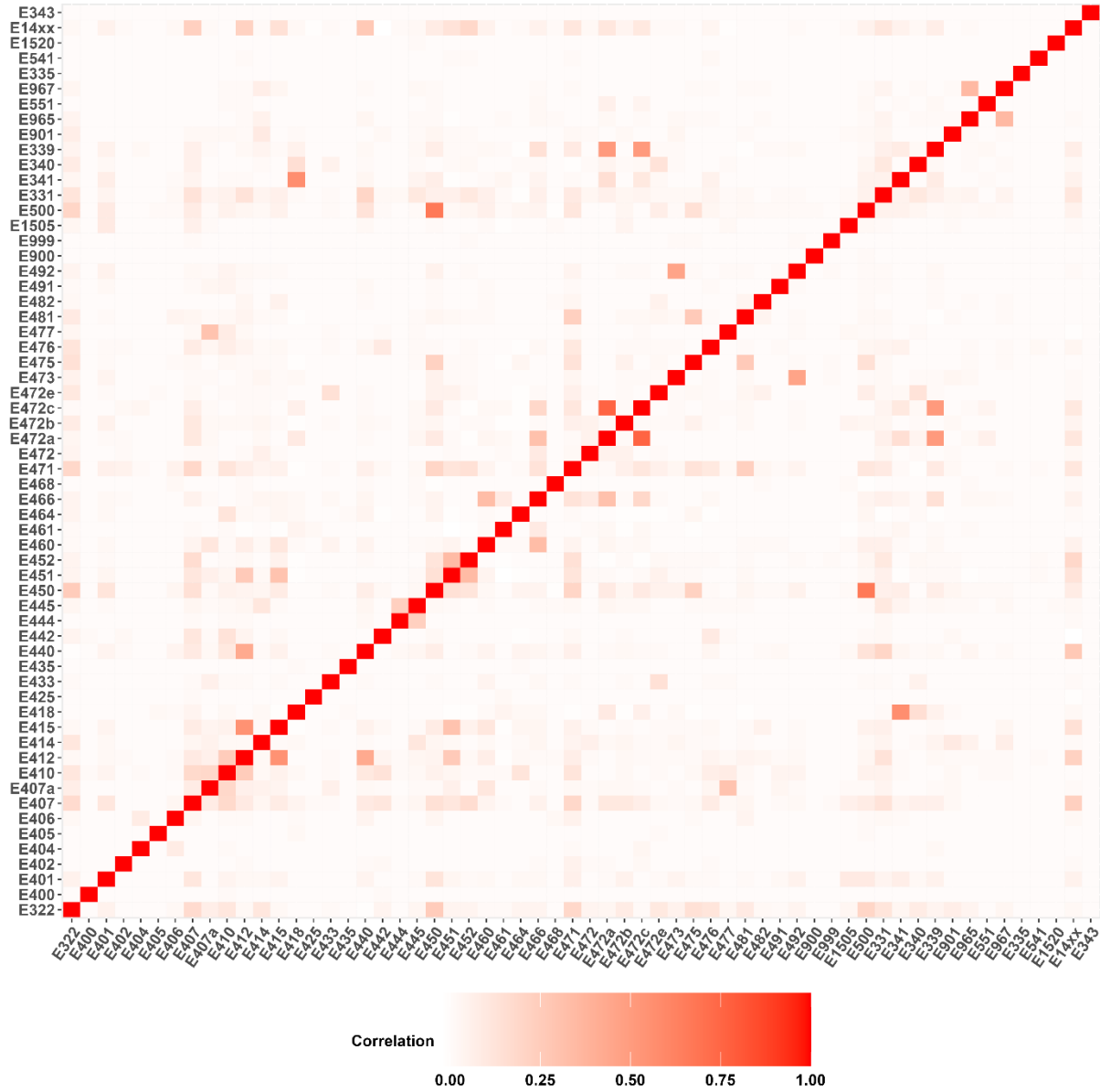


eData

eFigure1. Correlations between intakes of food additive emulsifiers among participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442).



eMethods

eMethod1. Method for the identification of under-reporters of energy intake

Participants who under-reported their energy intake were excluded from the analyses and were identified using the method from Black,[1,2] based on the original method developed by Goldberg et al.[3] This method relies on the hypothesis that the maintenance of a stable body weight requires a balance between energy intake and expenditure. The equations developed by Black account for the reported dietary energy intake, basal metabolic rate (calculated using Schofield's equations)[4], sex, age, height, weight, number of dietary records, physical activity level (PAL), and intra/inter-individual variability. As recommended by Black, the intra-individual coefficients of variations for BMR and PAL were fixed at 8.5 % and 15%, respectively. In addition, a PAL of 1.55 was used to reflect a "light" physical activity which is assumed to be attained by healthy, normally active individual living a sedentary lifestyle. Finally, some individuals identified as under-reporters of energy intakes using Black's method were not excluded, if they also reported recent weight variations, adherence to weight-loss restrictive diets, or declared the consumptions entered in their dietary records as unusually low compared to their habitual diets.

