

Supplementary material: Cadmium exposure in adults across Europe: Results from the HBM4EU aligned studies survey 2014-2020

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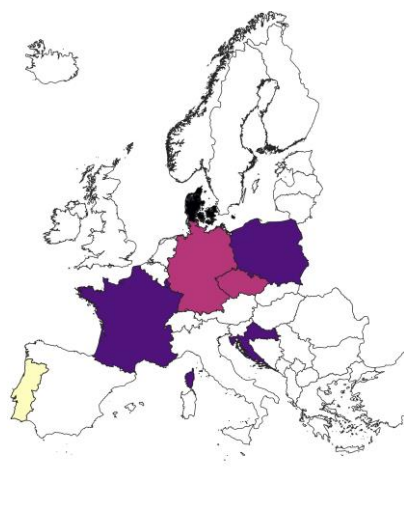
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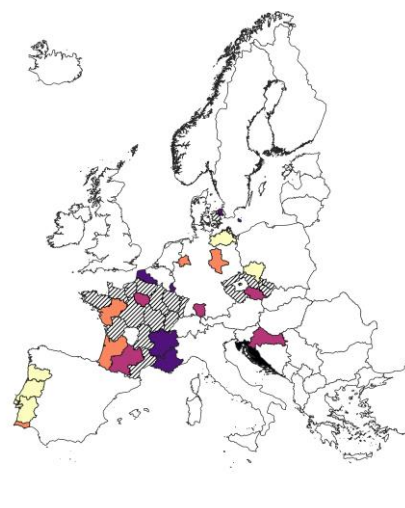
Cd in soil (mg/kg)

0.046 - 0.055
0.055 - 0.070
0.070 - 0.089
0.089 - 0.110
0.110 - 0.202



Cd in soil (mg/kg)

0.046 - 0.055
0.055 - 0.070
0.070 - 0.089
0.089 - 0.110
0.110 - 0.202
< 20 subjects



