The Italian national TDS

Intake of nutrients and exposure to contaminants of the Italian population

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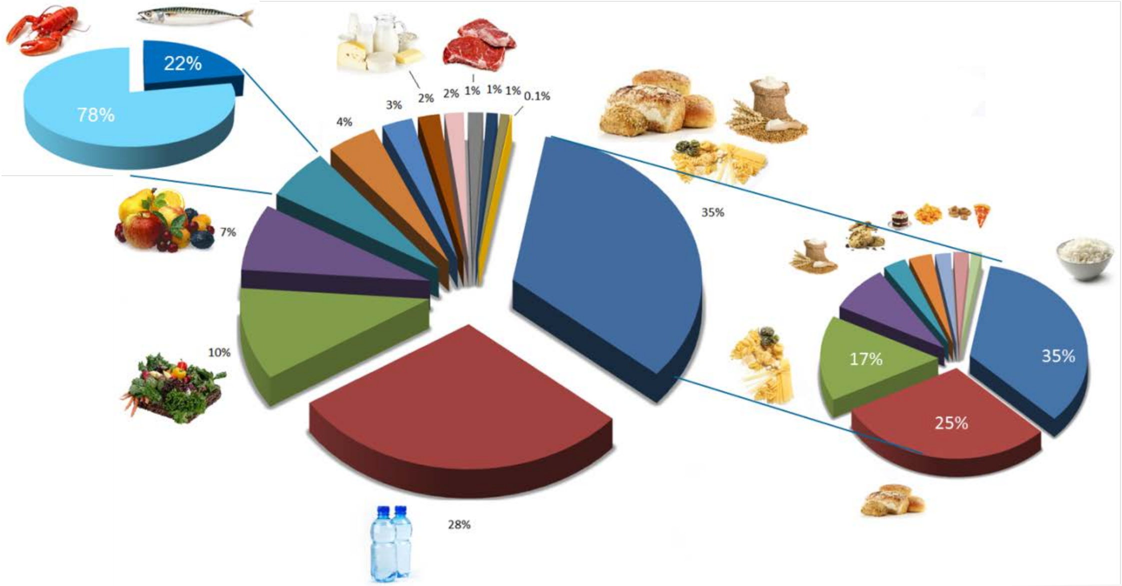


6th International Workshop on Total Diet Studies (TDS): Global Developments in TDS
Berline, 10-11 October 2022

Design of the Italian national TDS

Tailoring the Italian TDS to specific exposure assessment needs: an intermediate level of detail was chosen, with 51 core foods covered

- **Two extremes in TDS design**
  - **Screening approach**
    10-20 food groups
  - **Refined approach**
    200-300 food groups

- **Italian TDS 2012-2014**
  - **Food list**
    51 food groups
  - **Regional/geographical variability**
    Food groups from the 4 main Italian geographical areas not pooled: 204 final analytical samples

The numbers of the Italian TDS

- Substances
  65
- Geographical areas
  4
- Food groups
  51
- Elementary food samples collected
  >3000
- Estimated number of analytical readings
  23,000
- Individual exposure data
  Some dozen thousand

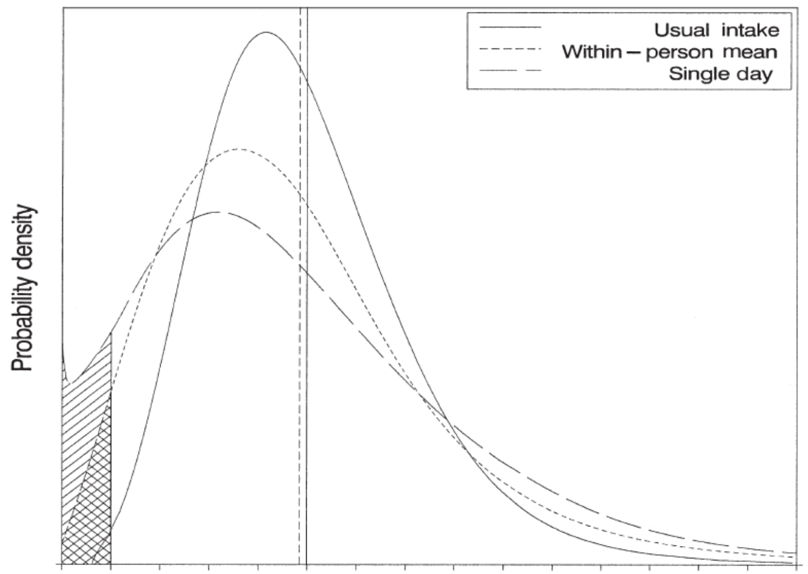
Exposure assessment and risk characterization strategy (1)

For chronic risk assessment calculations, there is a need for data on "usual" daily intake of a dietary component, commonly identified as the average daily intake over the past year

- **Dietary measurements** collected with 24-HR and dietary records cover **food consumption over a limited timeframe**, i.e. one day when one single measurement per subject is collected

- Limitation of the use of short-term food consumption instruments to estimate "usual" intake is that **individual diets can vary greatly from day to day**

- **Measured intakes over a limited number of days** incorporate considerable **within-person variability** making making them a **poor estimate of "usual" intake**



Dodd et al. 2006 (J Am Diet Assoc 106:1640)

Exposure assessment and risk characterization strategy (2)

Food consumption data at the basis of the TDS were 3-d individual dietary records: they were used as such to estimate the intake of nutrients and exposure to contaminants

- To translate **short-term measurements** of intake into **estimates of "usual" consumption** statistical modeling may be used. In the case of the food consumption data at the basis of the Italian TDS, **3-d individual dietary records** were collected. Therefore **consumption data were used as such** to estimate the intake of nutrients and exposure to contaminants

- **For nutrients** the **AR cut-point method** was used to estimate the **proportion of individuals whose intakes are not meeting their requirements**

  Conditions for validity of the method are: (1) intakes and requirements for the nutrient must be independent, (2) the distribution of requirements must be approximately symmetric around its mean, the AR, and (3) the variance of the distribution of requirements should be smaller than the variance of the usual intake distribution

