

N-3 POLYUNSATURATED FATTY ACID (N-3 PUFA) DIETARY INTAKE AND ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN ADULTS ON HEMODIALYSIS: THE DIET-HD MULTINATIONAL COHORT STUDY



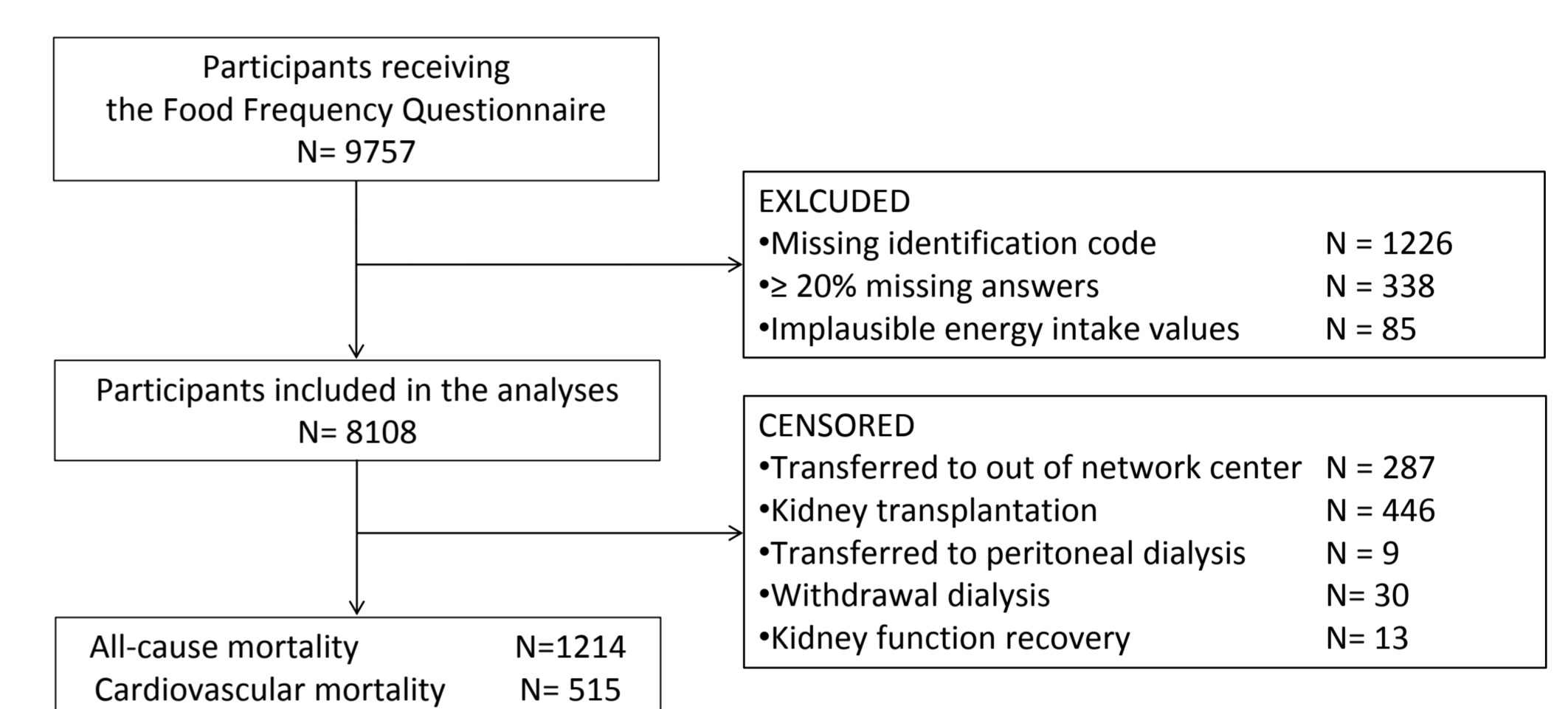
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Background Hemodialysis patients experience high mortality, largely due to cardiovascular disease (CVD). Interventions for CVD have been ineffective in this population and novel therapies are needed. N-3 PUFA is a novel intervention shown to reduce CV mortality by 10-30% in the general population compared to placebo. It is recommended in the general population for primary and secondary CV prevention but its role in hemodialysis (HD) is not well studied.