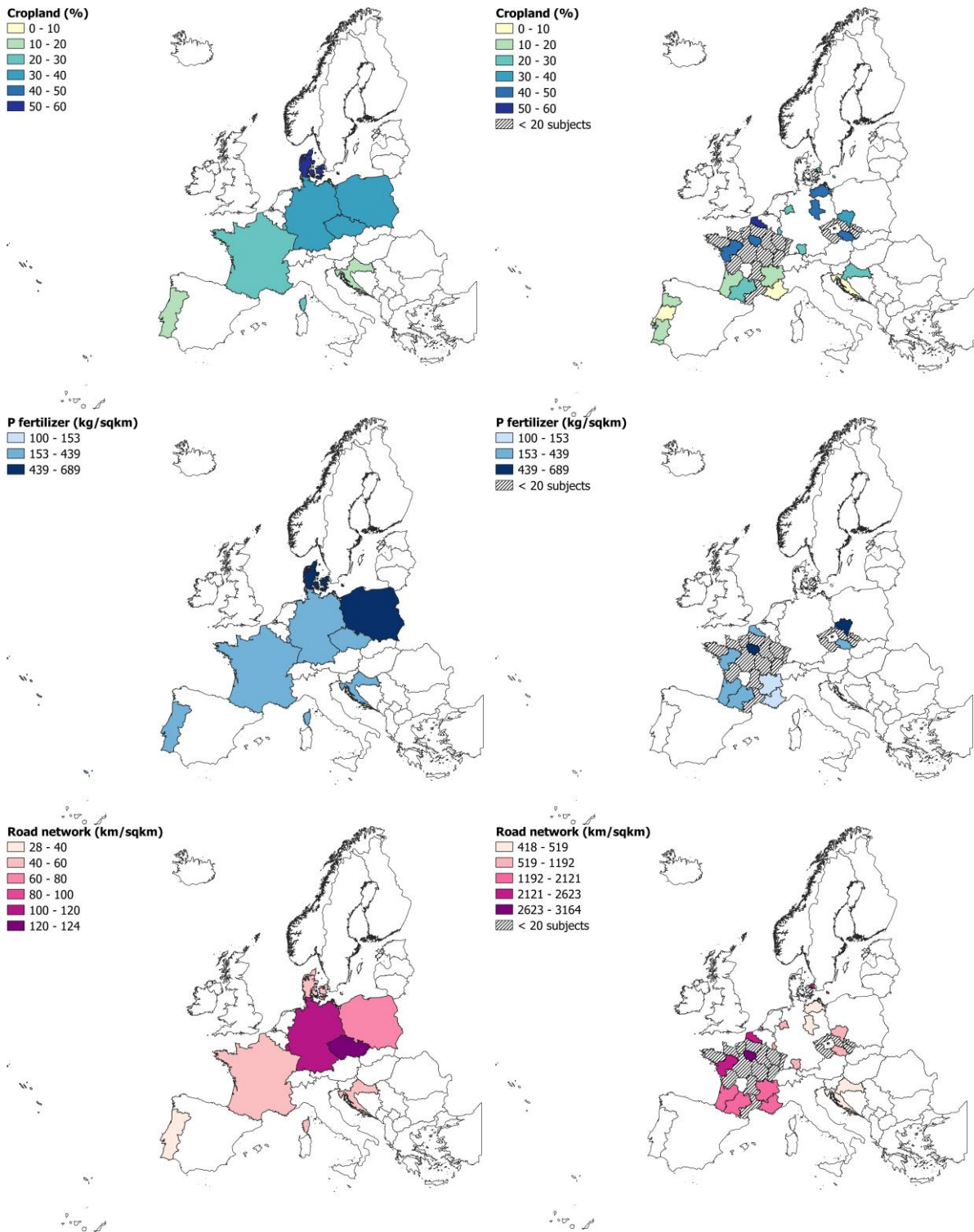


Figure S1. Distribution of external data obtained from available European databases on the country (left) and NUTS2 level (right).

Table S1. Characteristics of the study population based on the potential explanatory variables.

Country of the study	N	Local food (%)			N	Vegetarian diet (%)		N	Organ meat (%)			N	Cereals (%)			N	Drinking water source (%)		N	Type of drinking water (%)			
		1	2	3		Yes	No		1	2	3		1	2	3		Public	Private		Bottled	Tap	Ground	Other
ALL	300	23.7	68.0	8.3	1641	97.0	3.0	1976	77.7	21.2	1.1	1211	26.4	28.7	44.9	528	93.2	6.8	1187	37.4	57.3	2.1	3.2
Denmark	n.a	n.a.	n.a.	n.a.	n.a	n.a.	n.a.	n.a	n.a.	n.a.	n.a.	n.a	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a	n.a
Iceland	n.a	n.a.	n.a.	n.a.	180	97.2	2.8	n.a	n.a.	n.a.	n.a.	178	15.7	45.5	38.8	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Czech Republic	n.a	n.a.	n.a.	n.a.	300	96.7	3.3	296	59.4	39.2	1.4	296	3.0	23.0	74.0	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Poland	n.a	n.a.	n.a.	n.a.	n.a	n.a.	n.a.	228	43.0	53.1	3.9	227	61.7	34.4	3.9	228	100.0	0.0	228	78.9	21.1	0.0	0.0
Croatia	300	23.7	68.0	8.3	300	97.0	3.0	300	83.3	14.0	2.7	300	47.3	38.0	14.7	300	88.0	22.0	300	3.7	96.3	0.0	0.0
Portugal	n.a	n.a.	n.a.	n.a.	277	99.3	0.7	277	81.2	18.4	0.4	n.a	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	277	59.2	36.5	4.3	0.0
France	n.a	n.a.	n.a.	n.a.	295	99.0	1.0	376	82.4	17.6	0.0	n.a	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	382	23.3	63.4	3.4	9.9
Luxembourg	n.a	n.a.	n.a.	n.a.	n.a	n.a.	n.a.	210	91.0	9.0	0.0	210	0.5	2.8	96.7	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Germany	n.a	n.a.	n.a.	n.a.	289	93.1	6.9	289	99.0	1.0	0.0	n.a	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

Remarks: n.a. – not available. Frequencies of consumption for local food, organ meat, and cereals: 1 - less than once per month; 2 - at least once per month, but not more than 3 times per week; 3 - at least 4 times per week.

