REPUBLIC OF CYPRUS
MINISTRY OF HEALTH

ΓΧΚ SGL Γενικό Χημείο του Κράτους State General Laboratory

CY2026.EU

Preliminary results of the Risk Assessment of Copper in Cyprus: A Holistic Approach

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Why is Cyprus focusing on copper?

1. Main adverse health effect from copper exposure is related to its chronic liver toxicity.

Chronic toxicity:
Developmental and reproductive,
Carcinogenicity and genotoxicity,
Neurotoxicity and immunotoxicity

Acute copper toxicity:
gastrointestinal symptoms, haemolysis and damage in the gut, kidney and liver

Recently discovered bovine liver samples with copper concentrations higher than the MRL (30 mg/kg), triggered the need to perform a dietary exposure assessment of copper for the population in Cyprus.
Other challenges:
Copper is also an essential micronutrient, Background exposure, PPP residues, Lack of data for copper in supplements

2. Copper is a symbol of Cypriot heritage

- Copper is etymologically linked to the name of Cyprus (Cuprum), reflecting the island's ancient role as a major exporter of copper in the Eastern Mediterranean. *This connection is further supported by Cyprus' 5,000-year history as one of the Mediterranean's most significant copper producers.*
- Because of this deep-rooted connection, copper is often included as a target element in food and beverage studies, conducted by the scientific community in Cyprus.

Assessing dietary exposure to copper is particularly important for the Cypriot population, not only due to its potential toxicity, but also, because of its cultural and historical relevance.

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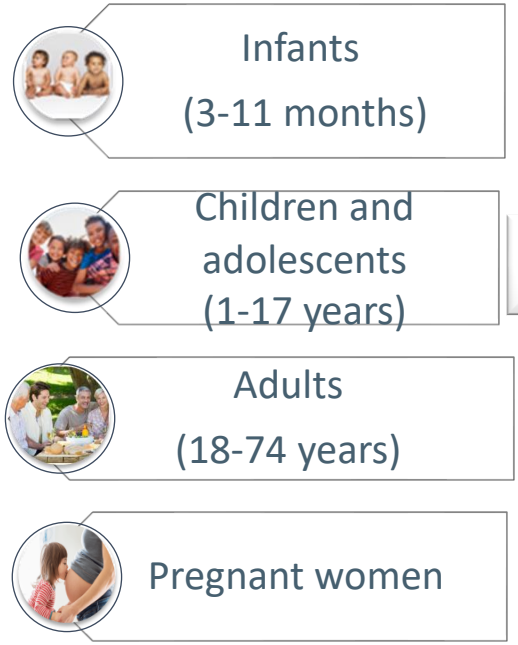
Dietary Risk Assessment tool

- Estimation of the chronic exposure assessment will be performed by using the SGL's risk assessment model **ImproRisk**, which is an open access RA model, built in R, fully compatible with the EFSA's food classification and description system FoodEx2.

- **Main advantages of ImproRisk (for Risk Assessors & Risk Managers)**:
  - Capability to upload food consumption datasets that include subjects with different demographic characteristics (gender, population class, area).
  - Dietary exposure estimation at individual level.
  - Automatic evaluation of the outcomes to identify statistically significant differences among subjects with different demographic characteristics.

Food Consumption data (EU Menu)



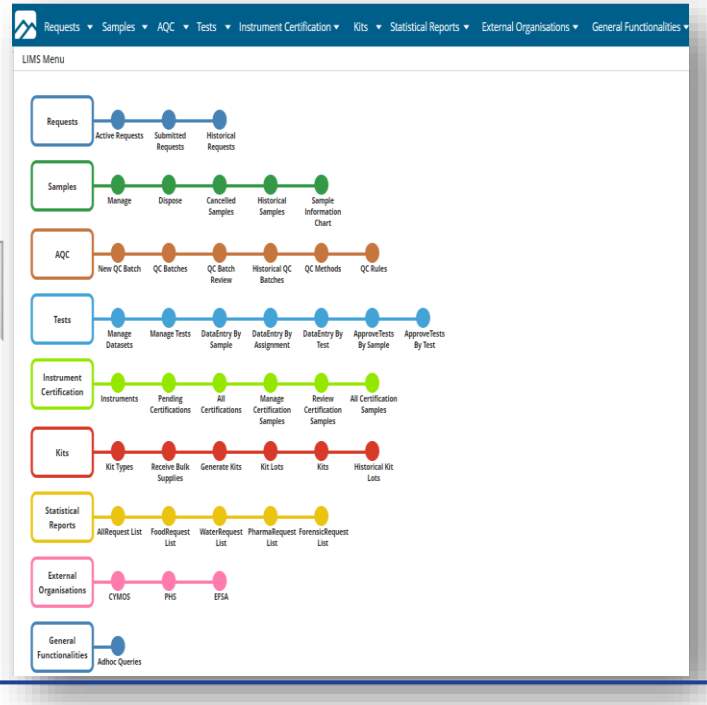
FoodEx2 coding

ImproRisk

SGL's Risk Assessment model

FoodEx2 coding

Chemical Occurrence data (SSD2)



