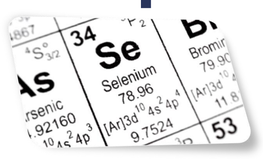
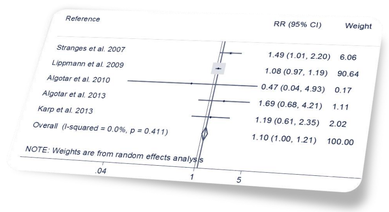
The 23rd Cochrane Colloquium Vienna, 3-7 October 2015
"Filtering the information overload for better decisions"

# Exploring inconsistencies between observational and experimental studies of selenium and diabetes risk




Marco Vinceti[1], Tommaso Filippini[1], Cinzia Del Giovane[1], Catherine M Crespi[2]

[1]University of Modena and Reggio Emilia and [2]Fielding School of Public Health, UCLA




## Background and aims

Observational and experimental epidemiologic studies that have addressed the relation between intake of the trace element selenium and cancer risk have yielded strongly conflicting results, as recently reported by a Cochrane review. Most observational studies suggest an inverse association with summary OR of 0.69 (95% CI 0.53-0.91), while randomized controlled trials (RCTs) have indicated a null or direct relation with summary RR of 1.02 (0.90-1.14) for studies with low risk of bias. Little is known about the replication of such inconsistencies when dealing with the risk of other chronic disease.

We investigated the results of observational and experimental studies linking selenium exposure to the occurrence of type 2 diabetes.

## Methods

After a literature search we identified 12 observational studies (8 cross-sectional and 4 cohort) and 5 RCTs. Using a random-effects model, we computed the summary relative risk (RR) of type-2 diabetes along with its 95% confidence interval (CI) in subjects with the highest versus the lowest selenium exposure category in observational studies, and in subjects allocated to selenium compared to placebo in the RCTs.

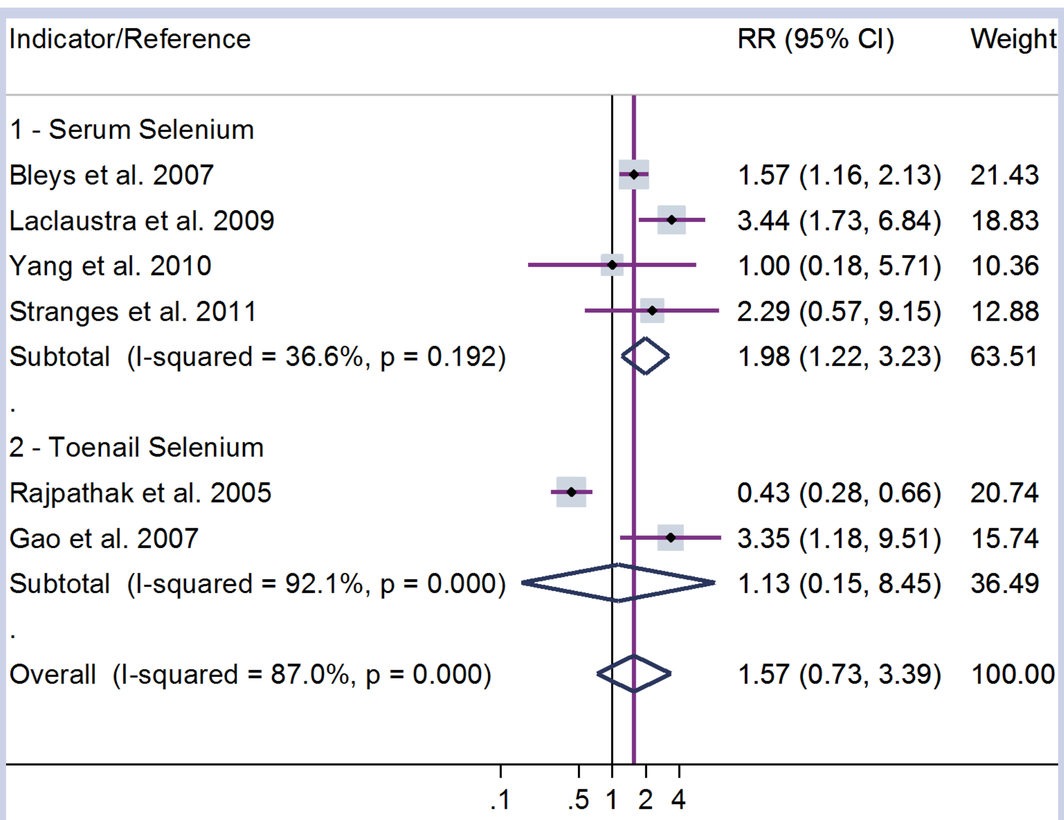



**Figure 1. Forest-plot of cross-sectional studies using serum (1) and toenail (2) selenium as exposure assessment method.**