Table S2. Results of study-specific linear regression models. The estimates are expressed as the fold change in Cd concentration for unit increase of the covariate.

Cd in urine (µg/g crt)	Estimate (95% CI)		
	Denmark	Iceland	Czech Republic
<i>n</i>	275	197	297
<i>Model R², p-value</i>	0.24, <0.001	0.34, <0.001	0.34, <0.001
Age (years)	1.03 (1.01-1.05)**	1.03 (1.01-1.04)**	1.05 (1.01-1.10)*
Sex (F vs. M)	1.48 (1.28-1.72)**	1.85 (1.61-2.13)**	1.26 (1.08-1.48)**
Smoking (yes vs. no)	1.15 (0.91-1.46)	1.03 (0.78-1.35)	1.01 (0.79-1.28)
Isced - low	1.00	1.00	1.00
Isced - medium	1.12 (0.88-1.43)	0.80 (0.59-1.10)	0.60 (0.23-1.56)
Isced - high	1.15 (0.91-1.46)	0.80 (0.59-1.08)	0.56 (0.22-1.44)
Sampling year	0.85 (0.66-1.10)	0.88 (0.74-1.04)	-
Vegetarian (yes vs. no)	-	-	1.48 (0.97-2.25)#
Cd in urine (µg/g crt)	Poland	Croatia	Portugal
<i>n</i>	227	300	277
<i>Model R², p-value</i>	0.04, 0.103	0.27, p<0.001	0.18, p>0.001
Age (years)	1.01 (1.00-1.03)	1.05 (1.04-1.07)**	1.05 (1.02-1.08)**
Sex (F vs. M)	1.13 (0.97-1.32)	1.28 (1.12-1.47)**	1.44 (1.20-1.72)**
Smoking (yes vs. no)	1.10 (0.89-1.34)	1.13 (0.98-1.31)	1.54 (1.27-1.87)**
Isced - low	-	-	1.00
Isced - medium	-	-	0.73 (0.58-0.92)**
Isced - high	-	-	0.80 (0.63-1.01)#
Sampling year	-	0.90 (0.78-1.03)	0.93 (0.74-1.18)
Vegetarian (yes vs. no)	-	1.36 (0.93-1.99)	-
Cereals consumption	1.06 (1.01-1.11)*	-	-
Organ meat consumption	-	0.95 (0.89-1.00)#	1.14 (0.95-1.37)
Meat consumption	-	-	0.93 (0.83-1.04)
Cd in urine (µg/g crt)	France	Luxembourg	Germany
<i>n</i>	381	210	289
<i>Model R², p-value</i>	0.32, p>0.001	0.24, p<0.001	0.19, p>0.001
Age (years)	1.02 (1.01-1.04)**	1.00 (0.98-1.02)	1.02 (1.00-1.04)#
Sex (F vs. M)	1.34 (1.17-1.54)**	1.40 (1.22-1.61)**	1.26 (1.13-1.41)**
Smoking (yes vs. no)	1.39 (1.19-1.61)**	1.23 (1.03-1.48)*	1.13 (0.95-1.35)*
Isced - low	1.00	1.00	-
Isced - medium	0.90 (0.57-1.42)	0.90 (0.65-1.24)	-
Isced - high	0.79 (0.51-1.23)	0.89 (0.65-1.21)	-
Sampling year	1.05 (0.93-1.18)	1.25 (1.10-1.43)**	0.95 (0.92-0.98)**
Vegetarian (yes vs. no)	-	-	1.53 (1.25-1.87)**
Organ meat consumption	-	0.85 (0.76-0.95)*	1.07 (0.97-1.19)
Drinking water: bottled	1.00	-	-
Drinking water: tap	1.00 (0.85-1.18)	-	-
Drinking water: ground	0.95 (0.64-1.40)	-	-
Drinking water: other	1.24 (0.96-1.60) #	-	-

p < 0.10, * p < 0.05, ** p < 0.01, - not included into the model. The models are additionally adjusted for creatinine. Consumption of food items is defined by the frequency: 0 = Never, 1 = Rarely: <1 time / month, 2 = Sometimes: <= 1 time / week but >= 1 time/month, 3 = Often: 2-3 times / week, 4 = Very Often: 4-6 times / week, 5 = Everyday: >= 7 times / week.