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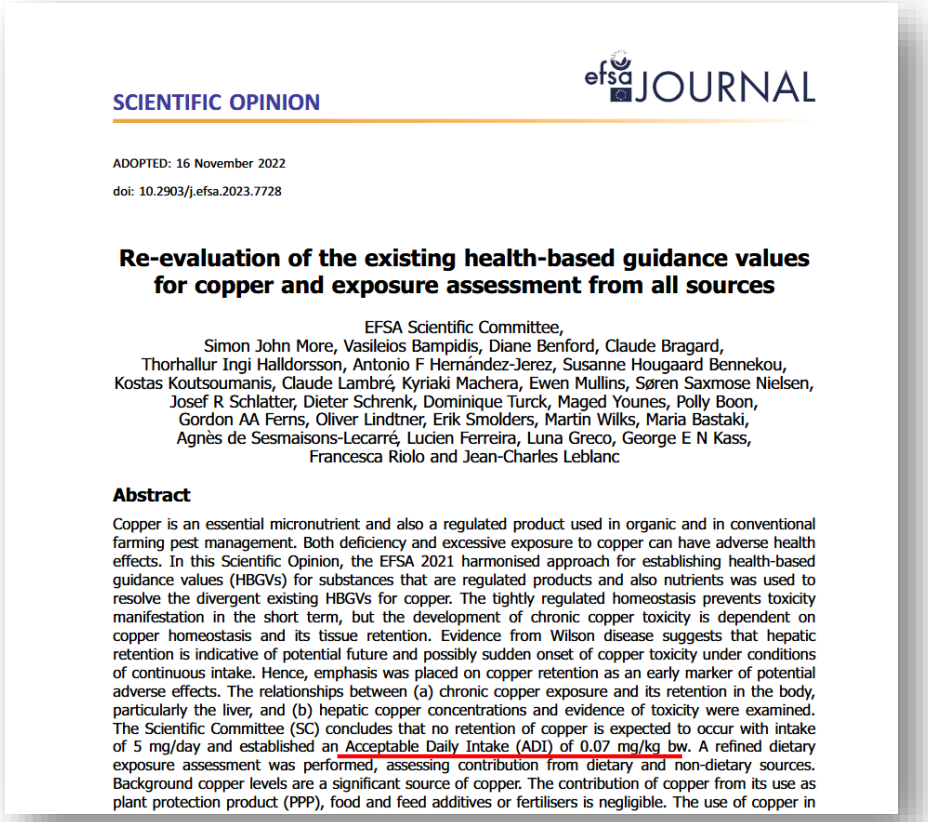
Data on Copper:

- Copper occurrence data in food were collected within the ***Official Control*** of the State General Laboratory of the Ministry of Health of Cyprus, during **2019-2024**.
- Analytical results from approximately **1300 food samples** are available from the contaminants and pesticide residue control plans.
- Substitution method will be applied for left censored data.
- Main food categories, according to the level 1 of FoodEx2: **meat**, **fish**, **milk**, **grains**, **vegetables** and **water**.
- Food consumption data: EU Menu Cyprus (2014 – 2018).

Risk characterization:

Risk characterization is performed using the health-based guidance values published in EFSA's Scientific Opinions and the EFSA Open FoodTox Database.

In this case, the latest EFSA's scientific opinion on the consumer risk assessment of copper will be taken into account.



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SCIENTIFIC OPINION

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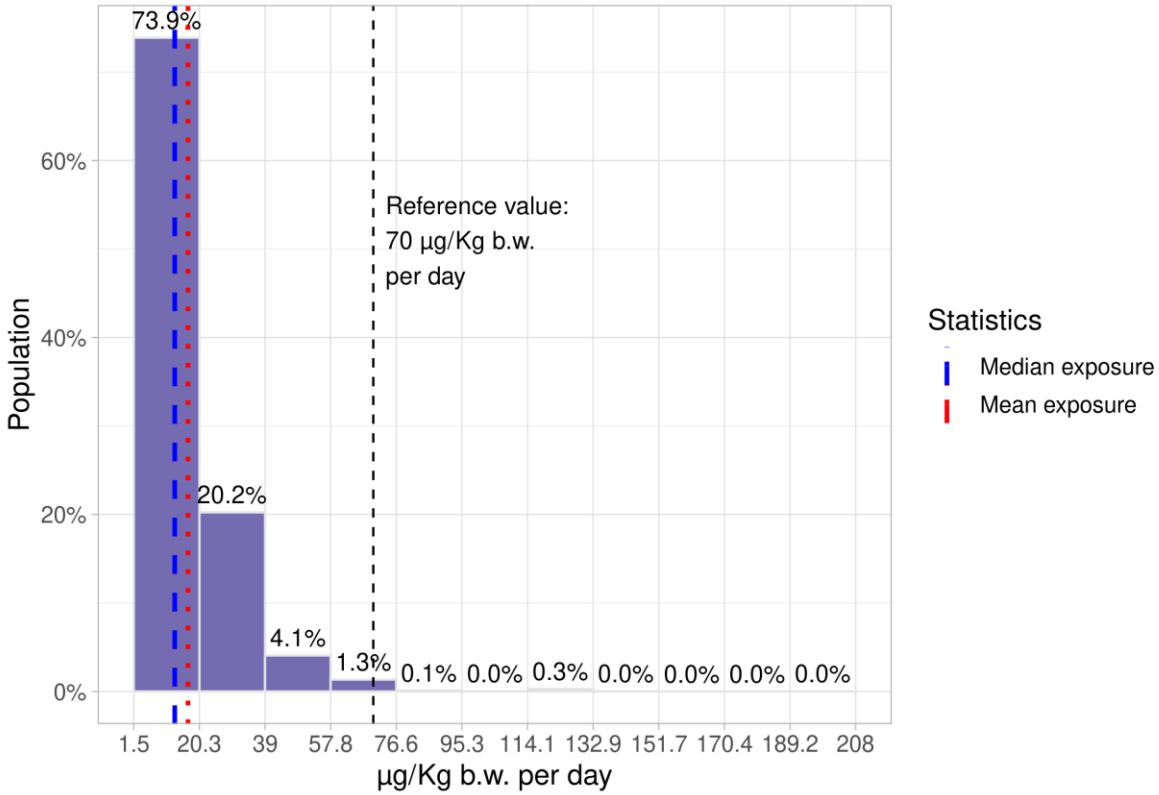
Re-evaluation of the existing health-based guidance values for copper and exposure assessment from all sources

