This is the peer reviewd version of the followng article:

Diet composition and serum levels of selenium species: A cross-sectional study / Filippini, Tommaso; Michalke, Bernhard; Wise, Lauren A.; Malagoli, Carlotta; Malavolti, Marcella; Vescovi, Luciano; Salvia, Chiara; Bargellini, Annalisa; Sieri, Sabina; Krogh, Vittorio; Ferrante, Margherita; Vinceti, Marco. - In: FOOD AND CHEMICAL TOXICOLOGY. - ISSN 0278-6915. - 115:(2018), pp. 482-490. [10.1016/j.fct.2018.03.048]

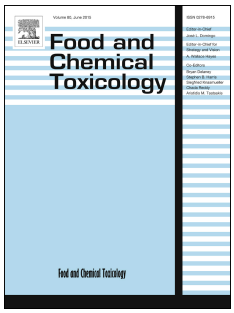
Terms of use:

The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

12/01/2025 22:02

(Article begins on next page)

Accepted Manuscript



Diet composition and serum levels of selenium species: A cross-sectional study

Tommaso Filippini, Bernhard Michalke, Lauren A. Wise, Carlotta Malagoli, Marcella Malavolti, Luciano Vescovi, Chiara Salvia, Annalisa Bargellini, Sabina Sieri, Vittorio Krogh, Margherita Ferrante, Marco Vinceti

PII: S0278-6915(18)30197-2

DOI: 10.1016/j.fct.2018.03.048

Reference: FCT 9684

To appear in: *Food and Chemical Toxicology*

Received Date: 16 January 2018

Revised Date: 14 March 2018

Accepted Date: 30 March 2018

Please cite this article as: Filippini, T., Michalke, B., Wise, L.A., Malagoli, C., Malavolti, M., Vescovi, L., Salvia, C., Bargellini, A., Sieri, S., Krogh, V., Ferrante, M., Vinceti, M., Diet composition and serum levels of selenium species: A cross-sectional study, *Food and Chemical Toxicology* (2018), doi: 10.1016/j.fct.2018.03.048.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

ACCEPTED MANUSCRIPT

Title: Diet composition and serum levels of selenium species: a cross-sectional study

Authors:

Tommaso Filippini[a], Bernhard Michalke[b], Lauren A. Wise[c], Carlotta Malagoli[a], Marcella Malavolti[a], Luciano Vescovi[d], Chiara Salvia[a], Annalisa Bargellini[a], Sabina Sieri[e], Vittorio Krogh[e], Margherita Ferrante[f], Marco Vinceti[a,c]

Affiliations:

[a]CREAGEN, Environmental, Genetic and Nutritional Epidemiology Research Center, Section of Public Health - Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, 287 Via Campi, 41125 Modena, Italy;

[b]Helmholtz Zentrum München GmbH, German Research Center for Environmental Health, Research Unit Analytical BioGeoChemistry, Ingolstädter Landstr. 1, 85764 Neuherberg, Germany

[c]Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA.

[d]IREN, Reggio Emilia and Piacenza, Italy;

[e]Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;

[f]Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", University of Catania, 87 Via S. Sofia, 95123, Catania, Italy.

Corresponding author: Marco Vinceti, CREAGEN – Section of Public Health - Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Via Campi 287, 41125 Modena, Italy (Tel. +39 059 2055481; fax +39 059 2055483; E-mail marco.vinceti@unimore.it)

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

1.1 Introduction

Selenium (Se) is a metalloid considered both essential and toxic to humans, depending on the level of exposure and its specific chemical species (Fairweather-Tait et al., 2011; Jablonska and Vinceti, 2015; Vinceti et al., 2009). Its relation to human health, specifically cancer (Vinceti et al., 2016a; Vinceti et al., 2017c; Vinceti et al., 2018; Wallenberg et al., 2014), diseases of the nervous system (Cicero et al., 2017; Mandrioli et al., 2017; Vinceti et al., 2017a; Vinceti et al., 2014), and other chronic diseases (Vinceti et al., 2016b; Vinceti et al., 2015b), is still unclear, despite the large number of epidemiologic studies on the topic. Recent laboratory studies have demonstrated toxicological potential of various organic and inorganic Se species (Galant et al., 2017; Li et al., 2012; Michalke et al., 2017b; Naderi et al., 2017; Oliveira et al., 2017; Pettem et al., 2017; Rezacova et al., 2016; Selvaraj et al., 2013).

The main source of Se exposure is dietary intake (Fairweather-Tait et al., 2011; Fan and Vinceti, 2015), though occupational environment, smoking, and air pollution may also contribute to Se exposure (Jablonska and Vinceti, 2015; Vinceti et al., 2013a). Detailed studies of dietary Se intake showed that cereals, meat, fish and dairy products are the main contributors to Se dietary intake in both European and Italian populations (Filippini et al., 2018; Gudmundsdottir et al., 2012; Lombardi-Boccia et al., 2003; Mariottini et al., 1995; Navarro-Alarcon and Cabrera-Vique, 2008). The assessment of Se intake based on individual food consumption must consider the large variation of Se content in foods, influenced by environmental and geographic variations of Se content in soil and water (Mariottini et al., 1995; Shacklette and Boerngen, 2013), use of Se supplemented fertilizers (Fairweather-Tait et al., 2010), the differences in Se bioavailability in foods of plant origin (Baskett et al., 2001; Terry et al., 2000), and the effect of self-supplementation with Se (Satia et al., 2006).

The few observational studies investigating Se content in food and its influence on Se blood levels have considered only the total amount of the trace element (Fairweather-Tait et al., 2011;

ACCEPTED MANUSCRIPT

Mariottini et al., 1995; Pennington et al., 1984; Rayman, 2008), and not the single Se species. Relatively few studies have assessed the levels of Se species in biological samples, including serum, cerebrospinal fluid and urine (Combs et al., 2011; Slotnick and Nriagu, 2006; Vinceti et al., 2015a; Vinceti et al., 2013b). These studies have shown large variation in Se species levels among individuals, probably related to the variations in dietary habits (Fairweather-Tait et al., 2011). However, little is known about the Se species contained in different food items that characterize human diet, and even less about the relation between intake of specific foods and blood levels of Se species.

Recently, interest in Se speciation in foods has increased (Castro Grijalba et al., 2017; Ruiz-de-Cenzano et al., 2017), mirroring the increased attention to Se speciation in human health and disease. Distinguishing between Se species is of major relevance given the different properties of inorganic selenium species, such as selenite and selenate, and of the organic forms including for instance selenomethionine (Lazard et al., 2017; Lee and Jeong, 2012; Michalke et al., 2017b; Oliveira et al., 2017; Vinceti et al., 2017b; Weekley and Harris, 2013), the markedly different and not entirely elucidated metabolism of various selenium species, and the limited bioavailability of inorganic Se forms such as selenate (B'Hymer and Caruso, 2006; Gammelgaard et al., 2012; Jager et al., 2016; Weekley and Harris, 2013). The main form of Se in foods is selenomethionine (Weekley and Harris, 2013), which can be incorporated into proteins as a mimic for the correspondent sulfur-amino acid methionine (Schubert et al., 1987), a phenomenon which may cause protein misfolding and Se toxicity (Plateau et al., 2017; Vinceti et al., 2013b).

In this study, we sought to assess the influence of dietary intake on serum levels of Se species in a sample of a Northern Italian population.

2.1 Methods

2.1.1. Study population

ACCEPTED MANUSCRIPT

The methodology for selection of study subjects has been described in detail elsewhere (Filippini et al., 2016; Vinceti et al., 2015a). Briefly, following approval of the study protocol by the Ethical Committee of the Policlinico University Hospital of Modena (n. 71/11), we randomly recruited fifty healthy subjects residing in Modena municipality without any relevant inflammatory disorder at the time of the recruitment, selected from sex- and age-specific subgroups through the databases of the Modena Municipality General Registry Office and using the Stata sample routine (Stata Corp., College Station, TX). Subjects were contacted from 2011 by land-line phone and invited to participate in the study. We recruited the 34% of contacted subjects and referred them to the Modena Health Unit to provide a fasting venous blood sample without any compensation apart from a complimentary breakfast.

Each participant completed a self-administered questionnaire collecting general demographic information, educational level, occupational history, smoking habits, and use of dietary supplements. In addition, we assessed their dietary habits through a validated semi-quantitative food frequency questionnaire (FFQ) specifically designed for the Central-Northern Italian population within the EPIC study (Pala et al., 2003; Pasanisi et al., 2002). A general explanation of modality of completion of the FFQ was provided to each subject soon after recruitment, and instructions were also included on the questionnaire. In addition, within each section of the questionnaire (e.g. main courses, side dishes, beverages, etc.) detailed instructions about how to answer were included. This questionnaire assessed the average frequency and amount of consumption of 188 food items over the previous year, permitting estimation of consumption of macro- and micro-nutrients (including Se). We did this using an *ad hoc* software program (Malagoli et al., 2015; Malavolti et al., 2013). In particular the estimation of Se intake was implemented through ascertainment and analysis of foods characterizing the typical Italian diet (Bottecchi and Vinceti, 2012). Food intake was reported in g/day for each food.