Table S3. Multilevel mixed regression models for the pooled European population with study as a random factor and inclusion of NUTS2-based variables. The estimates are expressed as the fold change in Cd concentration for unit increase of the covariate.

Cd in urine ($\mu\text{g/g crt}$)	Estimate (95% CI), Model 4	Estimate (95% CI), Model 5	Estimate (95% CI), Model 6	Estimate (95% CI), Model 7	Estimate (95% CI), Model 8
<i>n</i>	2173 (8 studies)	2173 (8 studies)	906 (3 studies)	1980 (7 studies)	501 (3 studies)
overall <i>p</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001
<i>var</i> BETWEEN	45 %	45 %	43 %	41 %	<0.01 %
Age (years)	1.03 (1.02-1.03)**	1.03 (1.02-1.04)**	1.02 (1.01-1.03)**	1.03 (1.02-1.03)**	1.02 (1.01-1.03)**
Sex (F vs. M)	1.30 (1.23-1.37)**	1.30 (1.23-1.37)**	1.23 (1.13-1.34)**	1.28 (1.21-1.35)**	1.34 (1.20-1.49)**
Smoking (yes vs. no)	1.26 (1.18-1.35)**	1.26 (1.17-1.35)**	1.23 (1.10-1.37)**	1.21 (1.13-1.30)**	1.27 (1.12-1.45)**
ISCED - low	1.00	1.00	1.00	1.00	1.00
ISCED - medium	0.92 (0.80-1.07)	0.93 (0.80-1.08)	0.87 (0.58-1.31)	0.98 (0.82-1.17)	0.80 (0.44-1.47)
ISCED - high	0.91 (0.79-1.05)	0.92 (0.80-1.06)	0.78 (0.52-1.18)	0.95 (0.80-1.13)	0.70 (0.38-1.26)
Sampling year	0.96 (0.93-1.00)#	0.97 (0.93-1.01)#	0.99 (0.89-1.10)	0.96 (0.92-0.99)*	0.94 (0.90-0.98)**
Cd in soil (mg/kg)	1.04 (0.35-3.12)	-	-	-	-
Cropland (10% change)	-	1.03 (1.00-1.06)#	-	-	-
P fertilizer (100 kg/km ²)	-	-	1.06 (1.03-1.09)**	-	-
Road density (km/km ²)	-	-	-	1.27 (1.15-1.40)**	-
Cd release (0.010 kg/km ²)	-	-	-	-	1.10 (1.01-1.19)*

$p < 0.10$, * $p < 0.05$, ** $p < 0.01$

Model 4 = adjusted for creatinine, sample type, age, sex, smoking, education, sampling year, and Cd in soil from LUCAS database (CZ, DE, DK, FR, CRO, LU, PL, PT);

Model 5 = adjusted for creatinine, sample type, age, sex, smoking, education, sampling year, and percent cropland from Eurostat (CZ, DE, DK, FR, CRO, LU, PL, PT);

Model 6 = adjusted for creatinine, sample type, age, sex, smoking, education, sampling year, and phosphate fertilizer application from Eurostat (CZ, FR, PL);

Model 7 = adjusted for creatinine, sample type, age, sex, smoking, education, sampling year, and road density from Eurostat (CZ, DE, DK, FR, CRO, LU, PL);

Model 8 = adjusted for creatinine, sample type, age, sex, smoking, education, sampling year, and Cd release from E-PRTR (CZ, DE, FR).

Table S4. Geometric means (96% confidence intervals) for the DEMOCOPHES study and HBM4EU Aligned Studies population groups of women.