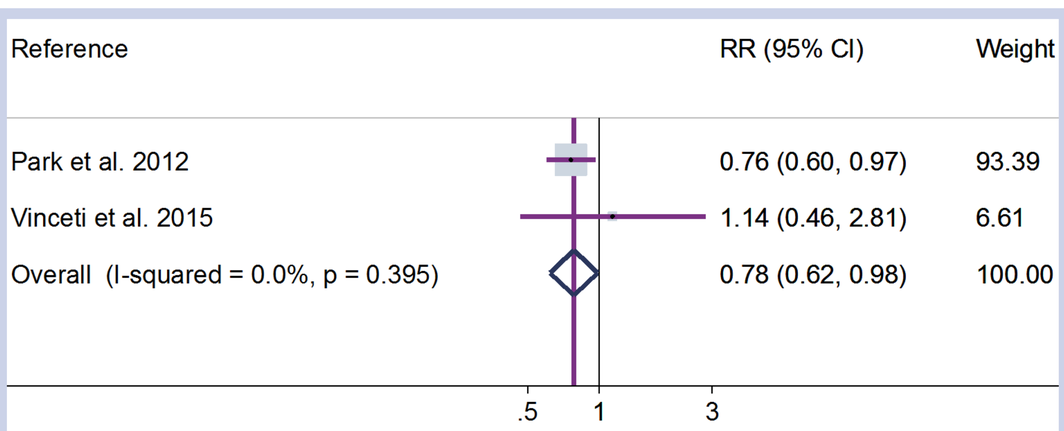



**Figure 2. Forest-plot of cohort studies using dietary selenium as exposure assessment method.**

## Results

Summary RRs were 1.98 (95% CI 1.22-3.23) and 1.13 (0.15-8.45) for cross-sectional studies using serum and toenail selenium for exposure assessment, respectively (Figure 1). Cohort studies based on toenail selenium yielded a summary RR of 0.78 (0.62-0.98)(Figure 2), while the only study assessing dietary selenium intake gave a RR of 2.39, (1.32-4.32). For RCTs, summary RR was 1.11 (1.00-1.22) among selenium-supplemented versus placebo. Results of different stratified analyses showed in Figure 3. A distinctive feature of the two observational studies (one cross-sectional and one prospective) that failed to find an excess diabetes risk associated with higher selenium exposure was that the subjects were health professionals. Age, gender, study area and other demographic characteristics did not appear to have influenced the results.

| | | Experimental | | Control | |
|---|---|---|---|---|---|
| Reference | Trial | Events | Total | Events | Total |
| Stranges et al. 2007 | NPC | 58 | 542 | 39 | 563 |
| Lippmann et al. 2009 | SELECT | 724 | 8028 | 669 | 8027 |
| Algotar et al. 2010 | WWT | 4 | 83 | 2 | 38 |
| Algotar et al. 2013 | NBT | 24 | 398 | 7 | 202 |
| Karp et al. 2013 | ECOG5597 | 26 | 839 | 12 | 465 |

**Table of RCTs with selenium-supplement treatment. Two RCTs have two intervention groups, 200/800 in WWT and 200/400 µg/Se/die in NBT. Other studies used supplements containing 200 µg/Se/die.**