In this study 21,708 participants (corresponding to 16.9% of the subjects) were considered as under-energy reporters and were excluded from the study. This proportion of under-reporters is common, for instance in the nationally representative INCA 3 study conducted in 2016 by the French Food Safety Agency [5] 18% of adult participants were identified as under-reporters using the Black method.

Several quality control operations were performed to account for over-reporting. Limitations in the online tool were set when participants reported the quantities of food consumed, aiming to alert them that the number they were about to enter was potentially an outlier, thereby encouraging double check and correction. Later on, during the data cleaning process, limitations were set per food category within one eating episode and per record for quantities; for instance, limitations for fruits were set for 3000 grams/day, 1500 grams/day for fish, 2000 grams/day for yoghurts, etc... if more than 10% of reported food items had outliers, then the full record was excluded. Otherwise, values were corrected to the maximum authorised values or standardised.

eMethod2. Detailed quantitative assessment of emulsifiers

The strength of our methodology relies in the precise qualitative assessment of additive exposure, i.e., presence/absence of a specific emulsifier in the food consumed. This unique level of detail is permitted by the fact that commercial names/brands of industrial product consumed were collected and matched with Open Food Facts, Oqali and GNPD databases providing the ingredient list and thus, presence of the specific emulsifier), at the time when the product was consumed. Thus, we only attribute a non-null dose of a specific additive to a given product declare by a participant if this specific product contains this specific additive.

Then, the quantitative assessment of the doses of additives in the products which contain a specific additive is challenging since manufacturers are not compelled to declare this information on the packaging. Hence the 3-step method used to assess doses in our cohort. In all, in the framework of the ADDITIVES project, we performed 2677 quantified analyses, corresponding to a total of 61 food additives in 196 different (generic) food items. "Pairs" (i.e. a specific additive in a specific food vector) selected for laboratory assays corresponded to the most frequently consumed and most emblematic commercial food/beverage items for a given additive. Specifically, for emulsifiers, we had access to 501 laboratory quantified analyses corresponding to 9 emulsifiers (E322, E339, E340, E341, E343, E440,

E450, E451, E452) in 37 (generic) food items (several commercial brands were tested per food item, e.g., in the case of milk chocolate, milk chocolate with nuts, creamy desserts, omega-3 enriched margarines, sausages, jams, chocolate mousse...). In addition to the assays carried out by certified laboratories, which were sent to us by the consumer association UFC Que Choisir, we contacted two companies (Mérieux & Eurofins) and the Direction Générale de la Consommation, de la Concurrence et de la Répression des Fraudes (DGCCRF) to carry out these assays. Only the additives listed in their catalogue could be measured. In case data was not available from this source, EFSA and GSFA doses were only applied if the specific food item did actually contain the specific emulsifier in the ingredients list. We used 1497 emulsifier data from EFSA (data available online in each EFSA Opinion + transmission of specific information by EFSA following an official Public Access to Document request PAD 2020/077), related to 58 food additive emulsifiers present in 237 food categories. EFSA collects many information from manufacturers related to their specific commercial products but for confidentiality reasons, only transfers information for generic food items or food groups (no brand-specific data). As regards GSFA, we used 5352 emulsifier data concerning 45 food additive emulsifiers coming from 226 food categories. As for EFSA, data from GSFA are not brand-specific but relate to generic food items or food categories.

eMethod3. Method for multiple imputation of missing values

Missing values for covariates were handled using multiple imputation by additive regression, bootstrapping, and predictive mean matching (n=20 imputed datasets) as implemented in the *Hmisc* R package.[6] Missing values were imputed for the following variables: physical activity level (13.8% of missing values), smoking status (0.1%), education level (0.9%), and BMI (1.3%).

eMethod4. Method for deriving dietary patterns by principal component analysis and corresponding factor loadings

Dietary patterns and emulsifier intake patterns were identified based on 20 food categories, using a principal component analysis conducted with the R package *FactoMineR*.^[7] The principal component analysis creates linear combinations (called principal components) of the initial set of variables, with the aim to group those that are correlated while explaining as much variation from the dataset as possible. We used the scree plot generated by the principal component analysis to select the retained principal components (with eigen values ≥ 2). For easier interpretation, we used the R “varimax” option to rotate the principal components orthogonally and maximise the independence of the retained principal components.