Cd in urine ($\mu\text{g/g crt}$)	ALL	n	DK	n	PL	n	CZ	n	PT	n	LU	n	DE	n	Reference
DEMOCOPHES ALL mothers	0.20 (0.19-0.20)	1685	0.12 (0.10-0.13)	142	0.38 (0.33-0.43)	119	0.21 (0.19-0.24)	117	0.16 (0.14-0.18)	117	0.22 (0.18-0.26)	56	0.18 (0.17-0.20)	108	den Hond et al., 2015; Schwendler et al. 2017
HBM4EU Aligned studies Females	0.20 (0.19-0.21)	1350	0.14 (0.12-0.15)	122	0.38 (0.35-0.41)	158	0.11 (0.10-0.13)	155	0.11 (0.09-0.12)	171	0.22 (0.20-0.24)	111	0.30 (0.28-0.33)	144	present study
DEMOCOPHES Non-smoking mothers	0.18 (0.18-0.19)	1272	0.11 (0.09-0.12)	123	0.36 (0.31-0.42)	81	0.21 (0.19-0.23)	94	0.13 (0.11-0.16)	68	0.21 (0.18-0.25)	51	-	-	Berglund et al., 2015
HBM4EU Aligned studies Non-smoking females	0.20 (0.19-0.21)	1117	0.13 (0.12-0.14)	117	0.38 (0.34-0.41)	144	0.11 (0.10-0.13)	133	0.10 (0.09-0.11)	129	0.21 (0.19-0.23)	92	-	-	present study

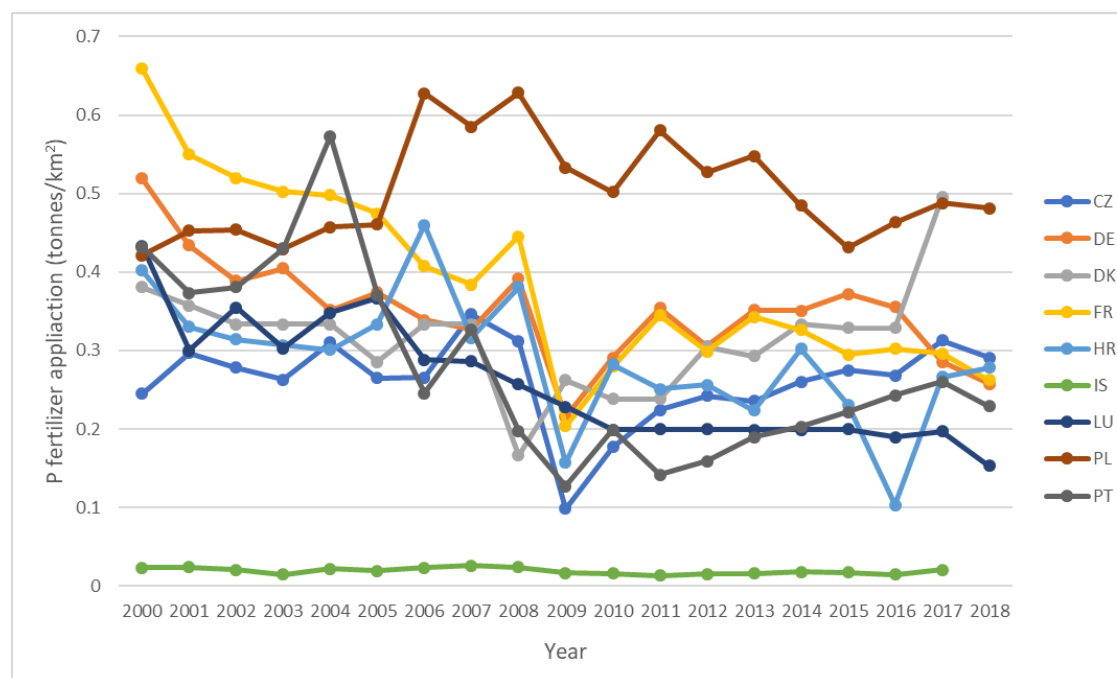


Figure S2. Application of phosphate fertilizer in tonnes per km^2 from 2000 to 2018 for each participating country. Data obtained from Eurostat.

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