- **For contaminants** the individual intake was compared with the **HBGVs** to establish the **percentage of the sample** exceeding them

Exposure assessment and risk characterization strategy (3)

Nutrients: EFSA Dietary Reference Values (DRVs)

- **Average Requirement (AR)** The level of nutrient intake that is enough for half of the people in a healthy group, given a normal distribution of requirements
- **Population Reference Intake (PRI)** The level of (nutrient) intake that is enough for virtually all healthy people in a group
- **Adequate Intake (AI)** The value estimated when a PRI cannot be established because an average requirement cannot be determined
- **Tolerable Upper intake Level (UL)** The maximum level of total chronic daily intake of a nutrient (from all sources) unlikely to pose a risk of adverse health effects

Contaminants: EFSA Health-based guidance values (HBGVs)

- **Tolerable daily/weekly intake (TDI or TWI)** The amount of a substance which can be consumed over a lifetime without presenting an appreciable risk to health
- **Benchmark-dose lower bound (BMDL)** A reference value derived from the Benchmark dose (BMD)* of low concern from a public health point of view

* The minimum dose of a substance that produces a clear, low level health risk, usually in the range of a 1-10% change in a specific toxic effect

Elements considered in the design of the Italian TDS

❑ Establishing the TDS food list and level of pooling

- Reference diet: the national individual food consumption survey
- Selection of the target population groups
- Characterization of the TDS food list (level of pooling)

❑ Sampling plan

- Addressing geographical variability: four main geographical areas
- Addressing seasonality: identification of the core foods to be sampled in different seasons
- Characterization of the TDS food shopping list: individual foods to be sampled
- Achieving representativeness by appropriate selection of sample collection premises

❑ Food collection and preparation

- Food collection and transport
- Kitchen preparation

❑ Chemical analysis

- Sample preparation for chemical analyses
- Performance criteria for analytical methods and analytical quality assurance

Design of the Italian TDS

Reference diet

National individual food consumption survey 'INRAN-SCAI 2005-06'

- Cross-sectional study where households were randomly selected after geographical stratification of the national territory
- Food consumption of 3323 subjects was assessed on 3 consecutive days through individual estimated dietary records

Public Health Nutrition 12:2504

TDS food list

Individual consumption data

Source: INRAN-SCAI 2005-06

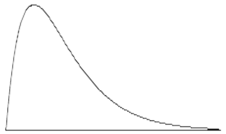
Food shopping list

Detailed description of products to be sampled for the 51 food groups

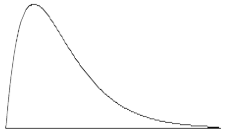
Sources: Annexes of INRAN-SCAI 2005-06, Istat and other official statistics, Market share data

Sampling, food preparation, chemical analysis (3 years)

Occurrence data



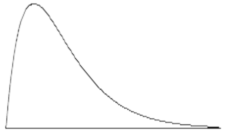
Consumption data



65 nutrients and contaminants

Intake data

By gender, age group, geographic area



Risk characterization

(comparison with DRVs/HBGVs)

Selection of the target population groups

Based on the individual data from the National Food Consumption Survey the following population (sub)groups were selected:

- **Two genders**
- Four age classes, i.e. **children** (3-9.9 years), **teenagers** (10-17.9 years), **adults** (18-64.9 years) and **elderly people** (≥ 65 years)
- A fifth age group - **infants and toddlers** (0–2.9 years) - was considered but limited statistics could be performed because of the sample size (*n* = 52) in the food consumption survey

TDS food list

TDS Food List showing the average daily consumption in g/d by food category in the total population (all ages, males and females), the percentage contribution of each food (in parenthesis), the percentage of consumers of each food and food category, the TDS sampling year, the number of TDS samples analysed (pooled samples) and collected at retail (individual sample)

Food categories	Consumption	Consumers (%)
Cereals, cereal products and substitutes	**258.4**	**99.8**
Bread	(40)	92.1
Pasta	(21)	91.1
Pizza	(3)	13.9
Rice	(6)	41.2
Wheat, other cereals and flours	(14)	84.1
Breakfast cereals	(1)	10.1
Biscuits	(5)	50.6
Savoury fine bakery products	(3)	38.0
Cakes and sweet snacks	(7)	44.4
Pulses, fresh and processed	**11.3**	**34.6**
Vegetables, fresh and processed	**211.2**	**99.6**
Leafy vegetables, fresh	(20)	84.0
Tomatoes, fresh	(20)	83.6
Other fruiting vegetables, fresh	(15)	64.3
Roots and onions, fresh	(9)	97.8
Other vegetables, fresh	(18)	82.9
Vegetables, processed	(17)	78.0
Spices and herbs	(1)	83.1

Food categories	Consumption	Consumers (%)
Potatoes, tubers and their products	**50.9**	**69.2**
Fruit, fresh and processed	**208.5**	**93.7**
Citrus fruit, fresh	(22)	46.9
Exotic fruit, fresh	(8)	38.9
Other fruit, fresh	(68)	83.1
Nuts, seeds, olives and their products, dried fruit	(1)	27.1
Meat, meat products and substitutes	**110.1**	**99.0**
Beef and veal, not preserved, excl. offal	(39)	75.2
Pork, not preserved, excl. offal	(12)	31.4
Poultry and game, not preserved, excl. offal	(19)	42.4
Other meats, not preserved, excl. offal	(5)	10.2
Ham, salami, sausages and other preserved meats, excl. offal	(25)	81.3
Offal, blood and their products	(1)	3.3
Fish, seafood and their products	**44.7**	**68.0**
Fish	(70)	62.0
Crustaceans and molluscs	(30)	21.8
Milk, milk products and substitutes	**198.0**	**99.2**
Milk, milk-based beverages, infant formula	(60)	78.6
Yoghurt and fermented milk	(10)	86.3
Cheese	(29)	96.7