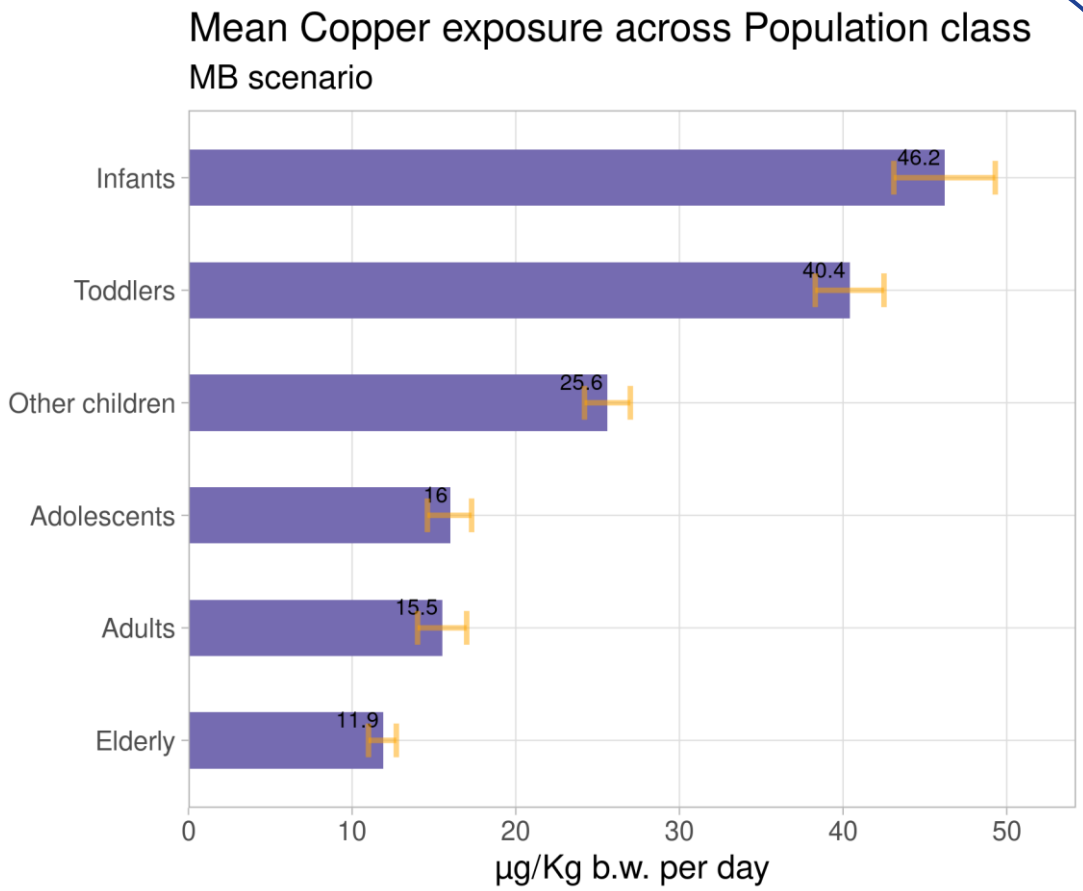
EFSA Scientific Committee,
Simon John More, Vasileios Bampidis, Diane Benford, Claude Bragard, Thorhallur Ingi Halldorsson, Antonio F Hernández-Jerez, Susanne Hougaard Bennekou, Kostas Koutsoumanis, Claude Lambré, Kyriaki Machera, Ewen Mullins, Søren Saxmose Nielsen, Josef R Schlatter, Dieter Schrenk, Dominique Turck, Maged Younes, Polly Boon, Gordon AA Ferns, Oliver Lindtner, Erik Smolders, Martin Wilks, Maria Bastaki, Agnès de Sesmaisons-Lecarré, Lucien Ferreira, Luna Greco, George E N Kass, Francesca Riolo and Jean-Charles Leblanc

Abstract

Copper is an essential micronutrient and also a regulated product used in organic and in conventional farming pest management. Both deficiency and excessive exposure to copper can have adverse health effects. In this Scientific Opinion, the EFSA 2021 harmonised approach for establishing health-based guidance values (HBGVs) for substances that are regulated products and also nutrients was used to resolve the divergent existing HBGVs for copper. The tightly regulated homeostasis prevents toxicity manifestation in the short term, but the development of chronic copper toxicity is dependent on copper homeostasis and its tissue retention. Evidence from Wilson disease suggests that hepatic retention is indicative of potential future and possibly sudden onset of copper toxicity under conditions of continuous intake. Hence, emphasis was placed on copper retention as an early marker of potential adverse effects. The relationships between (a) chronic copper exposure and its retention in the body, particularly the liver, and (b) hepatic copper concentrations and evidence of toxicity were examined. The Scientific Committee (SC) concludes that no retention of copper is expected to occur with intake of 5 mg/day and established an Acceptable Daily Intake (ADI) of 0.07 mg/kg bw. A refined dietary exposure assessment was performed, assessing contribution from dietary and non-dietary sources. Background copper levels are a significant source of copper. The contribution of copper from its use as plant protection product (PPP), food and feed additives or fertilisers is negligible. The use of copper in

Results of the Dietary Risk Assessment





Only 0.8% of the over all population exceeds the ADI. Mean copper exposure at 17 µg/Kg b.w. per day. This exposure is compared to EFSA's results for the pan European population.

Below 0.7% of the population of adults, elderly, adolescence and other children exceeds the ADI. 14.1% for the infants and 3.3% of the toddler's population exceeds the ADI. This is due to the much higher consumption of baby food in this population classes, where copper is also added as nutrient.