ACCEPTED MANUSCRIPT

2.1.2 Laboratory analysis

Blood samples were collected in a plastic tube (BD Vacutainer®, Becton Dickinson, Milan, Italy), immediately centrifuged for 10 min at 1000 x g and serum aliquots of 1 ml were stored at -15°C and kept continuously frozen until use. Selenium speciation analysis was performed at the Research Center for Environmental Health (Research Unit Analytical BioGeoChemistry, Neuherberg, Germany), using previously-described methodology (Solovyev et al., 2013; Vinceti et al., 2015a). To summarize, we slowly thawed samples in a refrigerator at 4°C, vortexed and subsequently analyzed them. Suprapure grade chemicals were used throughout. Selenite (Se(IV)), selenate (Se(VI)), selenomethionine-bound selenium (Se-Met), selenocysteine-bound selenium (Se-Cys), thioredoxin reductase-bound selenium (Se-TXNRD), glutathione peroxidase-bound selenium (Se-GPX), human serum albumin (HSA) and Tris buffer were from Sigma-Aldrich (Deisenhofen, Germany). We purchased certified Se and Rh stock standards (1000 mg/L) from CPI International, Santa Rosa, CA, USA, and we obtained ammonium acetate (NH_4Ac) and acetic acid (HAc) from Merck, Darmstadt, Germany. $Argon_{liq}$ and methane (99.999% purity) were purchased from Air Liquide (Kleeve, Germany). We prepared stock solutions of Se(IV) and Se(VI) at a concentration of 1000 mg Se/L by dissolving in MILLI-Q water (18.2 MΩ cm, Milli-Q system, Millipore, Bedford, MA, USA). HSA was prepared at a concentration of 1000 mg/L. Preparation of Se-HSA was performed by mixing 10 mg Se/L selenite with this stock solution and incubating for at least 14 days. Working standards of Se species were prepared daily from their stock standard solutions by appropriate dilution with Milli-Q H_2O. Since selenoprotein P-bound selenium (Se-SelenoP) is not commercially available as a standard compound, it can be prepared from serum using affinity chromatography (AFC) with the methodology previously described in detail (Solovyev et al., 2013).

We determined Se species Se(IV), Se(VI), Se-Met, Se-Cys, Se-TXNRD, Se-GPX, Se-SelenoP and Se-HSA in serum samples using anion exchange chromatography (IEC) coupled with

ACCEPTED MANUSCRIPT
inductively-coupled plasma dynamic reaction cell mass spectrometry (ICP-DRC-MS) according to methodologies implemented for biological matrices (Michalke and Berthele, 2011; Solovyev et al., 2013). See *Vinceti et al.* (Vinceti et al., 2015a) for the detailed experimental settings, Se species determination, and quality controls. When the concentration of a Se compound was lower than the detection limit of 0.02 μg/L, we inputted in the database half that value (0.01 μg/L) (Whitcomb and Schisterman, 2008).

2.1.3 Data analysis

In selecting food categories in the present study, we took into account both the typical dietary pattern of the Italian population (Turrini et al., 2001), the types of foods previously reported as being rich in Se and relevant sources of this metalloid (European Food Safety Authority, 2014; Filippini et al., 2018; Filippini et al., 2017a), and the ability of such plants, the so called 'Se accumulator' vegetables including garlic, onion and cabbage, to accumulate large amount of the element (Finley, 2005; Terry et al., 2000). The final list of foods we selected included cereals, meat (both processed and not-processed), milk and dairy products, eggs, fish and seafood, vegetables (further divided in 'Se-accumulator' and 'Se non-accumulator'), legumes, tubers (i.e. potatoes), mushrooms, fresh fruits, dry fruits, and sweets (including sugar, chocolate and cakes). We calculated the median and interquartile range (IQR) of the intake of these foods and food categories.

In order to reduce the influence of measurement error frequently associated with food frequency questionnaires, either under-reporting and over-reporting food intake, we adjusted the estimates for total energy intake using the Willett's residual method (Willett, 2013). We computed Pearson correlation coefficients along with 95% confidence intervals (CI) between serum Se species and food category intake, after testing for normality of the data. We also used both crude and multivariable linear regression models, taking into account variable such as sex, age and

ACCEPTED MANUSCRIPT
storage time, smoking habits and Se supplement use. We also performed a sensitivity analysis restricting the sample to subjects not taking Se-containing supplements.

When considering Se species in the analysis, we left apart Se-HSA and Se unknown species from the standard classification in organic and inorganic Se, for the uncertainties related to these forms (Vinceti et al., 2015a; Vinceti et al., 2013b) . After detecting a subject with extremely high and implausible levels of inorganic hexavalent Se(VI), 88.7 µg/L, we considered this sample as an outlier and removed the subject from all data analyses.

3.1 Results

Demographic and lifestyle characteristics of study participants have been reported in detail elsewhere (Vinceti et al., 2015a). Briefly, we recruited 50 subjects aged 35-70 years, males and females were equally represented. Nine (18%) participants were current-smokers, while twenty-six (52%) and fifteen (30%) were never- and former- smokers, respectively. Finally, nine (18%) subjects reported use of Se supplement at time of the blood sampling, with a mean additional intake due to these supplements of 28.6 µg/Se/day. The distribution of Se species in serum total population in selected subgroups is shown in Supplementary Table S1.

Figure 1 shows the distribution of overall dietary Se intake in the study population (median of 93.2 µg/day, interquartile range (IQR): 80.0-109) and in selected subgroups. No relevant differences across these groups were found, except for Se supplement users who were characterized by a lower background dietary Se intake compared with non-users (97.3 µg/day, IQR: 85.1-110, and 76.3 µg/day, IQR: 68.2-98.9 in non-users and users, respectively). The corresponding figure of total serum levels in Se supplement users and non-users were 138 µg/L (IQR: 113-139) and 118 µg/L (IQR: 107-127), mainly due concentration of organic Se forms, i.e. 82.2 µg/L (IQR: 58.5-92.7) and 66.4 µg/L (IQR: 30.4-83.5) (Supplementary Table S1).

ACCEPTED MANUSCRIPT

Usual intake of the main food categories is shown in Figure 2. Median consumption was 240.8 g/day (IQR: 181.6-340.2) for fresh fruits, 167.4 g/day (IQR: 77.4-214.7) for cereals, 161.6 g/day (IQR: 90.6-272.0) for milk and dairy products, followed by 124.4 g/day (IQR: 77.6-166.1) for meat and 119.5 g/day (IQR: 72.3-176.7) for vegetables. Figure 2 shows the foods yielding the highest Se contribution to overall dietary intake, primarily fish and seafood (~30%), meat (~20%) and cereals (~13%), followed by milk and dairy products (~11%) and vegetables (~7%) (see Supplementary Table S2). Table 1 shows Pearson correlation coefficients between Se intake and total serum Se and its species. Se intake was inversely correlated with organic species, especially Se-GPX but directly with Se-TXNRD, while positively correlated with inorganic forms. Exclusion of subjects taking Se-containing supplements gave comparable results.

Table 2 shows correlation coefficients between food categories and serum Se species. Considering total Se concentrations, we found a positive correlation with cereals and fresh fruits intake, but an inverse correlation with dairy products, mushrooms, vegetables, legumes and potatoes intake. Overall, organic Se concentrations were directly correlated with intake of dairy products and inversely correlated with intake of fish and seafood, legumes and dry fruits. Focusing on single organic Se species, Se-SelenoP, the most abundant form, showed an inverse correlation with intake of fresh fruits, and to a lesser extent with vegetables, legumes, and fish and seafood. Conversely, concentrations of Se-Cys, the only form being the one characterized in selenoproteins, were directly correlated with intake of cereals, eggs, vegetables, fresh fruits, legumes and mushrooms, while inversely correlated with intake of sweets. Se-Met showed a positive correlation with intake of dairy products, while Se-Met and Se-GPX negatively correlated with legume intake. Se-TXNRD showed positive correlation with cereal intake and opposite with sweet intake. Serum concentrations of inorganic Se, the most toxic Se species, were inversely correlated with consumption of dairy products and mushrooms, while directly correlated with intake of fish

ACCEPTED MANUSCRIPT
and seafood, legumes and dry fruits. Finally Se-HSA showed positive correlations with intake of cereals and fresh fruits, and inverse correlations with eggs, milk and dairy products.

Sensitivity analyses carried out using linear regression in crude and multivariable models (Supplementary Table S3 and Figure S1) generated similar results, as did analyses excluding subjects taking Se supplements (Supplementary Table S4).

4.1 Discussion

In our study population, we investigated correlations between food intake and serum levels of Se species, since diet (food consumption and dietary supplement use) is by far the most important determinant of Se exposure in the majority of individuals (European Food Safety Authority, 2014; Fairweather-Tait et al., 2011). Se concentration in foods could vary widely, mainly depending on soil content (Fairweather-Tait et al., 2011). Se from soil is generally absorbed by plants primarily as inorganic Se (mostly selenate) which, after translocation into the chloroplast, it is reduced to selenide, which in turn reacts with serine to form Se-Cys (Finley, 2005; Weekley and Harris, 2013). This was confirmed by Se speciation studies, which demonstrated that, in plants, organic Se species, especially selenomethionine and selenocysteine, are the predominant Se compounds, followed by inorganic species (Chan et al., 2010; Fox et al., 2002; Lyubenova et al., 2015; Montes-Bayon et al., 2002; Thavarajah et al., 2007; Whanger, 2002; Wolf and Goldschmidt, 2007). Accordingly, in our study we observed a strong positive correlation between intake of cereals, vegetables, legumes and fresh fruit and serum Se-Cys, while concerning inorganic forms only legumes demonstrated a positive correlation.

Our results showed little influence of meat intake on serum concentrations of Se species, despite the high Se content generally characterizing this food category, particularly liver and kidneys. Selenomethionine and selenocysteine appear to be the predominant species of Se in edible portions of meat (Bierla et al., 2008; Fairweather-Tait et al., 2011). However, the

ACCEPTED MANUSCRIPT
bioavailability of the Se in meat is difficult to assess, and the literature has yielded inconsistent evidence on this topic (Bugel et al., 2004; Fairweather-Tait et al., 2010; van der Torre et al., 1991).

Milk and dairy products generally contain higher amount of organic Se compounds, mainly selenomethionine and selenocysteine (Muniz-Naveiro et al., 2007; Phipps et al., 2008). Supplementation of animal feeding with organic Se species also demonstrated to be much more effective in increasing levels of Se in milk, while inorganic species showed limited effects (Ortman and Pehrson, 1999). Moreover, a study assessing the Se bioavailability of different types of milk showed that removal of the milk fat fraction increases its availability (Shen et al., 1996). Interestingly, our results showed a positive correlation between milk intake and overall organic species, particularly Se-Met, but an inverse correlation with Se(IV).

In our study, egg consumption was strongly correlated with circulating Se-Cys levels, but did not influence serum concentrations of the other Se species, except for a slight increase in Se(IV) levels and inorganic Se overall. Hen's eggs contain from 3 to 25 µg Se per whole egg, and Se-Cys and Se-Met are the predominant species (Lipiec et al., 2010).