Food categories	Consumption	Consumers (%)
Oils and fats	**40.4**	**99.7**
Olive oil	(81)	99.7
Other vegetable oils	(6)	41.8
Butter and creams	(10)	45.7
Other fats	(2)	17.9
Eggs	**20.9**	**74.3**
Alcoholic beverages	**91.0**	**74.5**
Regular wine	(70)	69.7
Beer, cider	(27)	16.6
Sweet wine, spumante, wine-based appetizers, spirits and liquors	(3)	13.2
Sweet products and substitutes	**33.1**	**93.2**
Ice cream and ice lolly	(30)	20.3
Chocolate and substitutes	(8)	22.7
Candies, jam and other sweet products (incl. sugar-free)	(10)	26.6
Sugar, fructose, honey and other nutritious sweeteners	(50)	84.9
Cocoa and cocoa-based powder	(2)	9.6
Water and other non-alcoholic beverages	**836.1**	**99.9**
Tap water (as such, in beverages or recipes)	(23)	57.1
Bottled water	(54)	76.5
Coffee, tea, and herbal tea	(15)	87.7

D'Amato et al. (2013) Ann Ist Super Sanità 49:272

Addressing geographical variability

Regional variability: Four cities were selected for food sampling to represent the four main geographical areas of Italy

Despite limitations due to budget issues this design allowed to **investigate geographical variability**, which is **rarely addressed in TDSs**

Occurrence data from each area were combined with **consumption data** for the same area to obtain **area-specific intake estimates**

D'Amato et al. (2013) Ann Ist Super Sanità 49:272

TDS food shopping list

The TDS food list was translated into a food shopping list, i.e. the list of individual food items to be sampled

Information sources to identify the specific products to be sampled

Details on **individual foods** listed in the annexes of the National Food Consumption Survey

Species, variety, origin and available national statistics were used to detail the types of **fresh food**

Food formulation, type of processing and market share data allowed to identify types and brands of the **packed foods** to be sampled at large-scale retail trade

Selection of sample collection premises

Sample collection premises were selected to ensure representativeness

- **Specific retail outlets were selected for each core food according to consumer habits**
- **Hyper and supermarket supplied by different distribution centres have been chosen so as to reflect the structure of food retailing in Italy**
- **Tap water is the only food in a TDS that is not bought: samples collected at different sites in each location**

  - **> 3000** products, i.e. **elementary samples**, were collected
  - Elementary samples were pooled into **944 individual samples**
  - Individual samples were pooled into the 51 core foods in each of the 4 areas, to yield **204 final analytical samples**
  - The **relative proportion** of each individual sample within the pooled sample reflects its importance in the average Italian diet

Kitchen preparation

Individual food samples that were not ready-to-eat were prepared and cooked according to normal consumer practices

- **Cooking was performed according to standard recipes for each geographical area**

- **For boiled food, salt was always added to boiling water in standardized conditions**
  - This in order to closely simulate actual household conditions, and considering aspects such as osmotic pressure, minimization of the loss of the analytes into cooking water, and the intention to capture full exposure

- **After cooking, samples were pooled into individual foods and finally pooled into the 51 core foods according to the proportions of the average diet**

Performance criteria for analytical methods and AQA

Analyses were performed in compliance with good laboratory practice and under strict quality control procedures

- Quality control (QC) included **internal QC**, i.e., use of control samples (calibrants, spiked samples, replicate samples) and of certified reference materials (CRMs), and **external QC**, i.e. participation to Proficiency Tests and Interlaboratory Comparisons with consistent good performance
- All analytical methods were **validated** for the food matrices and the analytes under study
- All analytical methods were adopted **after scrutiny of the limits of detection (LOD) and limits of quantification (LOQ)** achieved
  - In order to reduce uncertainties in exposure assessment it is important to minimize the number of analytical results that may fall below those limits (i.e. left-censored data) due to the dilution caused by the pooling process
  - As a result, except for mycotoxins, a negligible proportion of left-censored data was obtained

Example: certified and reference materials used for trace elements analysis

Cereals, cereal products and substitutes
NIST Durum 8436
NIST Rice Flour 1568a
Wheat flour IMEP-112
ERM BC-211 Rice Flour

Fish, seafood and their products
NRC Dorm-2
NRC Dorm-4 fish protein
ERM CE-278K
BCR Cod 422
DORM-3
SRM 2976 Mussel Tissue

Milk, milk products and substitutes
ERM-DB-150 Milk powder
BCR-063R Milk powder
BD150 skimmed milk powder

Vegetables fresh and processed
NIST Spinach 1570a
Cabbage 679
IAEA-359 cabbage

Meat, meat products and subsitutes
NIST Bovine Liver 1577c
NRC Bovine muscle RM 8414
BCR Pig Kidney BCR-186

Other core foods
NIST Typical diet 1548a

Water and other non-alcoholic beverages
CA021A Soft drinking water

Substances assessed in the Italian TDS

Nutrients

- **Essential elements**
  - Calcium, copper, iodine, iron, manganese, molybdenum, selenium, zinc: **8 substances**

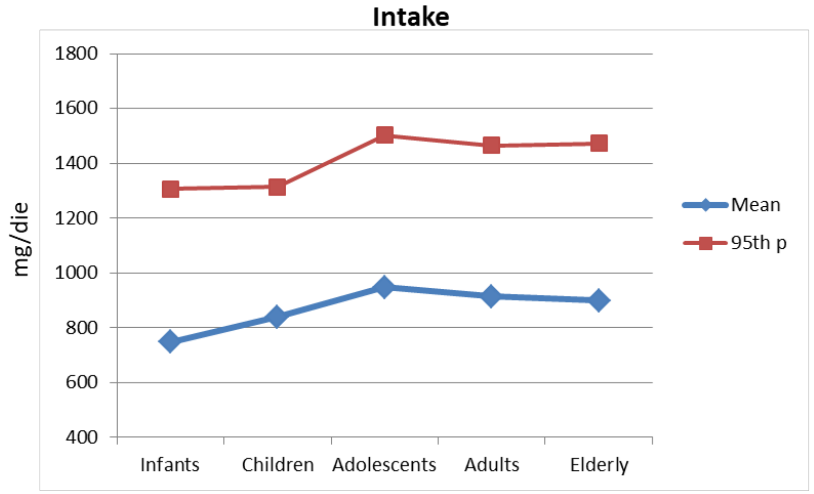
Contaminants

- **Non-essential elements**
  - Aluminum, cadmium, inorganic arsenic, lead, nickel, inorganic mercury, methyl-mercury, silver, uranium: **9 substances**
- **Dioxins & PCBs**
  - PCDDs (7), PCDFs (10), DL-PCBs (12), NDL-PCB (6 ‘indicators’): **35 substances**
- **Mycotoxins**
  - Aflatoxin B1, aflatoxin M1, citrinin, deoxynivalenol, fumonisin B1, ochratoxin A, HT-2/T-2 toxins, zearalenone: **9 substances**
- **Radionuclides**
  - ^{40}K, ^{134}Cs, ^{137}Cs, ^{90}Sr: **4 substances**

