draft and the missing sections should be written for publication.