The main Se species in fish appears to be selenomethionine, selenite and selenate (Cappon and Smith, 1982a, b; Fairweather-Tait et al., 2010; Moreda-Pineiro et al., 2013; Sele et al., 2018). Similarly, a speciation study in fish samples from Spain and Portugal showed that Se-Met was the most abundant species detected, and its amount varied depending on fish type, with the higher level in swordfish (93%), followed by tuna (46%) and sardines (28%) (Cabanero et al., 2005). In line with these studies, in our study population intake of fish and seafood showed a positive correlation with this (only) organic form, Se-Met, and with inorganic Se and more specifically both its forms, Se(IV) and (VI). A study yielded in Sweden men yielded consistent results, showing that plasma Se increased slightly with the increasing consumption of fish, with no such increases in glutathione peroxidase and selenoprotein P (Huang et al., 1995). In general, Se bioavailability from seafood appears to be low (Moreda-Pineiro et al., 2013), and shrimps intake does not appear to

ACCEPTED MANUSCRIPT
influence plasma and glutathione peroxidase activity (Bugel et al., 2001). In addition, though Se in seafood generally demonstrates good absorption and high bioavailability after consumption of Se-rich fish (Fox et al., 2004), plasma Se tends to be quickly cleared from other organs (Bugel et al., 2001). Conversely other studies supported a low bioavailability of selenium from fish (Meltzer et al., 1993), possibly due to its interaction with heavy metals, particularly mercury and arsenic (Burger and Gochfeld, 2013; Cabanero et al., 2007; Copat et al., 2014; Olmedo et al., 2013). Another reason explaining its bioavailability is the low conversion rate of inorganic Se into organic Se in the human, also taking into account the peculiar metabolic and catabolic pathways of inorganic Se (Cummins and Martin, 1967; Jager et al., 2016; Marschall et al., 2016; Suzuki et al., 2006).

Commercially and wild-grown mushrooms generally contain high Se levels (Cocchi et al., 2006; Pounis et al., 2014) and a wide spectrum of Se forms, i.e. Se-Met, Se-methylselenocysteine, Se-Cys, Se(IV) as well as several unidentified seleno-compounds (Falandysz, 2013). In our sample, we unexpectedly found null or inverse correlations of mushroom intake with most Se species, except for the slight positive association with Se-Cys. Possible explanations of these discrepancies are the different concentrations of Se species in the fruiting bodies of mushrooms, the biotransformation process of Se into organic compounds (Piepponen et al., 1983), and the speciation extraction procedures implemented (Diaz Huerta et al., 2006). For example, studies carried out on different species of Se-enriched mushrooms identified a major content alternatively of Se-Met or Se(IV) and Se-Cys (Bhatia et al., 2013; Stefanka et al., 2001). A low bioavailability of Se in mushrooms may also explain the low correlation we observed between intake of this food item and serum Se levels, possibly due to the high heavy metal content of mushrooms, thereby favoring Se excretion with the same mechanisms hypothesized for smoking (Vinceti et al., 2013a; Vinceti et al., 2000). The limited consumption of mushroom in the total diet characterizing our

ACCEPTED MANUSCRIPT

free-living study subjects likely contributes to explain the limited influence of this food item on serum Se levels.

Considering sweet products, intake in our study population was inversely correlated with Se-Cys, and more slightly with Se-TXNRD, but no relevant relation emerged with any other Se species. Previous studies have generally assessed only total Se serum concentrations in relation with sweet intake, though a study carried out in multiple sclerosis patients showed results consistent with our findings (Socha et al., 2014), although no such relation emerged in controls. However, other studies yielded conflicting results (Borawska et al., 2004; Letsiou et al., 2010), also depending on type of sweet products considered and on Se exposure status, with an inverse correlation below serum Se <70 µg/L and a positive one above that cut-point (Borawska et al., 2004).

We found a positive correlation between overall Se intake, as assessed through the food frequency questionnaire, and inorganic serum Se species, while no such correlation emerged for the other Se species. This could be due to the large influence of one dietary category (i.e. fish) on overall Se intake (Figure 2). However, other factors could have hampered the correlations. First, biosynthesis of selenoproteins and therefore requirement of Se are only partially regulated by Se intake and status (Sunde et al., 2009), and many other factors such as pro-oxidant stressors, intake of other factors such as methionine may be involved (Vinceti et al., 2013a). This means that foods containing pro-oxidant factors might induce higher body retention and levels of organic Se due to the induction of a reactive proteomic response, which upregulate the antioxidant Se-containing proteins and therefore increase circulating Se-Cys levels (Jablonska and Vinceti, 2015). Secondly, uptake and retention by peripheral tissues tend to be considerably higher for the Se organic forms than for inorganic ones (Jablonska and Vinceti, 2015; Labunskyy et al., 2014; Vinceti et al., 2009). In addition, two endocytic receptors are implicated in the tissue-specific uptake of SelenoP (Chiu-Ugalde et al., 2010; Olson et al., 2008; Olson et al., 2007), possible explaining the generally null or

ACCEPTED MANUSCRIPT
even inverse correlation of Se-SelenoP with most of food as opposed to Se-Cys. Finally, Se intake evaluated through the food frequency questionnaire reflects the long term dietary exposure over the last year, while levels in blood are influenced by the short-term dietary intake and also by other environmental exposures such as smoking and air pollution (Di Dato et al., 2017; Vinceti et al., 2017b; Vinceti et al., 2015a). In addition, since the relative distribution of Se species can differ between serum and other body compartments (Behne et al., 1996; Michalke et al., 2017a; Misra et al., 2012; Vinceti et al., 2017a), the associations we observed are specific to serum and do not necessarily apply to other matrices. Moreover, it is also worth noting that one (organic) Se species, Se-Met, was below the detection limit for half the sample, and therefore the results concerning this compound were incomplete and imprecise.

A few limitations of our study warrant discussion. First, a general caveat must be outlined: in this study, we assessed correlations between diet composition and blood Se species levels, but we did not have available information about food content of specific Se chemical forms, neither about the exact origin of the circulating Se species, which could derive either from foods and from endogenous metabolism of Se species, including ex-novo synthesis of organic Se forms (Bulteau and Chavatte, 2015; Cummins and Martin, 1967; Esaki et al., 1981; Gladyshev et al., 2016; Schmidt and Simonovic, 2012). Therefore, the observed correlations between food intake and circulating Se species could have been confounded by Se metabolism (Gladyshev et al., 2016; Schmidt and Simonovic, 2012), and in turn, influenced by diet composition, life-style variables and genetic factors (Vinceti et al., 2015a). Other factors that could have influenced correlations between food intake and serum levels of Se species in our study were intake of heavy metals, which are known to alter Se absorption, retention and bioavailability (Jablonska and Vinceti, 2015; Vinceti et al., 2013a).

Moreover, dietary information was collected with a self-administered food frequency questionnaire that, although validated for the Northern Italian population (Pasanisi et al., 2002),

ACCEPTED MANUSCRIPT

was originally implemented nearly 10 years before the administration to study population (Pala et al., 2003), and this might have introduced some slight misclassification in the assessment of dietary habits. In addition, the small sample size of the study was associated with a limited statistical precision of the point estimates, as shown by their wide confidence intervals. Finally, other sources of selenium exposure could have affected the correlation between food intake and serum Se, such as airborne Se from anthropogenic activities including motorized traffic pollution (Fan and Vinceti, 2015; Heck et al., 2014), volcanic emissions (Ferrante et al., 2013; Tolu et al., 2014), smoking (Bogden et al., 1981), and the use of shampoos containing selenium (LeBlanc et al., 1999), at least in some subjects. This may have induced some exposure misclassification for particularly for inorganic Se serum concentrations, which may be found at higher levels in highly polluted urban environments and have been associated to risk of chronic disease (Heck et al., 2014; Ito et al., 2011).

Our study is the first to investigate, to the best of our knowledge, the relation between dietary habits, extensively assessed through a validated food frequency questionnaire, and the circulating levels of Se species (Filippini et al., 2017b; Michalke, 2016; Michalke et al., 2009; Vinceti et al., 2013b), a relevant health issue taking into account the highly specific and in some cases even opposite biological effects of Se species. Another strength is that study subjects were randomly recruited from Modena residents, and their demographic characteristics and lifestyles (such as body mass index, educational attainments, occupational status and smoking habits) were similar to those characterizing the population of the entire Modena municipality, and more generally of Italy (Ferrante et al., 2012; Gruppo Tecnico PASSI Emilia-Romagna, 2012).

5.1 Conclusions

In this study, we found several correlations between food intake and serum Se species. The most toxic Se species, the inorganic ones, showed a positive correlation with intakes of fish,

ACCEPTED MANUSCRIPT

legumes and dry fruits, while a negative correlation emerged with intakes of milk and dairy products and mushrooms. Concerning organic Se species, the most abundant one - Se-SelenoP - showed inverse correlation with food intake, and specifically with fish, fresh fruits, vegetables, and legumes, while Se-Cys positively correlated with fresh fruits, potatoes, legumes and mushroom intake. If confirmed in future studies, these findings may have major implications when assessing the nutritional and toxicological potential of foods with reference to Se.

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

Table 1. Correlation between dietary estimate of Se intake and total Se serum and its species in all subjects (n=50) and in subjects not taking Se containing supplements. Pearson correlation coefficient (r) with 95% confidence interval (CI) reported.