65 substances

Nutrients:
some examples

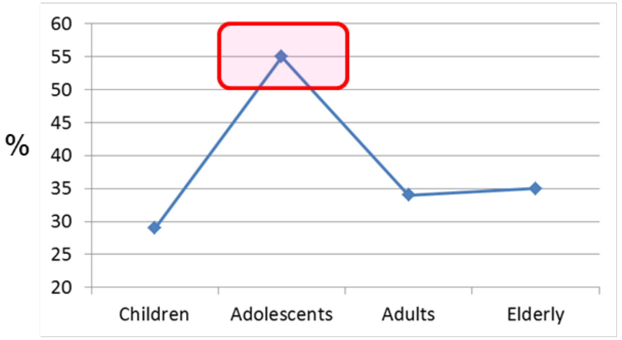
Calcium



Age (y)	**AR** (mg/d)	**PRI** (mg/d)
1–3	390	450
4–10	680	800
11–17	960	1150
18–24	860	1000
≥ 25	750	950

	Adults	Children/ Teenagers	
Italy 2012-2014	912	900	mg/d
France 2007-2009	786	659	mg/d

Estimated prevalence of inadequacy
(AR cut-point method)

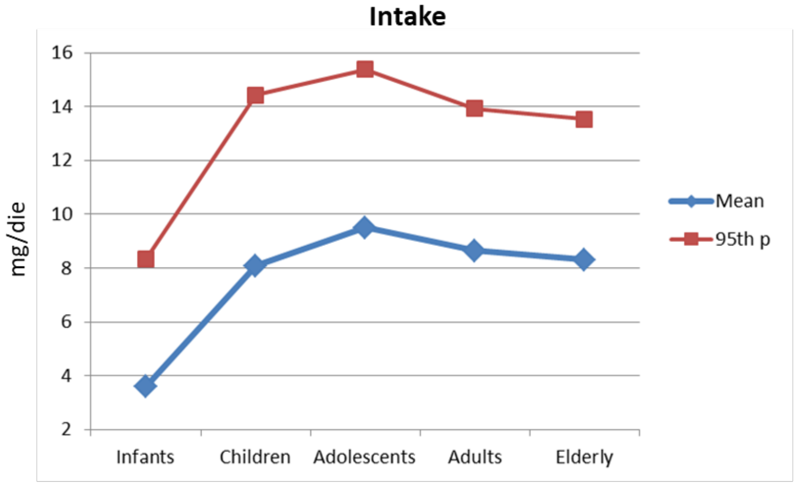


Milk and milk products
51%

Cereals and cereal products
16%

Vegetables
14%

Iron

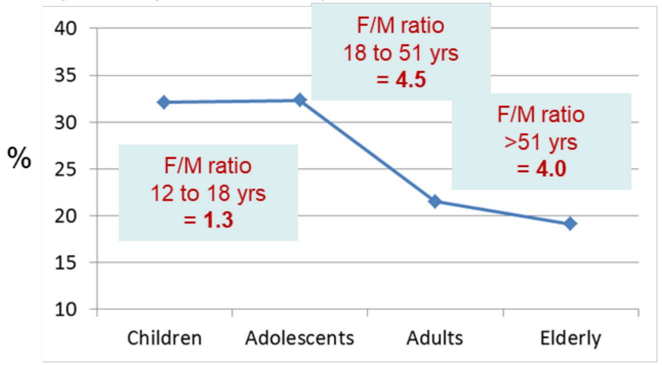


Age (y)	AR (mg/d)	PRI (mg/d)
7-11 mo	8	11
1–6	5	7
7–11	8	11
12–17 (M)	8	11
12–17 (F)	7	13
≥ 18 (M)	6	11
18-51 (F)	7	16*
≥ 51 (F)	6	11**

* Premenopausal
** Postmenopausal

	Adults	Children/ Teenager	
Italy 2012-2014	8.59	8.88	mg/d
France 2007-2009	7.71	6.57	mg/d

Estimated prevalence of inadequacy
(AR cut-point method)