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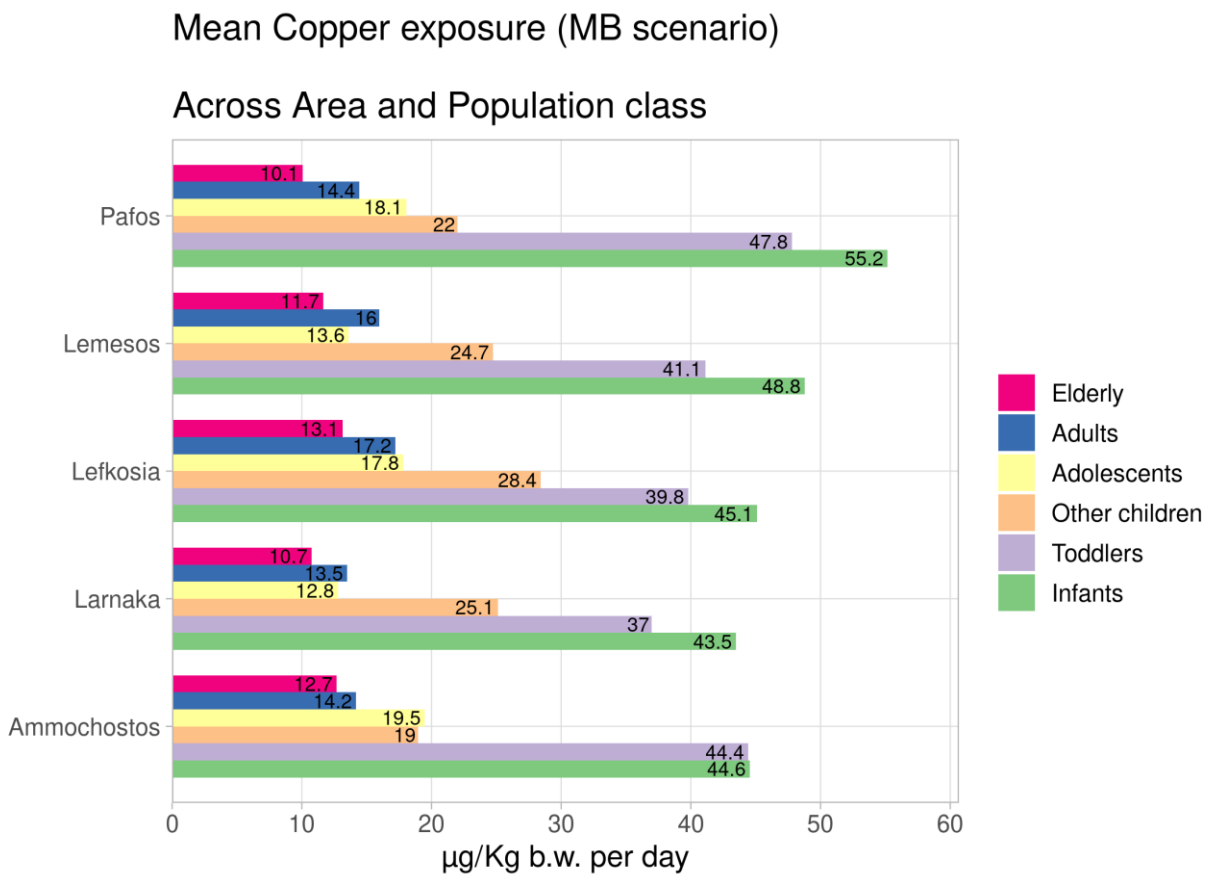
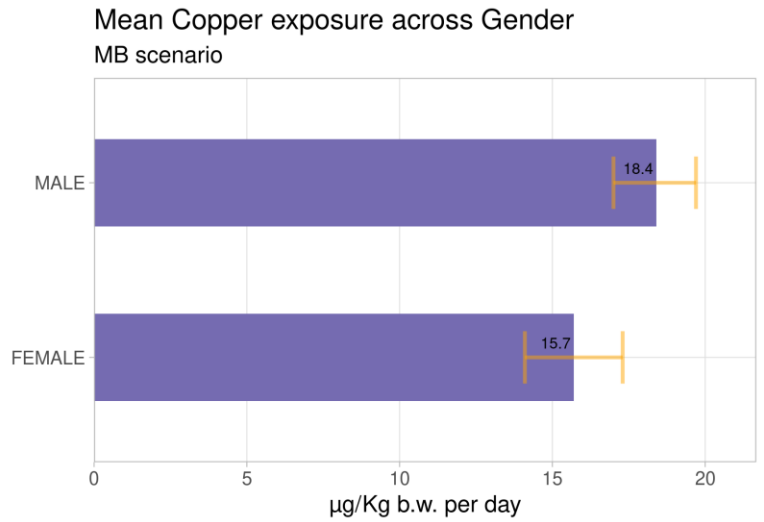
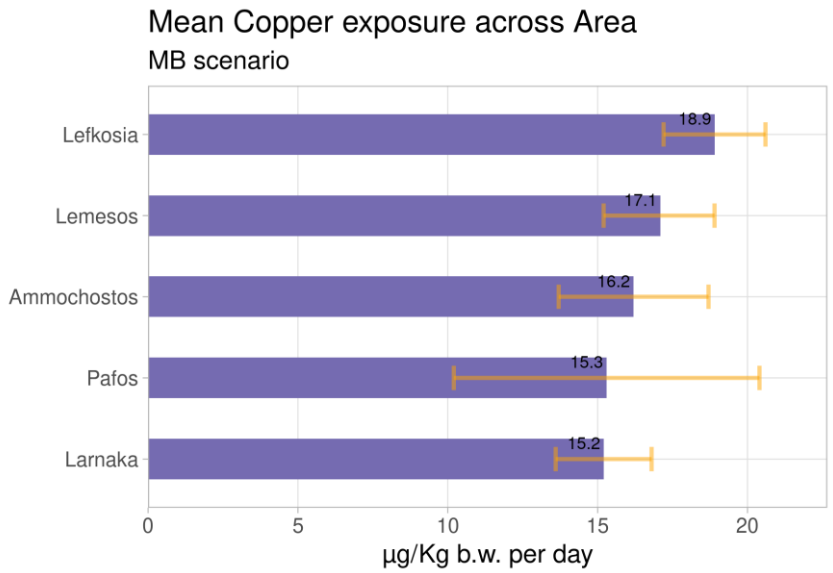
Results of the Dietary Risk Assessment







Similar results were observed in all areas in Cyprus. Higher exposure for infants and toddlers, and lower exposure for adults and elderly.

There was a statistically significant difference in the mean exposure, across genders and also across several areas.