	All subjects (N =50)			Not taking Se-suppl. (n=41)		
	r	95% CI	*P*	r	95% CI	*P*
Total Se	-0.104	(-0.372 to 0.179)	*0.472*	0.076	(-0.237 to 0.375)	*0.636*
Organic Se	-0.208	(-0.460 to 0.075)	*0.147*	-0.203	(-0.481 to 0.112)	*0.203*
Se-SelenoP	-0.058	(-0.331 to 0.224)	*0.687*	-0.151	(-0.438 to 0.164)	*0.346*
Se-Met	0.025	(-0.255 to 0.302)	*0.861*	0.073	(-0.240 to 0.373)	*0.649*
Se-Cys	-0.083	(-0.354 to 0.199)	*0.564*	0.048	(-0.263 to 0.351)	*0.764*
Se-GPX	-0.378	(-0.594 to -0.112)	*0.007*	-0.300	(-0.556 to 0.009)	*0.057*
Se-TXNRD	0.133	(-0.151 to 0.396)	*0.358*	0.263	(-0.049 to 0.528)	*0.097*
Inorganic Se	0.237	(-0.044 to 0.484)	*0.097*	0.344	(0.041 to 0.590)	*0.027*
Se(IV)	0.221	(-0.061 to 0.471)	*0.123*	0.333	(0.029 to 0.581)	*0.033*
Se(VI)	0.182	(-0.102 to 0.438)	*0.207*	0.205	(-0.110 to 0.482)	*0.199*
Se-HSA	0.014	(-0.265 to 0.291)	*0.923*	0.044	(-0.267 to 0.347)	*0.783*
Unknown spp	-0.106	(-0.373 to 0.178)	*0.465*	0.029	(-0.281 to 0.334)	*0.856*

ACCEPTED MANUSCRIPT

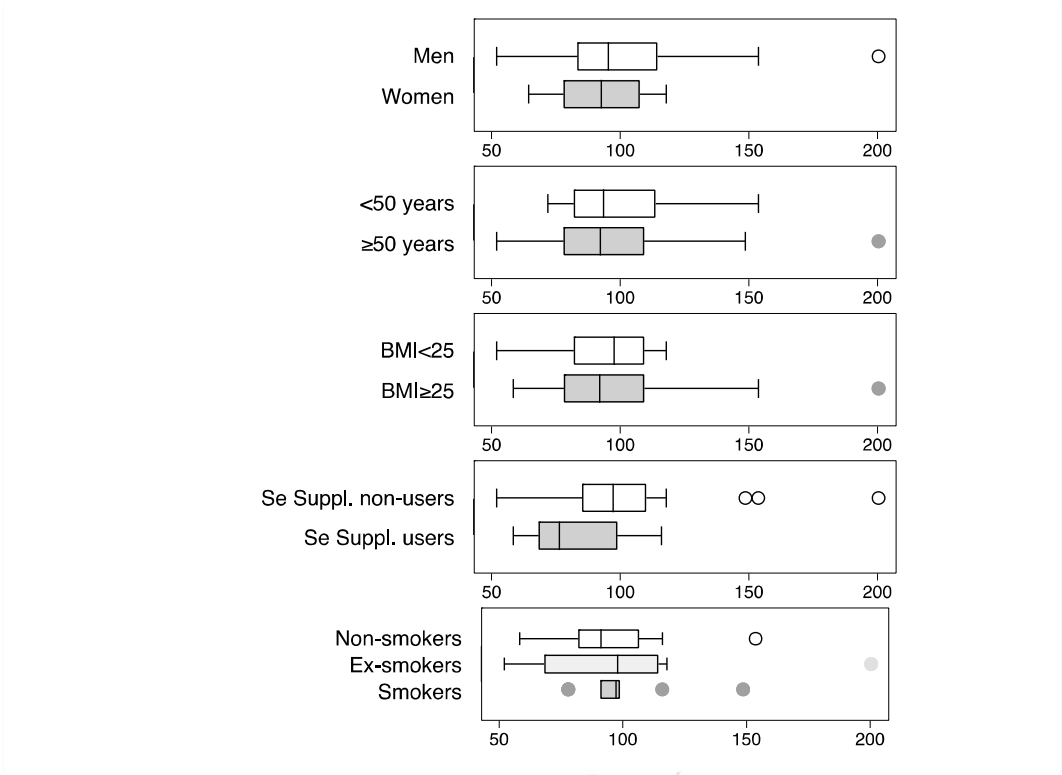
ACCEPTED MANUSCRIPT

Table 2. Correlation between Se serum and its species in selected food categories. Pearson correlation coefficient (r) with 95% confidence interval (CI) reported.

	Cereals			***Meat***			***Milk and dairy products***		
	r	**95% CI**	***P***	**r**	**95% CI**	***P***	**r**	**95% CI**	***P***
Total Se	0.214	(-0.068 to 0.465)	*0.135*	-0.026	(-0.303 to 0.254)	*0.855*	-0.297	(-0.531 to -0.020)	*0.036*
Organic Se	0.086	(-0.197 to 0.356)	*0.553*	-0.004	(-0.282 to 0.275)	*0.979*	0.152	(-0.152 to 0.413)	*0.292*
Se-SelenoP	0.040	(-0.241 to 0.315)	*0.783*	0.028	(-0.252 to 0.304)	*0.845*	0.071	(-0.211 to 0.343)	*0.623*
Se-Met	-0.146	(-0.408 to 0.138)	*0.310*	-0.040	(-0.315 to 0.241)	*0.781*	0.221	(-0.061 to 0.471)	*0.122*
Se-Cys	0.299	(0.022 to 0.533)	*0.035*	-0.018	(-0.294 to 0.262)	*0.903*	-0.010	(-0.288 to 0.269)	*0.945*
Se-GPX	-0.012	(-0.290 to 0.267)	*0.932*	-0.005	(-0.283 to 0.274)	*0.973*	0.113	(-0.171 to 0.380)	*0.433*
Se-TXNRD	0.164	(-0.119 to 0.423)	*0.253*	-0.105	(-0.372 to 0.179)	*0.470*	0.079	(-0.203 to 0.350)	*0.583*
Inorganic Se	-0.059	(-0.332 to 0.223)	*0.684*	0.008	(-0.271 to 0.285)	*0.957*	-0.180	(-0.436 to 0.104)	*0.211*
Se(IV)	-0.059	(-0.332 to 0.223)	*0.682*	0.011	(-0.268 to 0.288)	*0.941*	-0.205	(-0.457 to 0.078)	*0.154*
Se(VI)	-0.027	(-0.303 to 0.254)	*0.854*	-0.009	(-0.286 to 0.270)	*0.951*	0.021	(-0.258 to 0.298)	*0.882*
Se-HSA	0.156	(-0.127 to 0.417)	*0.278*	-0.025	(-0.301 to 0.255)	*0.862*	-0.286	(-0.522 to -0.008)	*0.044*
Unknown spp	-0.096	(-0.365 to 0.187)	*0.506*	-0.010	(-0.287 to 0.270)	*0.947*	-0.235	(-0.482 to 0.046)	*0.099*
	Eggs			***Fish and seafood***			***Mushrooms***		
	r	**95% CI**	***P***	**r**	**95% CI**	***P***	**r**	**95% CI**	***P***
Total Se	-0.025	(-0.301 to 0.255)	*0.863*	-0.088	(-0.358 to 0.195)	*0.543*	-0.212	(-0.463 to 0.071)	*0.139*
Organic Se	0.130	(-0.154 to 0.394)	*0.369*	-0.171	(-0.429 to 0.113)	*0.235*	-0.023	(-0.299 to 0.257)	*0.876*
Se-SelenoP	0.034	(-0.247 to 0.309)	*0.815*	-0.170	(-0.428 to 0.113)	*0.236*	-0.054	(-0.328 to 0.228)	*0.709*
Se-Met	-0.049	(-0.323 to 0.232)	*0.733*	0.130	(-0.154 to 0.394)	*0.370*	-0.015	(-0.292 to 0.264)	*0.916*
Se-Cys	0.251	(-0.029 to 0.495)	*0.078*	-0.048	(-0.322 to 0.234)	*0.743*	0.225	(-0.057 to 0.474)	*0.116*
Se-GPX	0.101	(-0.183 to 0.369)	*0.486*	-0.102	(-0.370 to 0.182)	*0.482*	-0.069	(-0.341 to 0.214)	*0.635*
Se-TXNRD	0.128	(-0.156 to 0.392)	*0.376*	0.092	(-0.192 to 0.361)	*0.527*	0.141	(-0.143 to 0.403)	*0.330*
Inorganic Se	0.144	(-0.140 to 0.406)	*0.319*	0.187	(-0.096 to 0.442)	*0.193*	-0.145	(-0.407 to 0.138)	*0.313*
Se(IV)	0.143	(-0.141 to 0.405)	*0.322*	0.171	(-0.113 to 0.429)	*0.236*	-0.128	(-0.392 to 0.156)	*0.377*
Se(VI)	0.072	(-0.210 to 0.344)	*0.617*	0.158	(-0.126 to 0.418)	*0.273*	-0.145	(-0.407 to 0.139)	*0.316*
Se-HSA	-0.284	(-0.521 to -0.006)	*0.046*	0.008	(-0.271 to 0.286)	*0.955*	-0.001	(-0.279 to 0.278)	*0.997*
Unknown spp	-0.199	(-0.452 to 0.084)	*0.166*	-0.054	(-0.328 to 0.228)	*0.708*	-0.176	(-0.433 to 0.108)	*0.222*
	Vegetables			***Legumes***			***Potatoes***		
	r	**95% CI**	***P***	**r**	**95% CI**	***P***	**r**	**95% CI**	***P***
Total Se	-0.188	(-0.443 to 0.095)	*0.190*	-0.218	(-0.468 to 0.064)	*0.128*	-0.295	(-0.530 to -0.019)	*0.037*
Organic Se	-0.037	(-0.312 to 0.244)	*0.800*	-0.223	(-0.472 to 0.064)	*0.120*	-0.051	(-0.325 to 0.230)	*0.723*
Se-SelenoP	-0.159	(-0.419 to 0.125)	*0.270*	-0.160	(-0.420 to 0.123)	*0.265*	-0.141	(-0.403 to 0.143)	*0.329*
Se-Met	-0.102	(-0.370 to 0.181)	*0.478*	-0.202	(-0.455 to 0.080)	*0.158*	0.006	(-0.272 to 0.284)	*0.965*
Se-Cys	0.405	(0.143 to 0.614)	*0.003*	0.188	(-0.095 to 0.443)	*0.190*	0.171	(-0.113 to 0.429)	*0.236*
Se-GPX	0.138	(-0.146 to 0.401)	*0.340*	-0.240	(-0.486 to 0.042)	*0.093*	0.090	(-0.193 to 0.360)	*0.533*
Se-TXNRD	-0.032	(-0.308 to 0.248)	*0.824*	0.124	(-0.160 to 0.389)	*0.392*	0.033	(-0.248 to 0.308)	*0.820*
Inorganic Se	-0.022	(-0.298 to 0.258)	*0.881*	0.190	(-0.094 to 0.445)	*0.186*	-0.085	(-0.355 to 0.198)	*0.558*
Se(IV)	-0.012	(-0.290 to 0.267)	*0.931*	0.191	(-0.093 to 0.445)	*0.184*	-0.129	(-0.393 to 0.155)	*0.373*
Se(VI)	-0.049	(-0.323 to 0.232)	*0.733*	0.085	(-0.198 to 0.355)	*0.555*	0.148	(-0.136 to 0.410)	*0.304*
Se-HSA	-0.106	(-0.374 to 0.177)	*0.462*	0.017	(-0.262 to 0.294)	*0.905*	-0.102	(-0.370 to 0.182)	*0.482*
Unknown spp	0.017	(-0.263 to 0.294)	*0.908*	-0.271	(-0.511 to 0.008)	*0.056*	-0.144	(-0.406 to 0.140)	*0.319*
	Fresh fruits			***Dry fruits***			***Sweets***		
	r	**95% CI**	***P***	**r**	**95% CI**	***P***	**r**	**95% CI**	***P***
Total Se	0.224	(-0.058 to 0.473)	*0.117*	-0.016	(-0.293 to 0.263)	*0.909*	-0.006	(-0.284 to 0.273)	*0.966*
Organic Se	-0.042	(-0.317 to 0.239)	*0.770*	-0.209	(-0.461 to 0.074)	*0.145*	0.041	(-0.240 to 0.316)	*0.778*
Se-SelenoP	-0.212	(-0.463 to 0.070)	*0.138*	-0.112	(-0.379 to 0.172)	*0.438*	0.128	(-0.156 to 0.393)	*0.374*
Se-Met	0.016	(-0.264 to 0.293)	*0.914*	-0.151	(-0.412 to 0.133)	*0.294*	0.120	(-0.164 to 0.385)	*0.408*
Se-Cys	0.484	(0.238 to 0.672)	*<0.001*	-0.074	(-0.345 to 0.209)	*0.609*	-0.425	(-0.629 to -0.166)	*0.002*
Se-GPX	0.114	(-0.170 to 0.380)	*0.430*	-0.147	(-0.409 to 0.136)	*0.306*	0.014	(-0.266 to 0.291)	*0.925*
Se-TXNRD	0.116	(-0.167 to 0.382)	*0.421*	-0.086	(-0.356 to 0.197)	*0.551*	-0.167	(-0.425 to 0.117)	*0.247*
Inorganic Se	0.062	(-0.221 to 0.334)	*0.670*	0.226	(-0.056 to 0.475)	*0.114*	0.039	(-0.242 to 0.314)	*0.789*
Se(IV)	0.054	(-0.228 to 0.327)	*0.711*	0.244	(-0.037 to 0.489)	*0.087*	0.036	(-0.245 to 0.311)	*0.805*
Se(VI)	0.063	(-0.219 to 0.336)	*0.663*	0.028	(-0.252 to 0.304)	*0.846*	0.031	(-0.249 to 0.307)	*0.828*
Se-HSA	0.217	(-0.066 to 0.467)	*0.130*	0.096	(-0.187 to 0.365)	*0.506*	-0.112	(-0.379 to 0.172)	*0.438*
Unknown spp	0.003	(-0.276 to 0.281)	*0.984*	-0.014	(-0.291 to 0.266)	*0.924*	0.052	(-0.230 to 0.326)	*0.719*