Methods The DIET-HD study is a cohort study (n=9235) conducted between January 2014 and January 2016 in 11 countries across Europe and South America. It aims to examine the association between nutrition and dietary patterns with major health outcomes in prevalent adult HD patients. All participants received a food frequency questionnaire validated for N-3 PUFA. Adjusted Cox regression analyses clustered by country were undertaken to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for CV and all-cause mortality associated with N-3 PUFA dietary intake.

Figure 1: Flow chart of patients' participation



Results Of 9757 patients, 8108 (83%) were included in the analysis (Figure 1 and Table 1). The median (interquartile range) dietary intake of n-3 PUFA was 1.2 (0.3 to 2.4) grams per week. It varied considerably among countries. However the majority of the study population consumed much less dietary n-3 PUFA than recommended for CV prevention. Even though patients in countries with lower incidence of mortality reported higher dietary intake of n-3 PUFA in aggregated data analysis (Figure 2), no association between dietary n-3 PUFA and mortality was observed in adjusted random effect analysis (Table 2), consistently across all countries (Figure 3).

Table 1 Table 1: Baseline characteristics of patients

Variable	Value
Age (years), mean (SD)	63.1 (15.0)
Male gender, n (%)	4707 (57.8)
Hypertension, n (%)	6232 (84.9)
Diabetes, n (%)	2338 (32.0)
Congestive heart failure, n (%)	1392 (19.1)
Myocardial infarction, n (%)	841 (11.6)
Stroke, n (%)	638 (8.8)
Albumin (g/L) mean (SD)	39.8 (3.8)
Serum phosphorus (mg/dL) mean (SD)	4.7 (1.4)
Hemoglobin (g/dL) mean (SD)	11.1 (1.3)
Time on dialysis (years), median (IQR)	3.6 (1.7- 6.8)
Kt/V urea, mean (SD)	1.7 (0.3)

Figure 2: Unadjusted incidence of cardiovascular and all-cause mortality and dietary intake of n-3 shown by country