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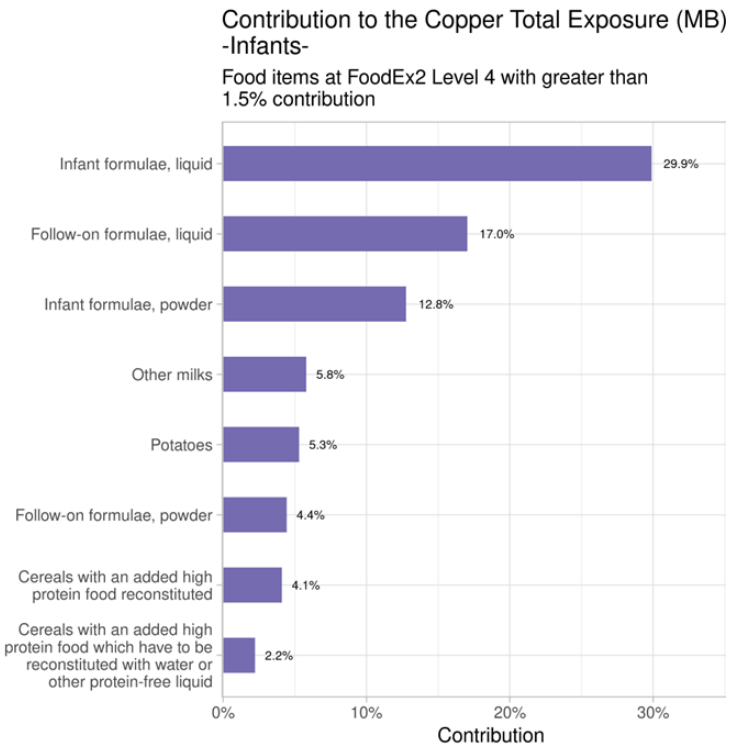
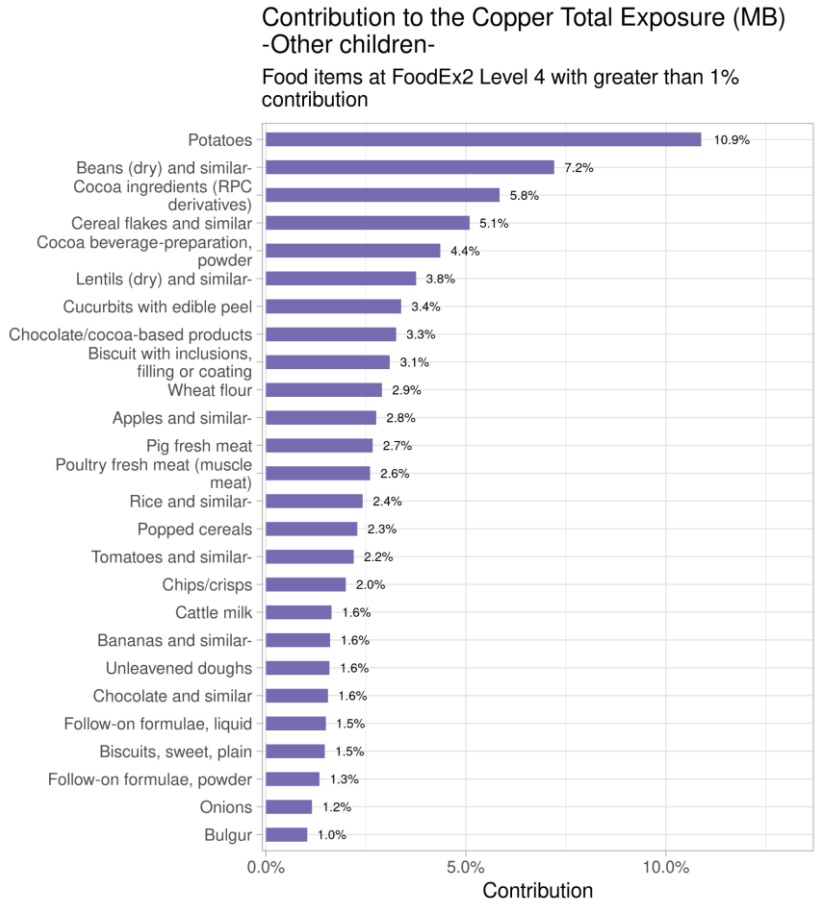
Results of the Dietary Risk Assessment

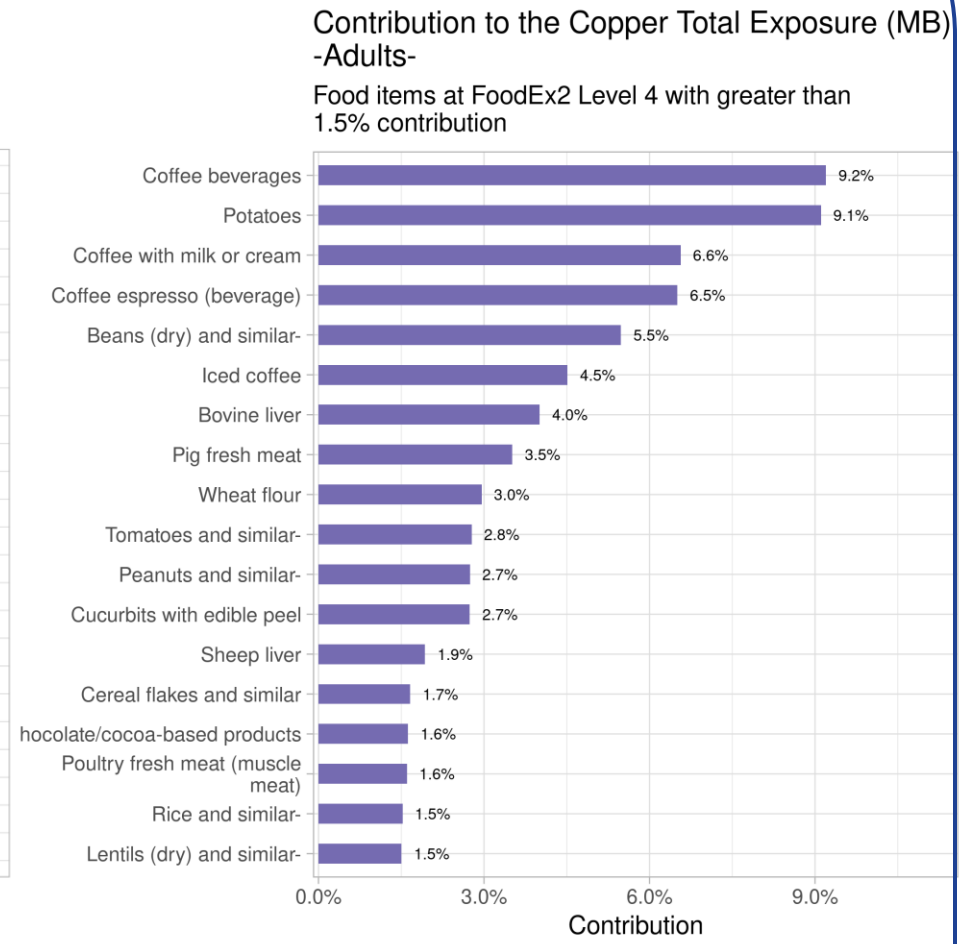
INFANTS



OTHER CHILDREN



ADULTS



For **infants** the highest contribution to copper intake was baby food (and similarly for toddlers).
For **other children**, potatoes, beans, cocoa and cereal are the main contributors.
In the case of **adults**, main contributors to copper exposure were coffee, potatoes, beans and mammal's liver.

