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How to Conduct A Good Meta-Analysis on Flavonoid Intake?

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COLUMN ARTICLE

Short Column

Meta-analysis has become an increasingly popular and valuable tool in flavonoid epidemiology, and major review articles often employ this methodology. Researchers performing a meta-analysis should have expertise in the exposure (in our case flavonoid intake), the outcome (e.g., mortality, chronic diseases, intermediate biomarkers), and the analysis (i.e., selection and abstraction of the appropriate articles, and the use of adequate statistical methods). The investigators are usually experts in the outcome and the analysis, but not in flavonoids. Therefore, this short column will provide several suggestions to increase the quality of future meta-analyses and to avoid some common mistakes related to flavonoid exposure.

Firstly, the use of "total flavonoids" can be misleading. On the one hand, many studies have not included all main six flavonoid classes (flavanols, flavonols, flavanones, flavones, anthocyanins, and isoflavones), especially in "old" studies. The availability of food composition tables on flavonoids was very limited until the development of the US Department of Agriculture database (USDA) in 2004 [1] and Phenol-Explorer database in 2009. Phenol-Explorer also contains data on other minor flavonoid classes (such as chalcones, dihydrochalcones, and dihydroflavonols) [2]. On the other hand, flavonoids form a large family of highly diverse chemical structures that may have both very different bioavailability [3] and bioactivity [4]. Therefore, in my opinion, it is more important to focus on the meta-analyses on separate flavonoid classes than on the entire family.

Secondly, the flavanol or flavan-3-ol class can have different definitions. The most accepted one divides it into three subclasses: monomers (catechins and epicatechins), oligomers and polymers (also called proanthocyanidins), and flavanol-derived compounds (theaflavins and thearubigins) [5]. However, the quality of the food composition data on thearubigins is very poor [6], and in my opinion it would be better to exclude them from the analysis. Despite this, the impact of thearubigins in a diet with a high consumption of black tea could be enormous, and in some populations thearubigins account for almost 50% of total flavonoids, such as in the UK [6]. Therefore, it is crucial to ensure that the consistent flavanol subclasses are used in all studies meta-analyzed.

Finally, flavonoid contents can be expressed as aglycones, such as in the USDA database [1], or as native glycosides, such as in Phenol-Explorer [2]. Differences in the intake estimates can be relatively large [7] but the risk estimates between intake and disease risk are almost identical [8]. In this case the authors can combine both results if they are using quantiles, but not if they are using continuous estimates of intake, particularly to conduct dose-response analysis.

Overall, to guarantee the quality of meta-analyses on flavonoids, it is important to take into account the flavonoid classes and subclasses included in the study, the way that

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the flavonoids are expressed (aglycones vs glycosides) and it is preferable to investigate flavonoid classes than "total flavonoids".

CONFLICT OF INTEREST

RZ-R declares no conflict of interest.

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