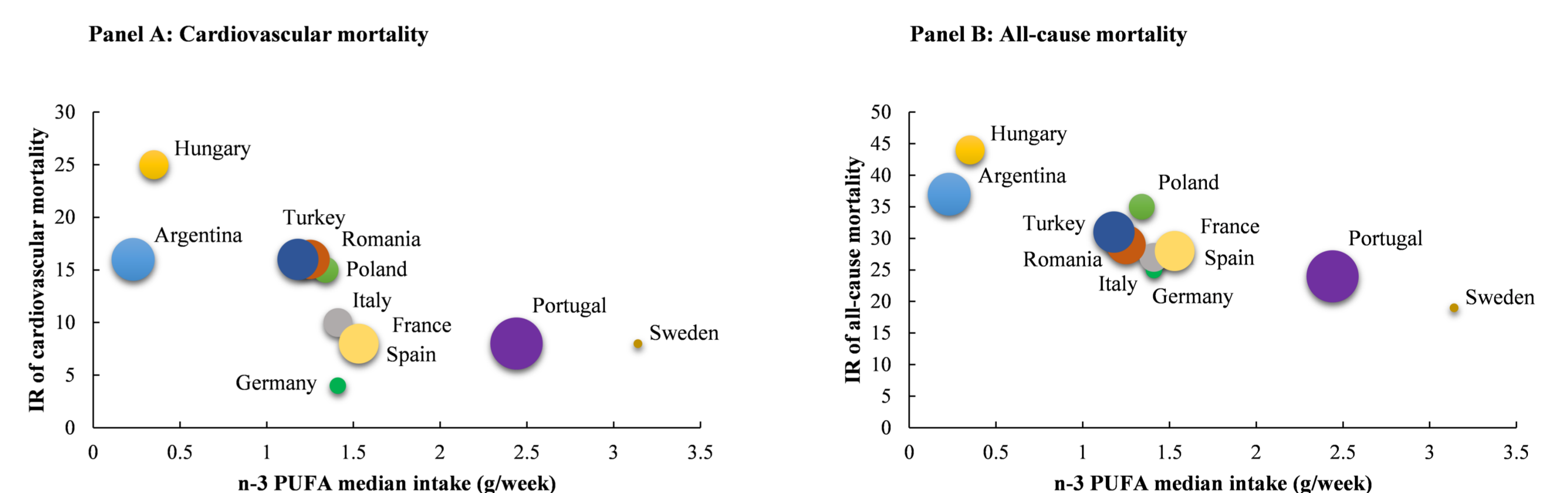
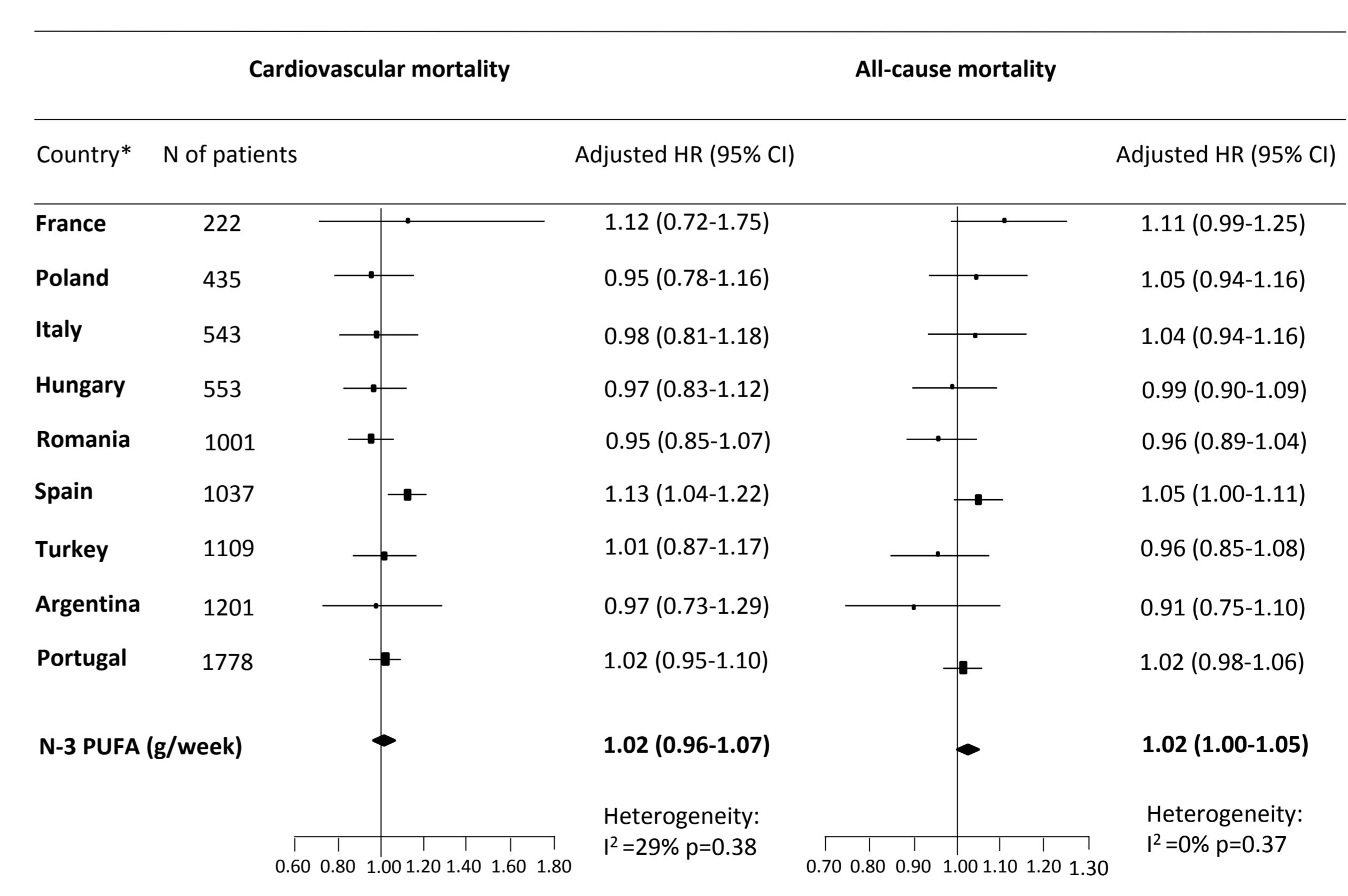