For further information: www.improrisk.com, dkafouris@sgl.moh.gov.cy

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Why add Human Biomonitoring (HBM) for Copper?

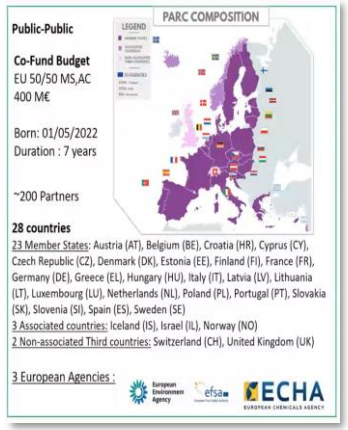
Dietary Risk Assessment

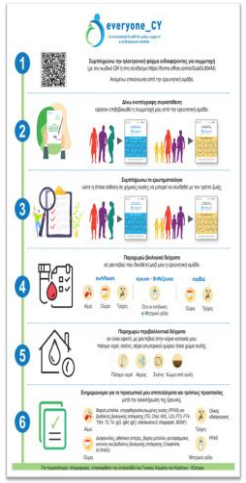
- Occurrence data + EU MENU consumption
- External exposure (mg/kg bw/day)
- Comparison with EFSA ADI

Why HBM?	Interpretation context
Provides **internal exposure marker** (urinary copper)	Copper is an **essential element** with tight homeostatic control
Supports Benchmarking - **comparisons with other European populations**	Urinary copper = **minor excretion pathway** biliary/fecal excretion is dominant
Helps identify **outliers or additional sources**   	**SG correction** improves interpretation of Spot/morning urine
	⚠ HBM supports **triangulation** (not a direct comparison with ADI)

HBM Cyprus – study design

Funded by the European Union





CY PARC Alignment Study "everyone_CY"

- ✓ **adults** of reproductive age (18-39y, N≥150)
- ✓ **children** (6-11y, N≥150)

- CY National Bioethics Committee approval
- Fieldwork: 9/2025-4/2026
- Copper is not a PARC priority chemical. Chosen as a national add-on for integrated copper assessment.
- Interpretation: urinary copper reflects a minor excretion pathway; copper is homeostatically regulated.

Pilot Copper Biomonitoring study

Samples collected up to 12/2025:

- ✓ **Adults**: N=54 ; **Children**: N=35
- ✓ Morning urine
- ✓ Personal data (PARC main questionnaires and sampling questionnaires)

- Measured:

Ούρα

- ✓ **copper in urine** by ICP-MS (PARC-approved, ISO/IEC 17025 accredited lab, LOQ=1.7 µg/L)
- ✓ **Specific Gravity (SG)**

- Primary reporting metric for comparison within the dataset (Levine/Fahy approach):

- ✓ SG-adjusted to SG_ref=1.020.

$$[Cu]_{SG\ adjusted} = [Cu]_{raw} \times \frac{(SG_{reference} - 1)}{(SG_{sample} - 1)}$$

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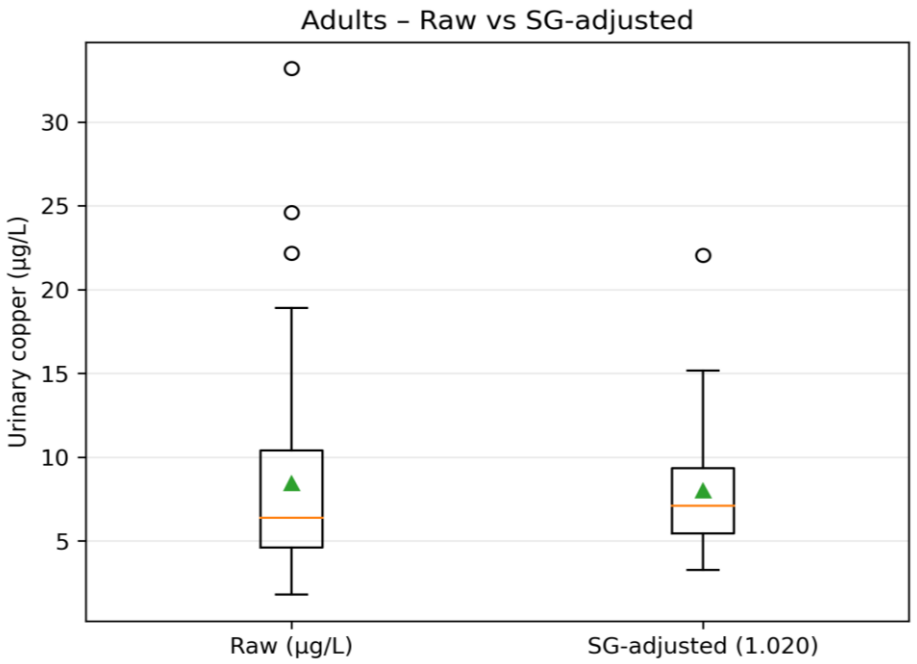
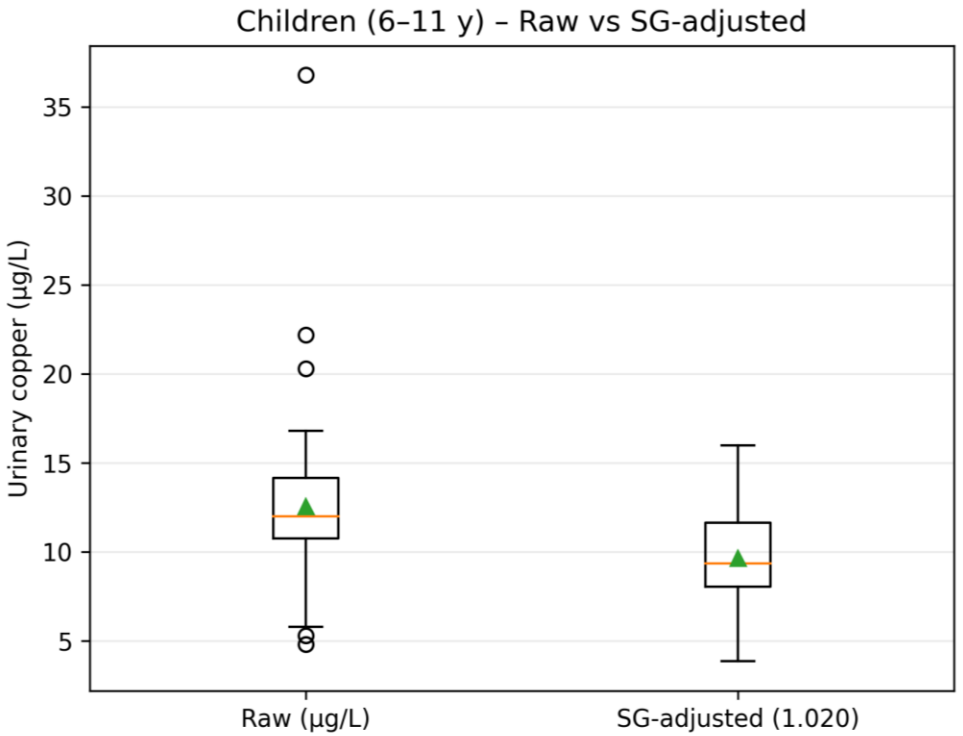
HBM Cyprus – urinary copper distribution (Adults and Children)