ACCEPTED MANUSCRIPT

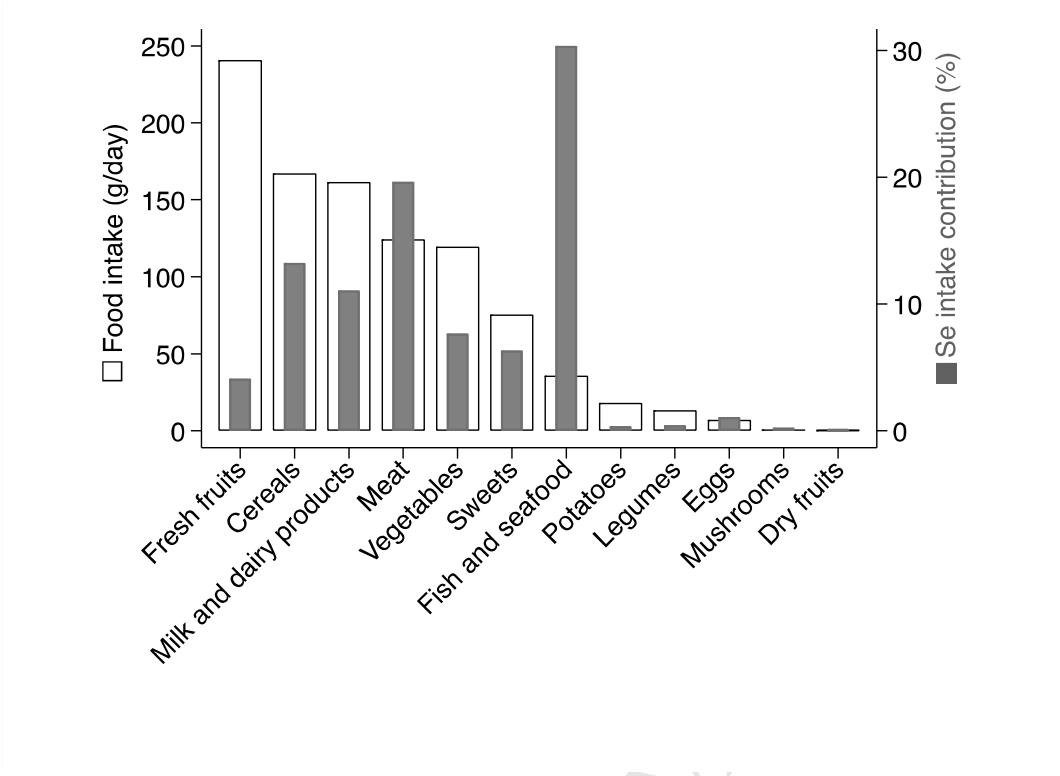
Figure 1. Distribution of dietary Se intake (µg/day) in selected subgroups (B). In the presented box plots, central rectangle spans from first to third quartile, and the segment inside the rectangle indicates median value, while "whiskers" above and below the box indicate minimum and maximum values, respectively.



ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

Figure 2. Distribution of intake (g/day) of selected foods with median (white bars) and their contribution (in percentage %) to overall Se intake (gray bars).



ACCEPTED MANUSCRIPT

References

B'Hymer, C., Caruso, J.A., 2006. Selenium speciation analysis using inductively coupled plasma-mass spectrometry. J Chromatogr A 1114, 1-20.
Baskett, C.K., V. L. Spate, V.L., Mason, M.M., Nichols, T.A., Williams, A., Dubman, I.M., Gudino, A., Denison, J., Morris, J.S., 2001. Long-term selenium status in humans. J Radioanal Nuc Chem 249, 429-435.
Behne, D., Gessner, H., Kyriakopoulos, A., 1996. Information on the selenium status of several body compartments of rats from the selenium concentrations in blood fractions, hair and nails. J Trace Elem Med Biol 10, 174-179.
Bhatia, P., Aureli, F., D'Amato, M., Prakash, R., Cameotra, S.S., Nagaraja, T.P., Cubadda, F., 2013. Selenium bioaccessibility and speciation in biofortified Pleurotus mushrooms grown on selenium-rich agricultural residues. Food Chem 140, 225-230.
Bierla, K., Dernovics, M., Vacchina, V., Szpunar, J., Bertin, G., Lobinski, R., 2008. Determination of selenocysteine and selenomethionine in edible animal tissues by 2D size-exclusion reversed-phase HPLC-ICP MS following carbamidomethylation and proteolytic extraction. Anal Bioanal Chem 390, 1789-1798.
Bogden, J.D., Kemp, F.W., Buse, M., Thind, I.S., Louria, D.B., Forgacs, J., Llanos, G., Moncoya Terrones, I., 1981. Composition of tobaccos from countries with high and low incidences of lung cancer. I. Selenium, polonium-210, Alternaria, tar, and nicotine. J Natl Cancer Inst 66, 27-31.
Borawska, M.H., Witkowska, A.M., Hukalowicz, K., Markiewicz, R., 2004. Influence of dietary habits on serum selenium concentration. Ann Nutr Metab 48, 134-140.
Bottecchi, I., Vinceti, M., 2012. [Trace elements in foods. Analysis of diet of Reggio Emilia and Modena], Department of Publich Health. University of Modena and Reggio Emilia, p. 124.
Bugel, S., Sandstrom, B., Skibsted, L.H., 2004. Pork meat: a good source of selenium? J Trace Elem Med Biol 17, 307-311.
Bugel, S.H., Sandstrom, B., Larsen, E.H., 2001. Absorption and retention of selenium from shrimps in man. J Trace Elem Med Biol 14, 198-204.
Bulteau, A.L., Chavatte, L., 2015. Update on selenoprotein biosynthesis. Antioxid Redox Signal 23, 775-794.
Burger, J., Gochfeld, M., 2013. Selenium and mercury molar ratios in commercial fish from New Jersey and Illinois: variation within species and relevance to risk communication. Food Chem Toxicol 57, 235-245.
Cabanero, A.I., Carvalho, C., Madrid, Y., Batoreu, C., Camara, C., 2005. Quantification and speciation of mercury and selenium in fish samples of high consumption in Spain and Portugal. Biol Trace Elem Res 103, 17-35.
Cabanero, A.I., Madrid, Y., Camara, C., 2007. Mercury-selenium species ratio in representative fish samples and their bioaccessibility by an in vitro digestion method. Biol Trace Elem Res 119, 195-211.
Cappon, C.J., Smith, J.C., 1982a. Chemical form and distribution of mercury and selenium in canned tuna. J Appl Toxicol 2, 181-189.
Cappon, C.J., Smith, J.C., 1982b. Chemical form and distribution of mercury and selenium in edible seafood. J Anal Toxicol 6, 10-21.
Castro Grijalba, A., Fiorentini, E.F., Wuilloud, R.G., 2017. Ionic liquid-assisted separation and determination of selenium species in food and beverage samples by liquid chromatography coupled to hydride generation atomic fluorescence spectrometry. J Chromatogr A 1491, 117-125.
Chan, Q., Afton, S.E., Caruso, J.A., 2010. Selenium speciation profiles in selenite-enriched soybean (Glycine Max) by HPLC-ICPMS and ESI-ITMS. Metallomics 2, 147-153.