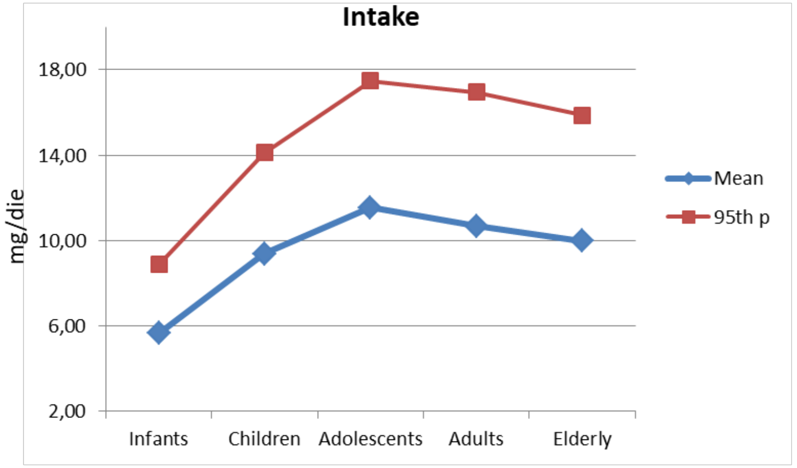
Cereals and cereal products
35%

Vegetables
19%

Meat and meat products
14%

with Fish and seafood **19%**

Zinc

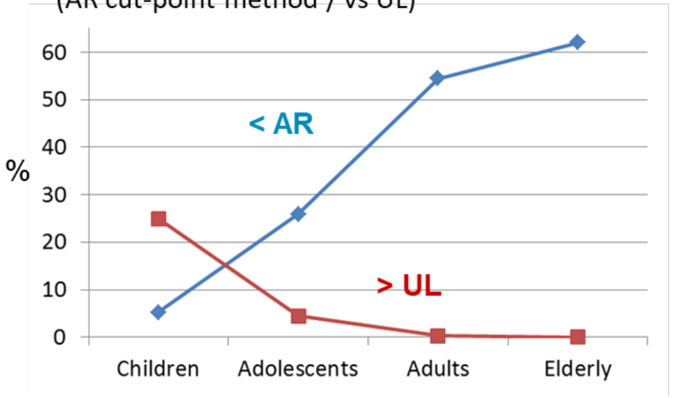


Age (y)	AR (mg/d)	PRI (mg/d)	UL (mg/d)
7-11 mo	2.4	2.9	
1–3	3.6	4.3	7
4–6	4.6	5.5	10
7–10	6.2	7.4	13
11–14	8.9	9.4	18
15–17 (M)	11.8	12.5	22
15–17 (F)	9.9	10.4	22
≥ 18 (M)	11,0	14.0*	25
≥ 18 (F)	10.2	11.0*	25

* assuming a level of phytate intake of 900 mg/day

	Adults	Children/ Teenager	
Italy 2012-2014	10.55	10.59	mg/d
France 2007-2009	7.93	6.43	mg/d

Estimated prevalence of inadequacy/excess
(AR cut-point method / vs UL)

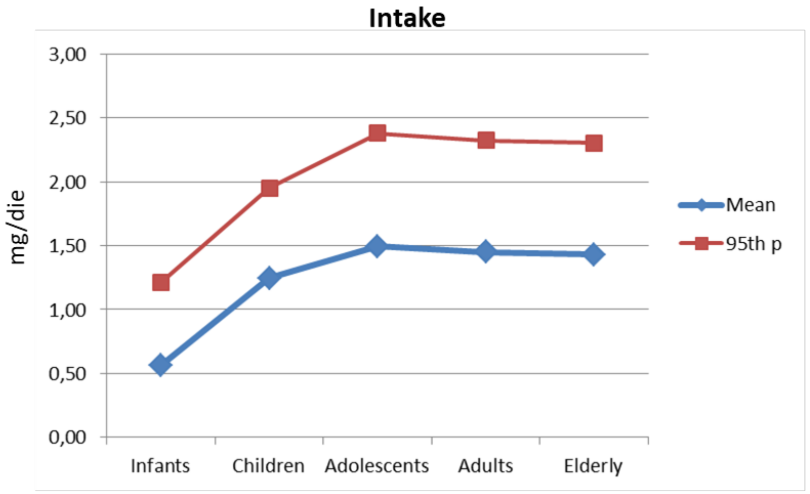


Meat and meat products
39%

Cereals and cereal products
32%

Milk and milk products
24%

Copper

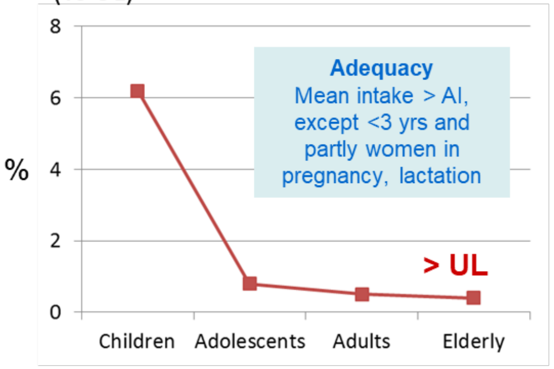


Age (y)	AI (mg/d) ♂	AI (mg/d) ♀	UL (mg/d)
7-11 mo	0.4	0.4	
1–3	0.7	0.7	1
4–6	1.0	1.0	2
7–10	1.0	1.0	3
11–14	1.3	1.1	4
15–17	1.3	1.1	4
≥ 18	1.6	1.3	5

Pregnancy, lactation: 1.5 mg/day

	Adults	Children/ Teenager	
Italy 2012-2014	1.45	1.39	mg/d
France 2007-2009	1.94	0.93	mg/d

Estimated prevalence of excess
(vs UL)

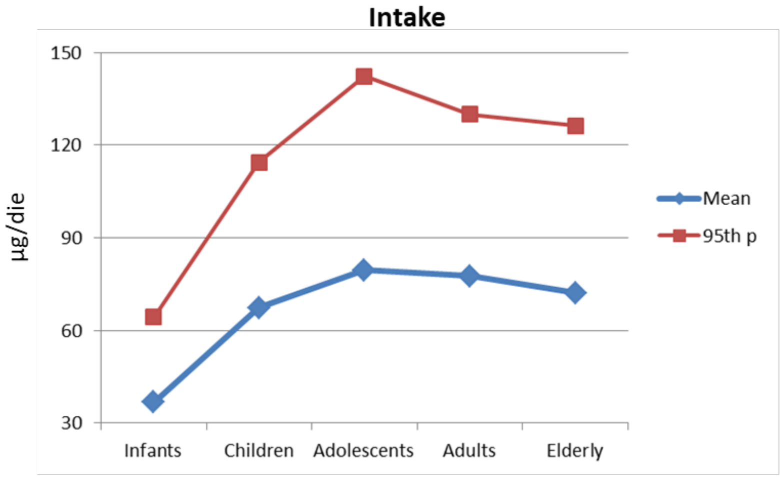


Cereals and cereal products
40%

Vegetables
15%

Meat and meat products
11%

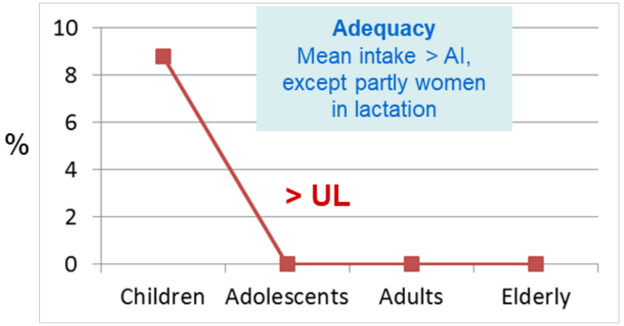
Selenium



Age (y)	AI (µg/d)	UL (µg/d)
7–11 mo	15	
1–3	15	60
4–6	20	90
7–10	35	130
11–14	55	200
15–17	70	250
≥ 18	70	300
Pregnancy	70	
Lactation	85	