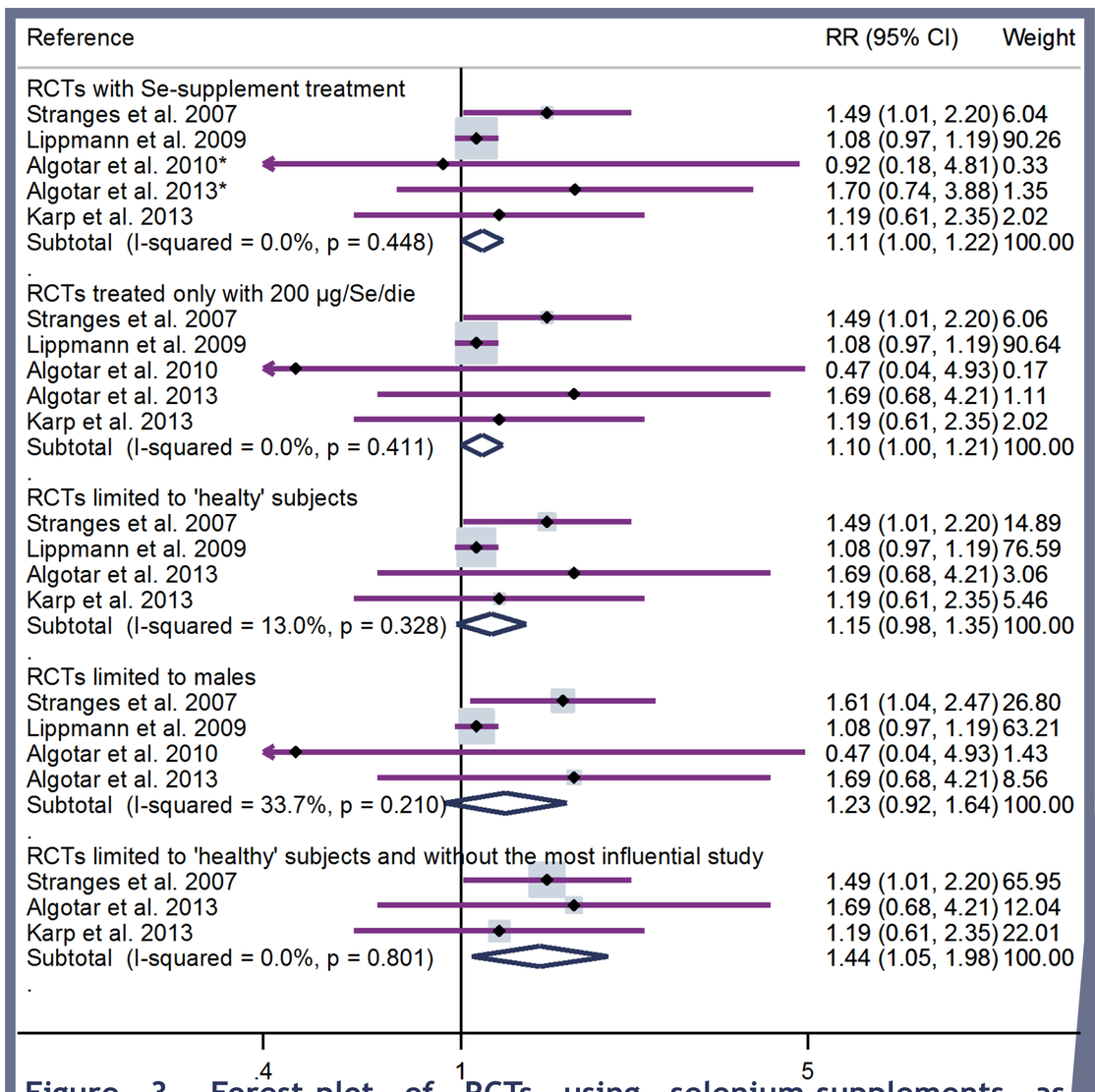



**Figure 3. Forest-plot of RCTs using selenium-supplements as intervention. Summary RRs are presented for all studies and into different stratified analyses.**

## Conclusions

These results suggest that the ability of observational studies to predict results of RCTs when addressing the health effects of selenium may differ on the basis of the outcome studied (diabetes versus cancer) as well as the indicator used for exposure assessment and the type of population under study.

Prof. Marco Vinceti, Department of Diagnostic, Clinic and Public Health Medicine - University of Modena and Reggio Emilia.
Via Campi 287 - 41125, Modena. *marco.vinceti@unimore.it*

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

Creagen

Environmental, Genetic and Nutritional Epidemiology Research Center

Cochrane

UNIVERSITAS STUDIORUM MUTINENSIS ET REGIENSIS
1175