Table 2. Adjusted association of dietary n-3 PUFA and clinical characteristics with cardiovascular and all cause-mortality

	Cardiovascular mortality		All-cause mortality	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
N-3 PUFA tertile (g/week)				
Lowest (<0.7)	1.00 (reference)		1.00 (reference)	
Middle (0.37-1.7)	0.80 (0.64-1.00)	0.05	0.95 (0.82-1.09)	0.45
Highest (≥1.7)	1.13 (0.88-1.45)	0.34	1.08 (0.92-1.28)	0.34
N-6 PUFA tertile (g/week)				
Lowest (<31)	1.00 (reference)		1.00 (reference)	
Middle (31-61)	1.01 (0.80-1.28)	0.92	1.01 (0.86-1.18)	0.92
Highest (≥61)	0.95 (0.73-1.25)	0.73	1.14 (0.96-1.36)	0.14
Age (1 year increase)	1.04 (1.03-1.05)	<.0001	1.04 (1.04-1.05)	<.0001
Men	1.09 (0.89-1.34)	0.39	1.09 (0.96-1.24)	0.20
Smoker (former/current vs never)	1.26 (1.01-1.57)	0.05	1.17 (1.01-1.35)	0.04
Myocardial infarction (yes vs no)	2.29 (1.80-2.91)	<.0001	1.67 (1.42-1.97)	<.0001
Albumin tertile (g/L)				
Lowest (<38)	1.00 (reference)		1.00 (reference)	
Middle (38-40)	0.60 (0.46-0.77)	<.001	0.49 (0.41-0.57)	<.0001
Highest (≥40)	0.50 (0.38-0.66)	<.0001	0.37 (0.31-0.44)	<.0001
Body mass index (kg/m²)				
< 18	1.00 (reference)		1.00 (reference)	
18-24	0.79 (0.52-1.19)	0.26	0.67 (0.52-0.86)	<.001
25-29	0.58 (0.38-0.89)	0.01	0.50 (0.39-0.65)	<.0001
≥30	0.49 (0.31-0.77)	<.0001	0.44 (0.34-0.58)	<.0001
Kt/V	0.66 (0.48-0.90)	0.01	0.69 (0.56-0.84)	<.001
Energy intake (kcal/week)	1.00 (1.00-1.00)	-	1.00 (1.00-1.00)	-

Figure 3. Adjusted association of dietary n-3 PUFA with cardiovascular and all cause-mortality by country



*Hazard ratios for Germany and Sweden were not estimable due to the low number of outcome events

Conclusion There was no association between dietary n-3 PUFA and CV or all-cause mortality in this multinational hemodialysis cohort. Dietary n-3 PUFA intake was much lower than recommended to prevent CV disease, that may in part explain our findings.

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