ACCEPTED MANUSCRIPT
Chiu-Ugalde, J., Theilig, F., Behrends, T., Drebes, J., Sieland, C., Subbarayal, P., Kohrle, J., Hammes, A., Schomburg, L., Schweizer, U., 2010. Mutation of megalin leads to urinary loss of selenoprotein P and selenium deficiency in serum, liver, kidneys and brain. Biochem J 431, 103-111.
Cicero, C.E., Mostile, G., Vasta, R., Rapisarda, V., Signorelli, S.S., Ferrante, M., Zappia, M., Nicoletti, A., 2017. Metals and neurodegenerative diseases. A systematic review. Environ Res 159, 82-94.
Cocchi, L., Vescovi, L., Petrini, L.E., Petrini, O., 2006. Heavy metals in edible mushrooms in Italy. Food Chem 98, 277-284.
Combs, G.F., Jr., Watts, J.C., Jackson, M.I., Johnson, L.K., Zeng, H., Scheett, A.J., Uthus, E.O., Schomburg, L., Hoeg, A., Hoefig, C.S., Davis, C.D., Milner, J.A., 2011. Determinants of selenium status in healthy adults. Nutr J 10, 75.
Copat, C., Vinceti, M., D'Agati, M.G., Arena, G., Mauceri, V., Grasso, A., Fallico, R., Sciacca, S., Ferrante, M., 2014. Mercury and selenium intake by seafood from the Ionian Sea: A risk evaluation. Ecotoxicol Environ Saf 100, 87-92.
Cummins, L.M., Martin, J.L., 1967. Are selenocystine and selenomethionine synthesized in vivo from sodium selenite in mammals? Biochemistry 6, 3162-3168.
Di Dato, C., Gianfrilli, D., Greco, E., Astolfi, M., Canepari, S., Lenzi, A., Isidori, A.M., Giannetta, E., 2017. Profiling of selenium absorption and accumulation in healthy subjects after prolonged L-selenomethionine supplementation. J Endocrinol Invest 40, 1183-1190.
Diaz Huerta, V., Fernandez Sanchez, M.L., Sanz-Medel, A., 2006. An attempt to differentiate HPLC-ICP-MS selenium speciation in natural and selenised Agaricus mushrooms using different species extraction procedures. Anal Bioanal Chem 384, 902-907.
Esaki, N., Nakamura, T., Tanaka, H., Suzuki, T., Morino, Y., Soda, K., 1981. Enzymatic synthesis of selenocysteine in rat liver. Biochemistry 20, 4492-4496.
European Food Safety Authority, 2014. Scientific Opinion on Dietary Reference Values for selenium. EFSA Journal 12, 3846.
Fairweather-Tait, S.J., Bao, Y., Broadley, M.R., Collings, R., Ford, D., Hesketh, J.E., Hurst, R., 2011. Selenium in human health and disease. Antioxid Redox Signal 14, 1337-1383.
Fairweather-Tait, S.J., Collings, R., Hurst, R., 2010. Selenium bioavailability: current knowledge and future research requirements. Am J Clin Nutr 91, 1484S-1491S.
Falandysz, J., 2013. Review: on published data and methods for selenium in mushrooms. Food Chem 138, 242-250.
Fan, A.M., Vinceti, M., 2015. Selenium and its compounds, Hamilton & Hardy's Industrial Toxicology. John Wiley & Sons, Inc., pp. 205-228.
Ferrante, G., Minardi, V., Possenti, V., Quarchioni, E., Masocco, M., Salmaso, S., Braggion, M., Campostrini, S., Baldissera, S., Gruppo Tecnico, P., 2012. [Smoke: prevalence is decreasing, but the gap between socioeconomic categories remains]. Epidemiol Prev 36, 371.
Ferrante, M., Fiore, M., Ledda, C., Cicciu, F., Alonzo, E., Fallico, R., Platania, F., Di Mauro, R., Valenti, L., Sciacca, S., 2013. [Monitoring of heavy metals and trace elements in the air, fruits and vegetables and soil in the province of Catania (Italy)]. Ig Sanita Pubbl 69, 47-54.
Filippini, T., Cilloni, S., Malavolti, M., Violi, F., Malagoli, C., Tesauro, M., Bottecchi, I., Ferrari, A., Vescovi, L., Vinceti, M., 2018. Dietary intake of cadmium, chromium, copper, manganese, selenium and zinc in a Northern Italy community. Journal of Trace Elements in Medicine and Biology.
Filippini, T., Ferrari, A., Michalke, B., Grill, P., Vescovi, L., Salvia, C., Malagoli, C., Malavolti, M., Sieri, S., Krogh, V., Bargellini, A., Martino, A., Ferrante, M., Vinceti, M., 2017a. Toenail selenium as an indicator of environmental exposure: A cross-sectional study. Mol Med Rep 15, 3405-3412.
Filippini, T., Michalke, B., Grill, P., Malagoli, C., Malavolti, M., Vescovi, L., Sieri, S., Krogh, V., Cherubini, A., Maffeis, G., Lucchini, R., Ferrante, M., Vinceti, M., 2017b. Determinants of serum manganese levels in an Italian population. Mol Med Rep 15, 3340-3349.

ACCEPTED MANUSCRIPT
Filippini, T., Michalke, B., Malagoli, C., Grill, P., Bottecchi, I., Malavolti, M., Vescovi, L., Sieri, S., Krogh, V., Cherubini, A., Maffeis, G., Modenesi, M., Castiglia, P., Vinceti, M., 2016. Determinants of serum cadmium levels in a Northern Italy community: A cross-sectional study. Environ Res 150, 219-226.
Finley, J.W., 2005. Selenium accumulation in plant foods. Nutr Rev 63, 196-202.
Fox, P.M., LeDuc, D.L., Hussein, H., Lin, Z.-q., Terry, N., 2002. Selenium Speciation in Soils and Plants, Biogeochemistry of Environmentally Important Trace Elements. American Chemical Society, pp. 339-354.
Fox, T.E., Van den Heuvel, E.G., Atherton, C.A., Dainty, J.R., Lewis, D.J., Langford, N.J., Crews, H.M., Luten, J.B., Lorentzen, M., Sieling, F.W., van Aken-Schneyder, P., Hoek, M., Kotterman, M.J., van Dael, P., Fairweather-Tait, S.J., 2004. Bioavailability of selenium from fish, yeast and selenate: a comparative study in humans using stable isotopes. Eur J Clin Nutr 58, 343-349.
Galant, L.S., Braga, M.M., de Souza, D., de Bem, A.F., Sancineto, L., Santi, C., da Rocha, J.B.T., 2017. Induction of reactive oxygen species by diphenyl diselenide is preceded by changes in cell morphology and permeability in Saccharomyces cerevisiae. Free Radic Res 51, 657-668.
Gammelgaard, B., Sturup, S., Christensen, M.V., 2012. Human urinary excretion and metabolism of (82)Se-enriched selenite and selenate determined by LC-ICP-MS. Metallomics 4, 149-155.
Gladyshev, V.N., Carlson, B.A., Hatfield, D.L., 2016. Pathways in De Novo Biosynthesis of Selenocysteine and Cysteine in Eukaryotes, in: D.L. Hatfield, U. Schweizer, P.A. Tsuji, V.N. Gladyshev (Eds.), Selenium: Its Molecular Biology and Role in Human Health. Springer International Publishing, Cham, pp. 39-45.
Gruppo Tecnico PASSI Emilia-Romagna, 2012. Sovrappeso e obesità in Emilia-Romagna: dati del sistema di sorveglianza PASSI (anni 2008-2011).
Gudmundsdottir, E.Y., Gunnarsdottir, I., Thorlacius, A., Reykdal, O., Gunnlaugsdottir, H., Thorsdottir, I., Steingrimsdottir, L., 2012. Blood selenium levels and contribution of food groups to selenium intake in adolescent girls in Iceland. Food Nutr Res 56.
Heck, J.E., Park, A.S., Qiu, J., Cockburn, M., Ritz, B., 2014. Risk of leukemia in relation to exposure to ambient air toxics in pregnancy and early childhood. Int J Hyg Environ Health 217, 662-668.
Huang, W., Akesson, B., Svensson, B.G., Schutz, A., Burk, R.F., Skerfving, S., 1995. Selenoprotein P and glutathione peroxidase (EC 1.11.1.9) in plasma as indices of selenium status in relation to the intake of fish. Br J Nutr 73, 455-461.
Ito, K., Mathes, R., Ross, Z., Nadas, A., Thurston, G., Matte, T., 2011. Fine particulate matter constituents associated with cardiovascular hospitalizations and mortality in New York City. Environ Health Perspect 119, 467-473.
Jablonska, E., Vinceti, M., 2015. Selenium and human health: Witnessing a Copernican revolution? J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 33, 328-368.
Jager, T., Drexler, H., Goen, T., 2016. Human metabolism and renal excretion of selenium compounds after oral ingestion of sodium selenate dependent on trimethylselenium ion (TMSe) status. Arch Toxicol 90, 149-158.
Labunskyy, V.M., Hatfield, D.L., Gladyshev, V.N., 2014. Selenoproteins: molecular pathways and physiological roles. Physiol Rev 94, 739-777.
Lazard, M., Dauplais, M., Blanquet, S., Plateau, P., 2017. Recent advances in the mechanism of selenoamino acids toxicity in eukaryotic cells. Biomol Concepts 8, 93-104.
LeBlanc, A., Dumas, P., Lefebvre, L., 1999. Trace element content of commercial shampoos: impact on trace element levels in hair. Sci Total Environ 229, 121-124.
Lee, K.H., Jeong, D., 2012. Bimodal actions of selenium essential for antioxidant and toxic pro-oxidant activities: the selenium paradox (Review). Mol Med Rep 5, 299-304.