- Children show higher raw values partly reflecting concentration;
- SG-adjustment reduces dilution-driven variability in spot/morning urine and improves comparability.

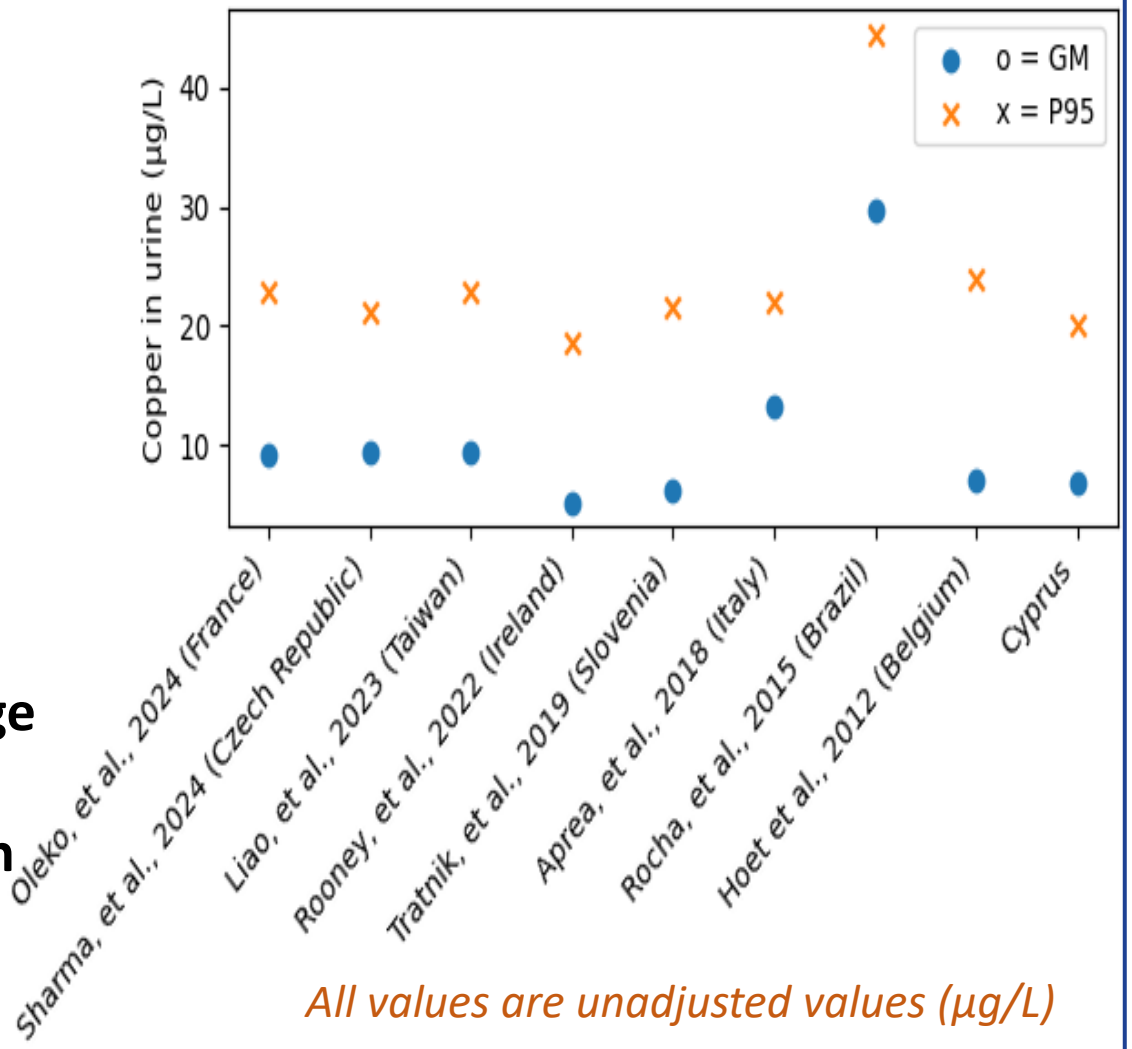
ADULTS	[Cu] Raw (µg/L)	[Cu] SG-adjusted (µg/L; SG_ref=1.020)
GM	6.83	7.36
Median (P50)	6.38	7.08
P95	20.05	14.63

CHILDREN	[Cu] Raw (µg/L)	[Cu] SG-adjusted (µg/L; SG_ref=1.020)
GM	11.54	9.25
Median (P50)	12.00	9.36
P95	20.87	14.26

Cyprus Compared to published European General Population Studies

Urinary Copper (unadjusted) in Adults

Country	Study	GM (µg/L)	P95 (µg/L)
France	Oleko 2024	9.08	22.95
Czech Republic	Sharma 2024 (Young Adults)	9.41	21.1
Ireland	Rooney 2022	5.1–5.6	18.6–27.1
Slovenia	Tratnik 2019	4.66–6.26	21.6–22.5
Italy	Aprea 2018	10.6–13.3	21.9–25.5
Belgium	Hoet 2012	6.94	23.9 (P97.5)
Cyprus	**This study**	**6.83** (M-F=6.70-6.92)	**20.05** (M-F=18.91-19.47)



- Cyprus GM (6.8 µg/L) lies within the **lower-middle range** of European background levels.
- Cyprus P95 (~20 µg/L) is **fully consistent with European upper percentiles** (≈20–25 µg/L).
- No evidence of systemic population-wide elevation.