	Adults	Children/ Teenager	
Italy 2012-2014	76.5	74.2	mg/d
France 2007-2009	64.4	41.5	mg/d

Estimated prevalence of excess
(vs UL)



Cereals and cereal products
33%

Fish and seafood
22%

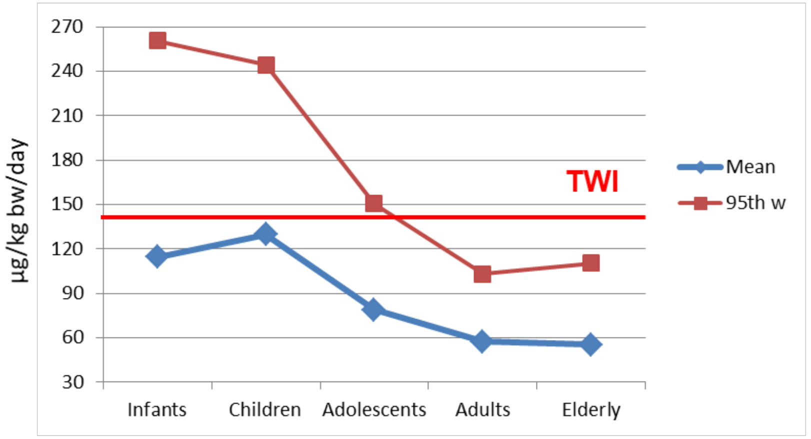
Meat and meat products
13%

Vegetables
11%

Milk and milk products
11%

Contaminants: some examples

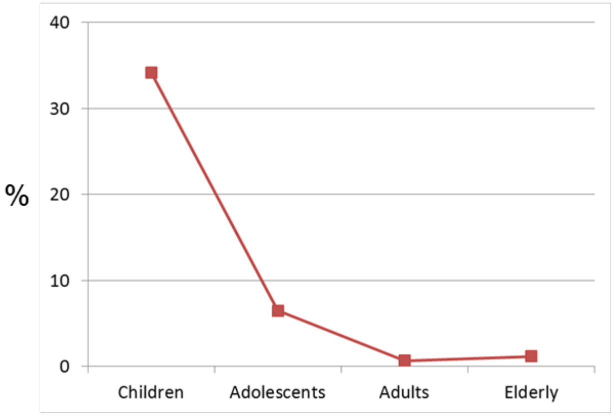
Aluminum



TWI 1 mg/kg bw/week

	Adults	Children/ Teenager	
Italy 2012-2014	56.9	101.1	µg/kg bw/day
France 2007-2009	40.3	62.2	µg/kg bw/day

Estimated prevalence of intakes >HBGV



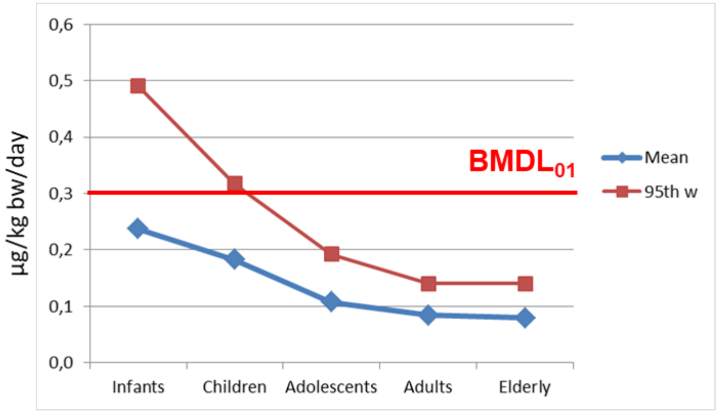
Vegetables
36%

Cereals and cereal products
29%

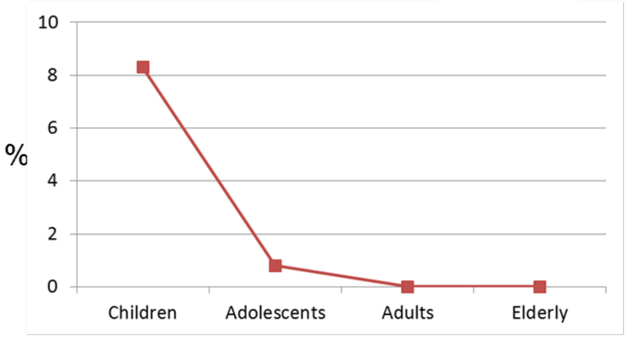
Sweet products
9%

Inorganic arsenic

Intake



Estimated prevalence of intakes >BMDL



$BMDL_{01}$ 0.3 µg/kg bw/day
(range 0.3-8 µg/kg bw/day)

Under the assumption that the same speciation of the chromatographed arsenic applies to the non-extracted portion of total arsenic (ca. 16% difference in exposure with measured inorganic As)

	Adults	Children/ Teenagers	
Italy 2012-2014	0.08	0.14	µg/kg bw/day
France 2007-2009	0.24-0.28	0.30-0.39	µg/kg bw/day