ACCEPTED MANUSCRIPT
Letsiou, S., Nomikos, T., Panagiotakos, D., Pergantis, S.A., Fragopoulou, E., Antonopoulou, S., Pitsavos, C., Stefanadis, C., 2010. Dietary habits of Greek adults and serum total selenium concentration: the ATTICA study. Eur J Nutr 49, 465-472.
Li, J.L., Li, H.X., Li, S., Gao, X.J., Xu, S.W., Tang, Z.X., 2012. Effects of Selenoprotein W gene expression by selenium involves regulation of mRNA stability in chicken embryos neurons. Biometals 25, 459-468.
Lipiec, E., Siara, G., Bierla, K., Ouerdane, L., Szpunar, J., 2010. Determination of selenomethionine, selenocysteine, and inorganic selenium in eggs by HPLC-inductively coupled plasma mass spectrometry. Anal Bioanal Chem 397, 731-741.
Lombardi-Boccia, G., Aguzzi, A., Cappelloni, M., Di Lullo, G., Lucarini, M., 2003. Total-diet study: dietary intakes of macro elements and trace elements in Italy. Br J Nutr 90, 1117-1121.
Lyubenova, L., Sabodash, X., Schroder, P., Michalke, B., 2015. Selenium species in the roots and shoots of chickpea plants treated with different concentrations of sodium selenite. Environ Sci Pollut Res Int 22, 16978-16986.
Malagoli, C., Malavolti, M., Agnoli, C., Crespi, C.M., Fiorentini, C., Farnetani, F., Longo, C., Ricci, C., Albertini, G., Lanzoni, A., Veneziano, L., Virgili, A., Pagliarello, C., Santini, M., Fanti, P.A., Dika, E., Sieri, S., Krogh, V., Pellacani, G., Vinceti, M., 2015. Diet quality and risk of melanoma in an Italian population. J Nutr 145, 1800-1807.
Malavolti, M., Malagoli, C., Fiorentini, C., Longo, C., Farnetani, F., Ricci, C., Albertini, G., Lanzoni, A., Reggiani, C., Virgili, A., Pagliarello, C., Santini, M., Fanti, P.A., Dika, E., Sieri, S., Krogh, V., Pellacani, G., Vinceti, M., 2013. Association between dietary vitamin C and risk of cutaneous melanoma in a population of Northern Italy. Int J Vitam Nutr Res 83, 291-298.
Mandrioli, J., Michalke, B., Solovyev, N., Grill, P., Violi, F., Lunetta, C., Conte, A., Sansone, V.A., Sabatelli, M., Vinceti, M., 2017. Elevated levels of selenium species in cerebrospinal fluid of amyotrophic lateral sclerosis patients with disease-associated gene mutations. Neurodegener Dis 17, 171-180.
Mariottini, E., Capel, R., Bigazzi Grasso, C., 1995. Selenium content in foods. J Prev Med Hyg 36, 55-60.
Marschall, T.A., Bornhorst, J., Kuehnelt, D., Schwerdtle, T., 2016. Differing cytotoxicity and bioavailability of selenite, methylselenocysteine, selenomethionine, selenosugar 1 and trimethylselenonium ion and their underlying metabolic transformations in human cells. Mol Nutr Food Res 60, 2622-2632.
Meltzer, H.M., Bibow, K., Paulsen, I.T., Mundal, H.H., Norheim, G., Holm, H., 1993. Different bioavailability in humans of wheat and fish selenium as measured by blood-platelet response to Increased dietary Se. Biol Trace Elem Res 36, 229-241.
Michalke, B., 2016. Review about the manganese speciation project related to neurodegeneration: An analytical chemistry approach to increase the knowledge about manganese related parkinsonian symptoms. J Trace Elem Med Biol 37, 50-61.
Michalke, B., Berthele, A., 2011. Contribution to selenium speciation in cerebrospinal fluid samples. J Anal Atom Spectrom 26, 165-170.
Michalke, B., Halbach, S., Nischwitz, V., 2009. JEM spotlight: metal speciation related to neurotoxicity in humans. J Environ Monit 11, 939-954.
Michalke, B., Solovyev, N., Vinceti, M., 2017a. Se-speciation investigations at neural barrier (NB), Se2017—200 Years of Selenium Research 1817–2017, Stockholm, 2017.
Michalke, B., Willkommena, D., Drobyshevb, E., Solovyev, N., 2017b. The importance of speciation analysis in neurodegeneration research. Trends Analyt Chem (in press).
Misra, S., Peak, D., Chen, N., Hamilton, C., Niyogi, S., 2012. Tissue-specific accumulation and speciation of selenium in rainbow trout (*Oncorhynchus mykiss*) exposed to elevated dietary selenomethionine. Comp Biochem Physiol C Toxicol Pharmacol 155, 560-565.

ACCEPTED MANUSCRIPT
Montes-Bayon, M., LeDuc, D.L., Terry, N., Caruso, J.A., 2002. Selenium speciation in wild-type and genetically modified Se accumulating plants with HPLC separation and ICP-MS/ES-MS detection. Journal of Analytical Atomic Spectrometry 17, 872-879.
Moreda-Pineiro, J., Moreda-Pineiro, A., Romaris-Hortas, V., Dominguez-Gonzalez, R., Alonso-Rodriguez, E., Lopez-Mahia, P., Muniategui-Lorenzo, S., Prada-Rodriguez, D., Bermejo-Barrera, P., 2013. In vitro bioavailability of total selenium and selenium species from seafood. Food Chem 139, 872-877.
Muniz-Naveiro, O., Dominguez-Gonzalez, R., Bermejo-Barrera, A., Bermejo-Barrera, P., Cocho, J.A., Fraga, J.M., 2007. Selenium speciation in cow milk obtained after supplementation with different selenium forms to the cow feed using liquid chromatography coupled with hydride generation-atomic fluorescence spectrometry. Talanta 71, 1587-1593.
Naderi, M., Salahinejad, A., Jamwal, A., Chivers, D.P., Niyogi, S., 2017. Chronic dietary selenomethionine exposure induces oxidative stress, dopaminergic dysfunction, and cognitive impairment in adult zebrafish (*Danio rerio*). Environ Sci Technol 51, 12879-12888.
Navarro-Alarcon, M., Cabrera-Vique, C., 2008. Selenium in food and the human body: a review. Sci Total Environ 400, 115-141.
Oliveira, C.S., Piccoli, B.C., Aschner, M., Rocha, J.B.T., 2017. Chemical speciation of selenium and mercury as determinant of their neurotoxicity. Adv Neurobiol 18, 53-83.
Olmedo, P., Hernandez, A.F., Pla, A., Femia, P., Navas-Acien, A., Gil, F., 2013. Determination of essential elements (copper, manganese, selenium and zinc) in fish and shellfish samples. Risk and nutritional assessment and mercury-selenium balance. Food Chem Toxicol 62, 299-307.
Olson, G.E., Winfrey, V.P., Hill, K.E., Burk, R.F., 2008. Megalin mediates selenoprotein P uptake by kidney proximal tubule epithelial cells. J Biol Chem 283, 6854-6860.
Olson, G.E., Winfrey, V.P., Nagdas, S.K., Hill, K.E., Burk, R.F., 2007. Apolipoprotein E receptor-2 (ApoER2) mediates selenium uptake from selenoprotein P by the mouse testis. J Biol Chem 282, 12290-12297.
Ortman, K., Pehrson, B., 1999. Effect of selenate as a feed supplement to dairy cows in comparison to selenite and selenium yeast. J Anim Sci 77, 3365-3370.
Pala, V., Sieri, S., Palli, D., Salvini, S., Berrino, F., Bellegotti, M., Frasca, G., Tumino, R., Sacerdote, C., Fiorini, L., Celentano, E., Galasso, R., Krogh, V., 2003. Diet in the Italian EPIC cohorts: presentation of data and methodological issues. Tumori 89, 594-607.
Pasanisi, P., Berrino, F., Bellati, C., Sieri, S., Krogh, V., 2002. Validity of the Italian EPIC questionnaire to assess past diet. IARC Sci Publ 156, 41-44.
Pennington, J.A., Wilson, D.B., Newell, R.F., Harland, B.F., Johnson, R.D., Vanderveen, J.E., 1984. Selected minerals in foods surveys, 1974 to 1981/82. J Am Diet Assoc 84, 771-780.
Pettem, C.M., Weber, L.P., Janz, D.M., 2017. Cardiac and metabolic effects of dietary selenomethionine exposure in adult zebrafish. Toxicol Sci 159, 449-460.
Phipps, R.H., Grandison, A.S., Jones, A.K., Juniper, D.T., Ramos-Morales, E., Bertin, G., 2008. Selenium supplementation of lactating dairy cows: effects on milk production and total selenium content and speciation in blood, milk and cheese. Animal 2, 1610-1618.
Piepponen, S., Liukkonen-Lilja, H., Kuusi, T., 1983. The selenium content of edible mushrooms in Finland. Z Lebensm Unters Forsch 177, 257-260.
Plateau, P., Saveanu, C., Lestini, R., Dauplais, M., Decourty, L., Jacquier, A., Blanquet, S., Lazard, M., 2017. Exposure to selenomethionine causes selenocysteine misincorporation and protein aggregation in *Saccharomyces cerevisiae*. Sci Rep 7, 44761.
Pounis, G., Costanzo, S., Persichillo, M., de Curtis, A., Sieri, S., Vinceti, M., Zito, F., Di Castelnuovo, A.F., Donati, M.B., de Gaetano, G., Iacoviello, L., Moli-sani Project, I., 2014. Mushroom and dietary selenium intakes in relation to fasting glucose levels in a free-living Italian adult population: the Moli-sani Project. Diabetes Metab 40, 34-42.