All values are unadjusted values (µg/L)

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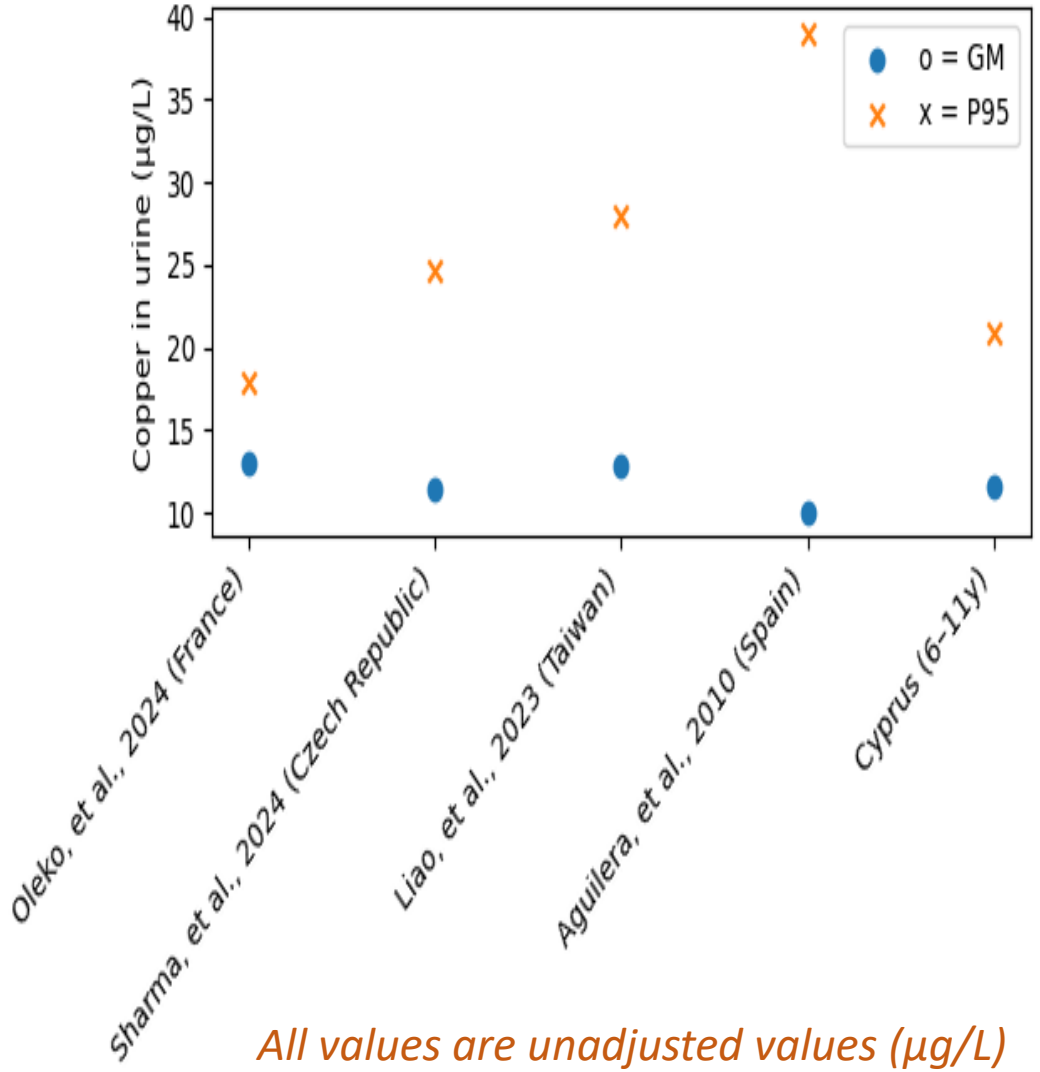
Cyprus Compared to published European General Population Studies

Urinary Copper (unadjusted) in Children

Country	Study	GM (µg/L)	P95 (µg/L)
France	Oleko 2025	13.06	17.83
Czech Republic	Sharma 2026	11.51	24.6
Spain	Aguilera 2010	10.02–10.15	32.18–39.06
Cyprus	**This Study**	**11.56**	**20.96**



- Cyprus children GM (11.56 µg/L) falls **within European background range (≈10–13 µg/L)**.
- Cyprus P95 (~21 µg/L) lies **below or within reported European upper percentiles**.
- Slightly higher GM in children vs adults is consistent with other European datasets.

All values are unadjusted values (µg/L)

For further information: akatsonouri@sgl.moh.gov.cy

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Conclusions

- **Dietary risk assessment** indicates that chronic exposure is **below the ADI for >99%** of the population (exceedance confined to the upper tail).

- Higher dietary exposure is predicted for **infants/toddlers**, mainly driven by milk/formula consumption.

- **HBM** supports benchmarking and outlier review; it **does not provide a direct conversion to ADI** exceedance for copper.

- HBM in **adults & school-age children** shows urinary copper distributions broadly comparable to published general-population studies.
(Infants/toddlers, who are predicted to have higher dietary exposure, were not assessed).

- **Next steps**:

  - ✓ integrate supplement intake, investigate potential water/plumbing contribution by utilizing data collected with PARC Aligned Studies Questionnaires

  - ✓ consider targeted sampling in younger age groups if needed.

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Acknowledges

To:

- EFSA for its continuous support

- CY-SGL Risk Assessment Unit
- SGL's Human Biomonitoring Lab
- CY-EFSA Focal Point Network
- CY-EFSA Communication Expert Network

Thank you for your attention!!