Cereals and cereal products
35%

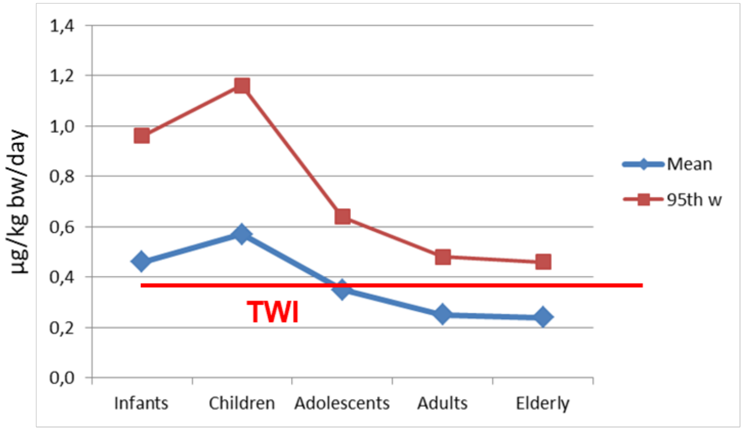
Water and non-alcoholic beverages
28%

Vegetables
11%

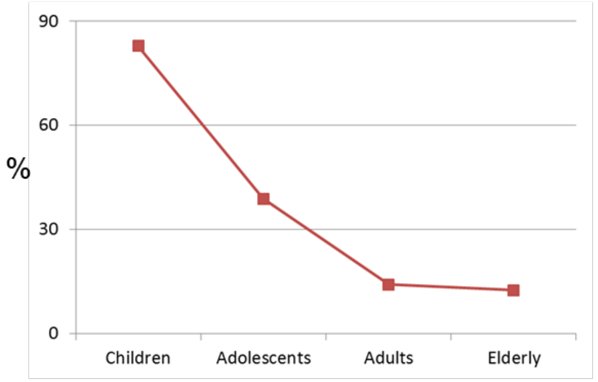
Cubadda et al. (2016) Food Chem Toxicol 98:148

Cadmium

Intake



Estimated prevalence of intakes >HBGV



TWI 2.5 µg/kg bw/week

	Adults	Children/ Teenagers	
Italy 2012-2014	0.25	0.45	µg/kg bw/day
France 2007-2009	0.16	0.24	µg/kg bw/day

Cereals and cereal products
35%

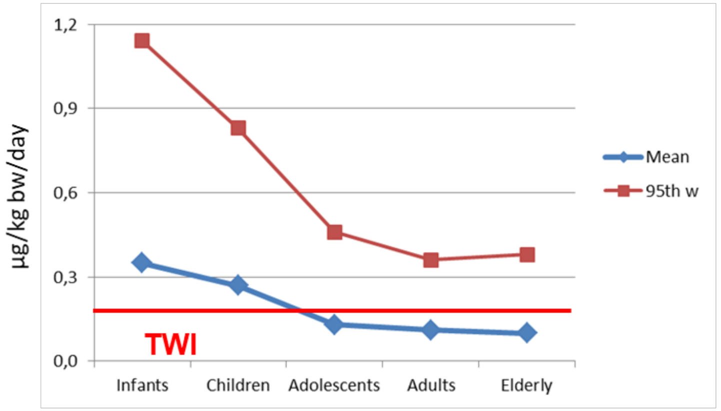
Vegetables
29%

Fish and seafood
15%

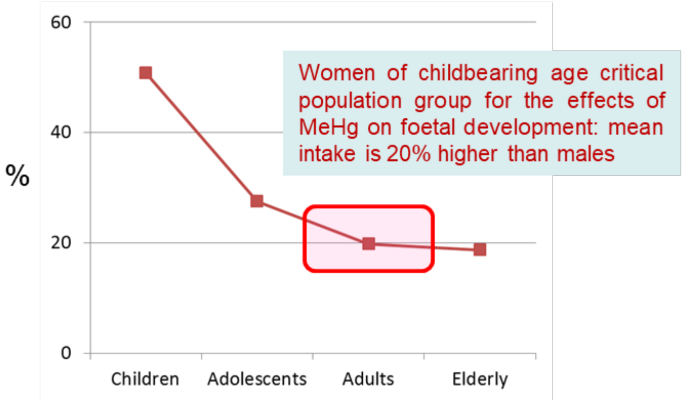
Potatoes and tubers
13%

Methylmercury

Intake



Estimated prevalence of intakes >HBGV



TWI 1.3 µg/kg bw/week

Note: conservative approach assuming that 100% and 80% of total Hg is present as MeHg in fish meat and in crustaceans/ molluscs, respectively

	Adults	Children/ Teenagers	
Italy 2012-2014	0.11	0.19	µg/kg bw/day
France 2007-2009	0.017	0.022	µg/kg bw/day