ACCEPTED MANUSCRIPT
Rayman, M.P., 2008. Food-chain selenium and human health: emphasis on intake. Br J Nutr 100, 254-268.
Rezacova, K., Canova, K., Bezrouk, A., Rudolf, E., 2016. Selenite induces DNA damage and specific mitochondrial degeneration in human bladder cancer cells. Toxicol In Vitro 32, 105-114.
Ruiz-de-Cenzano, M., Rochina-Marco, A., Cervera, M.L., de la Guardia, M., 2017. Evaluation of the content of antimony, arsenic, bismuth, selenium, tellurium and their inorganic forms in commercially baby foods. Biol Trace Elem Res 180, 355-365.
Satia, J.A., King, I.B., Morris, J.S., Stratton, K., White, E., 2006. Toenail and plasma levels as biomarkers of selenium exposure. Ann Epidemiol 16, 53-58.
Schmidt, R.L., Simonovic, M., 2012. Synthesis and decoding of selenocysteine and human health. Croat Med J 53, 535-550.
Schubert, A., Holden, J.M., Wolf, W.R., 1987. Selenium content of a core group of foods based on a critical evaluation of published analytical data. J Am Diet Assoc 87, 285-299.
Sele, V., Ørnsrud, R., Sloth, J.J., Berntssen, M.H.G., Amlund, H., 2018. Selenium and selenium species in feeds and muscle tissue of Atlantic salmon. Journal of Trace Elements in Medicine and Biology 47, 124-133.
Selvaraj, V., Tomblin, J., Yeager Armistead, M., Murray, E., 2013. Selenium (sodium selenite) causes cytotoxicity and apoptotic mediated cell death in PLHC-1 fish cell line through DNA and mitochondrial membrane potential damage. Ecotoxicol Environ Saf 87, 80-88.
Shacklette, H.T., Boerngen, J.G., 2013. Element concentrations in soils and other surficial materials of the conterminous United States, Washington.
Shen, L., Van Dael, P., Luten, J., Deelstra, H., 1996. Estimation of selenium bioavailability from human, cow's, goat and sheep milk by an in vitro method. Int J Food Sci Nutr 47, 75-81.
Slotnick, M.J., Nriagu, J.O., 2006. Validity of human nails as a biomarker of arsenic and selenium exposure: A review. Environ Res 102, 125-139.
Socha, K., Kochanowicz, J., Karpinska, E., Soroczynska, J., Jakoniuk, M., Mariak, Z., Borawska, M.H., 2014. Dietary habits and selenium, glutathione peroxidase and total antioxidant status in the serum of patients with relapsing-remitting multiple sclerosis. Nutr J 13, 62.
Solovyev, N., Berthele, A., Michalke, B., 2013. Selenium speciation in paired serum and cerebrospinal fluid samples. Anal Bioanal Chem 405, 1875-1884.
Stefanka, Z., Ipolyi, I., Dernovics, M., Fodor, P., 2001. Comparison of sample preparation methods based on proteolytic enzymatic processes for Se-speciation of edible mushroom (*Agaricus bisporus*) samples. Talanta 55, 437-447.
Sunde, R.A., Raines, A.M., Barnes, K.M., Evenson, J.K., 2009. Selenium status highly regulates selenoprotein mRNA levels for only a subset of the selenoproteins in the selenoproteome. Biosci Rep 29, 329-338.
Suzuki, K.T., Doi, C., Suzuki, N., 2006. Metabolism of 76Se-methylselenocysteine compared with that of 77Se-selenomethionine and 82Se-selenite. Toxicol Appl Pharmacol 217, 185-195.
Terry, N., Zayed, A.M., De Souza, M.P., Tarun, A.S., 2000. Selenium in Higher Plants. Annu Rev Plant Physiol Plant Mol Biol 51, 401-432.
Thavarajah, D., Vandenberg, A., George, G.N., Pickering, I.J., 2007. Chemical form of selenium in naturally selenium-rich lentils (Lens culinaris L.) from Saskatchewan. J Agric Food Chem 55, 7337-7341.
Tolu, J., Thiry, Y., Bueno, M., Jolivet, C., Potin-Gautier, M., Le Hecho, I., 2014. Distribution and speciation of ambient selenium in contrasted soils, from mineral to organic rich. Sci Total Environ 479-480, 93-101.
Turrini, A., Saba, A., Perrone, D., Cialfa, E., D'Amicis, A., 2001. Food consumption patterns in Italy: the INN-CA Study 1994-1996. Eur J Clin Nutr 55, 571-588.

ACCEPTED MANUSCRIPT
van der Torre, H.W., Van Dokkum, W., Schaafsma, G., Wedel, M., Ockhuizen, T., 1991. Effect of various levels of selenium in wheat and meat on blood Se status indices and on Se balance in Dutch men. Br J Nutr 65, 69-80.
Vinceti, M., Ballotari, P., Steinmaus, C., Malagoli, C., Luberto, F., Malavolti, M., Giorgi Rossi, P., 2016a. Long-term mortality patterns in a residential cohort exposed to inorganic selenium in drinking water. Environ Res 150, 348-356.
Vinceti, M., Burlingame, B., Filippini, T., Naska, A., Bargellini, A., Borella, P., 2016b. The epidemiology of selenium and human health, in: D.L. Hatfield, U. Schweizer, P.A. Tsuji, V.N. Gladyshev (Eds.), Selenium: Its molecular biology and role in human health. Springer International Publishing, Cham, pp. 365-376.
Vinceti, M., Chiari, A., Eichmuller, M., Rothman, K.J., Filippini, T., Malagoli, C., Weuve, J., Tondelli, M., Zamboni, G., Nichelli, P.F., Michalke, B., 2017a. A selenium species in cerebrospinal fluid predicts conversion to Alzheimer's dementia in persons with mild cognitive impairment. Alzheimers Res Ther 9, 100.
Vinceti, M., Crespi, C.M., Malagoli, C., Del Giovane, C., Krogh, V., 2013a. Friend or foe? The current epidemiologic evidence on selenium and human cancer risk. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 31, 305-341.
Vinceti, M., Filippini, T., Cilloni, S., Bargellini, A., Vergoni, A.V., Tsatsakis, A., Ferrante, M., 2017b. Health risk assessment of environmental selenium: Emerging evidence and challenges (Review). Mol Med Rep 15, 3323-3335.
Vinceti, M., Filippini, T., Cilloni, S., Crespi, C.M., 2017c. The epidemiology of selenium and human cancer. Adv Cancer Res 136, 1-48.
Vinceti, M., Filippini, T., Del Giovane, C., Dennert, G., Zwahlen, M., Brinkman, M., Zeegers, M.P., Horneber, M., D'Amico, R., Crespi, C.M., 2018. Selenium for preventing cancer. Cochrane Database Syst Rev Issue 1, CD005195.
Vinceti, M., Grill, P., Malagoli, C., Filippini, T., Storani, S., Malavolti, M., Michalke, B., 2015a. Selenium speciation in human serum and its implications for epidemiologic research: a cross-sectional study. J Trace Elem Med Biol 31, 1-10.
Vinceti, M., Grioni, S., Alber, D., Consonni, D., Malagoli, C., Agnoli, C., Malavolti, M., Pala, V., Krogh, V., Sieri, S., 2015b. Toenail selenium and risk of type 2 diabetes: the ORDET cohort study. J Trace Elem Med Biol 29, 145-150.
Vinceti, M., Mandrioli, J., Borella, P., Michalke, B., Tsatsakis, A., Finkelstein, Y., 2014. Selenium neurotoxicity in humans: bridging laboratory and epidemiologic studies. Toxicol Lett 230, 295-303.
Vinceti, M., Maraldi, T., Bergomi, M., Malagoli, C., 2009. Risk of chronic low-dose selenium overexposure in humans: insights from epidemiology and biochemistry. Rev Environ Health 24, 231-248.
Vinceti, M., Rovesti, S., Bergomi, M., Vivoli, G., 2000. The epidemiology of selenium and human cancer. Tumori 86, 105-118.
Vinceti, M., Solovyev, N., Mandrioli, J., Crespi, C.M., Bonvicini, F., Arcolin, E., Georgoulopoulou, E., Michalke, B., 2013b. Cerebrospinal fluid of newly diagnosed amyotrophic lateral sclerosis patients exhibits abnormal levels of selenium species including elevated selenite. Neurotoxicology 38, 25-32.
Wallenberg, M., Misra, S., Wasik, A.M., Marzano, C., Bjornstedt, M., Gandin, V., Fernandes, A.P., 2014. Selenium induces a multi-targeted cell death process in addition to ROS formation. J Cell Mol Med 18, 671-684.
Weekley, C.M., Harris, H.H., 2013. Which form is that? The importance of selenium speciation and metabolism in the prevention and treatment of disease. Chem Soc Rev 42, 8870-8894.
Whanger, P.D., 2002. Selenocompounds in plants and animals and their biological significance. J Am Coll Nutr 21, 223-232.

ACCEPTED MANUSCRIPT
Whitcomb, B.W., Schisterman, E.F., 2008. Assays with lower detection limits: implications for epidemiological investigations. Paediatr Perinat Epidemiol 22, 597-602.
Willett, W.C., 2013. Nutritional epidemiology. Third Edition. Oxford University Press, New York.
Wolf, W.R., Goldschmidt, R.J., 2007. Updated estimates of the selenomethionine content of NIST wheat reference materials by GC-IDMS. Anal Bioanal Chem 387, 2449-2452.

ACCEPTED MANUSCRIPT

ACCEPTED MANUSCRIPT

Highlights:

- Selenium species concentrations in serum shows different correlation pattern with food intake
- Inorganic selenium positively correlates with intake of fish, legumes and dry fruits, and negatively with dairy products
- Organic selenocysteine-bound selenium positively correlated with intake of cereals, eggs, vegetables and fresh fruits, and negatively with sweets

ACCEPTED MANUSCRIPT