Fish and seafood
100%

Fish 89%

Seafood 11%

Dioxins and dioxin-like PCBs

Contributors to exposure: detailed food sources

PCDD/Fs

Cereals and cereal products
50%

Meat and meat products
24%

Fish
11%

Milk and milk products plus butter
7%

→ mainly Cheese

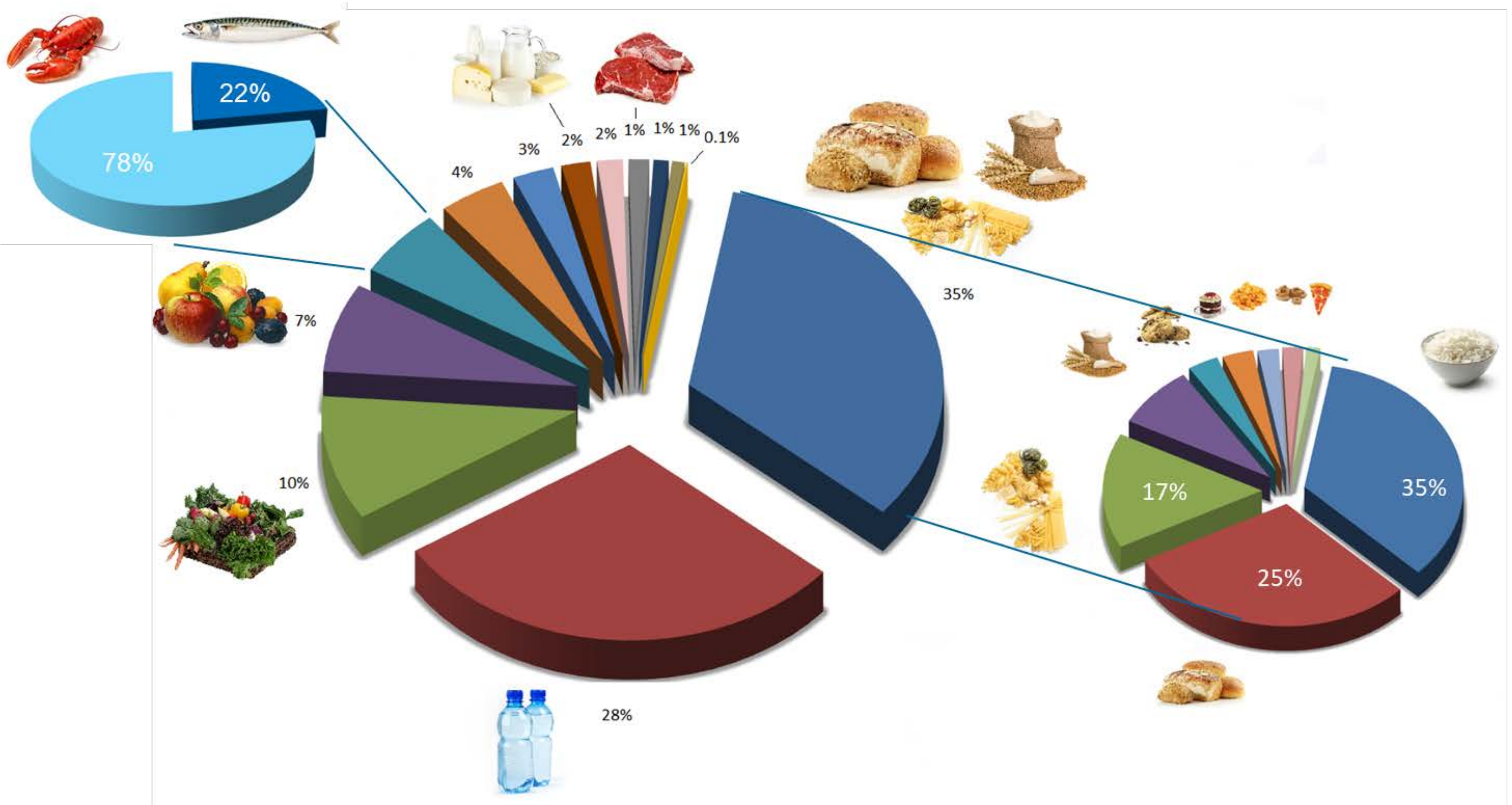
DL-PCBs

Fish
86%

Milk and milk products plus butter
9%

→ Butter 7% + Cheese 2%

Detailing contribution to intake at the level of core food



Example of the level of detail provided by TDS data
exposure to inorganic As in Italy (total population)

Prioritization of contaminants

Rank	Substance	Medium intake/HBGV	% population > HBGV	Other considerations
1	Aflatoxin B1	MOE = 8,500	19*	Genotoxic carcinogen, MOE of 2-4,000 in children and adolescents, respectively
2	Cadmium	78%	21%	% children population > HBGV is 83%
3	Methylmercury	63%	22%	Less priority compared to Cd due to the conservative approach behind EA
4	T-2/HT-2	55-112%	16%	LB-UB uncertainty
5	Nickel	65%	12%	Chronic effects. For acute toxicity 0.3% of the population <MOE **
6	Lead	50% ***	7%	Effects on children without treshold, there is no MOE accounted for
7	Inorg. arsenic	31%	1%	There is no MOE accounted for, exposure ca be doubled by er in spe eas
8	Aluminum	44%	4%	% children population > HBGV is 34%
9	OTA	Variable	Variable	In at least on site, transient exposure > HBGV
10	Dioxins+DL-PCBs	19-26%	0.6%	Up to 8% children might have an e

Changed with the new BMDL: ↓priority (rank 1)

Changed with the new HBGV: ↓priority (rank 5)

Changed with the new HBGV: ↑priority (rank 10)

* Percentage of population having a MOE < 10,000

** This is the average total diet, for acute effects indivdual foods in the specific meal are important

*** Children only considered

TDS as a tool for prioritization of substances for refined risk assessment

Conclusions

- The Italian national TDS addressed **8 nutrients and 57 contaminants**, i.e. a total of **65 substances**
- Dietary intake was estimated for the **whole population** and **selected population groups** according to age, sex, region
- For **contaminants** the mean exposure was compared with the HBGVs and the proportion of individuals exceeding them was estimated
- Exposure to contaminants is generally in the **low or medium-low range** when compared to other TDSs
- Intake of **nutrients** is also showing in most cases adequate supply and absence of excess exposure
- Overall the national TDS highlighted the **quality of the Italian total diet** for both the nutrients and the contaminants investigated
- However some substances deserve attention as the intake in critical population groups might be lead to health risks: a **prioritization** has been proposed for follow up and dedicated studies

TDS publications finalized

Cubadda F., Iacoponi F., Ferraris F., D'Amato M., Aureli F., Raggi A., Sette S., Turrini A., Mantovani A. 2020. Dietary exposure of the Italian population to nickel: the national Total Diet Study. *Food and Chemical Toxicology* **146**:111813.
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[doi: 10.1016/j.fct.2016.10.015]

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[doi: 10.4415/ANN_13_03_07]

Cubadda F., Aureli A., D'Amato M, Raggi A., Mantovani A., Silano M., Di Sandro A., Ferri G., Agrimi U. 2018. Lo Studio di Dieta Totale Nazionale: assunzione di nutrienti ed esposizione a contaminanti nella popolazione italiana. *Notiziario dell'Istituto Superiore di Sanità* **31**(10):3-8 *[In Italian]* [https://www.iss.it/documents/20126/45616/ultimo_ONLINE_10_.pdf/c6d9544e-7751-3e13-4e91-0b8dc830efeb?t=1581099722406]

More soon: stay tuned!

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Questions?

THANK YOU FOR YOUR ATTENTION