The variable coefficients derived from the selected principal components are called factor loadings. A positive factor loading indicates a positive contribution of the variable to the principal component, whereas a negative factor loading indicates a negative contribution. For the interpretation of the two principal components selected, we considered the variables contributing the most to the component, i.e. with loading coefficients under -0.25 or over 0.25. We then label the principal components descriptively, based on the most contributing variables. Finally, we calculated an adherence score to each principal component and for each participant, using the food categories or emulsifier factor loadings to weigh the sum of all observed intakes. Thus, the adherence score measures a participant’s diet conformity to the identified dietary pattern or emulsifier intake pattern.

In the analyses of dietary patterns, we identified a healthy pattern (explaining 10.88% of the variance), which was characterized by higher intakes of fish and seafood, fruits, unsweetened soft drinks, vegetables, and wholegrains, along with lower intakes of sweetened soft drinks. In contrast, we identified a Western pattern (explaining 7.9% of the variance), which was characterized by higher intakes of fat and sauces, potatoes and tubers, and soups and broths.

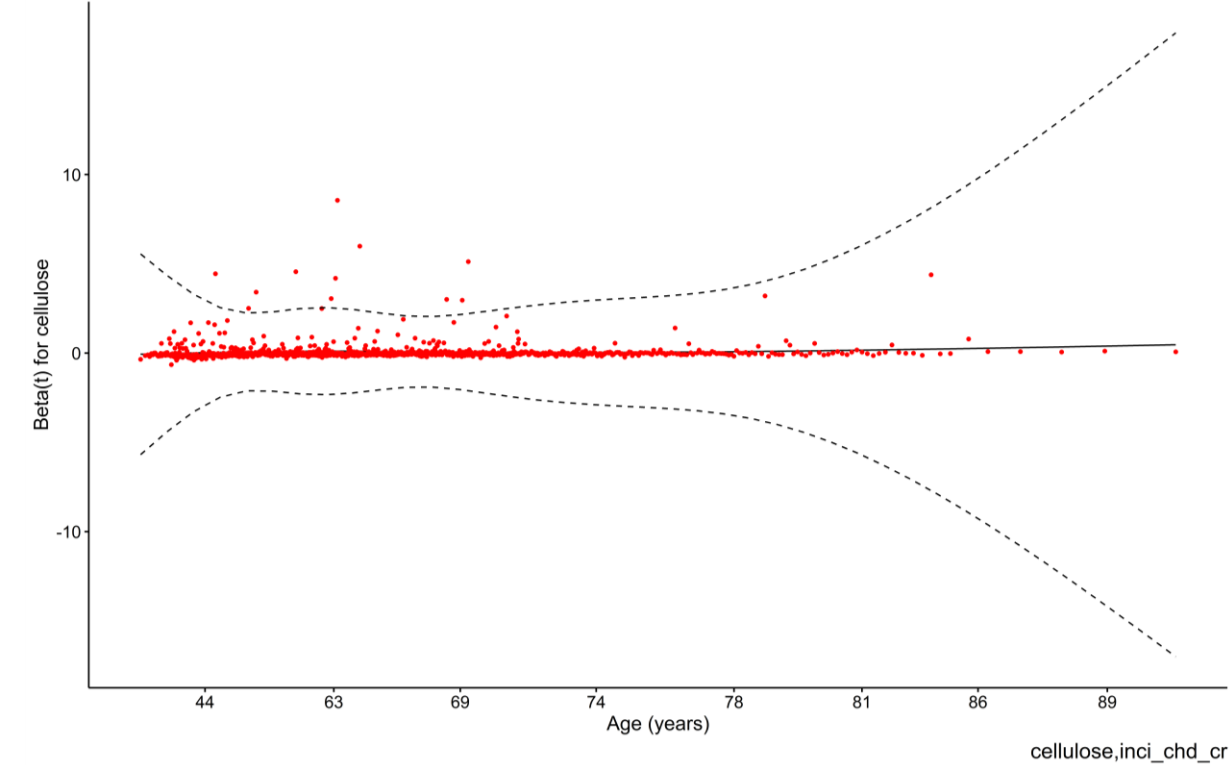
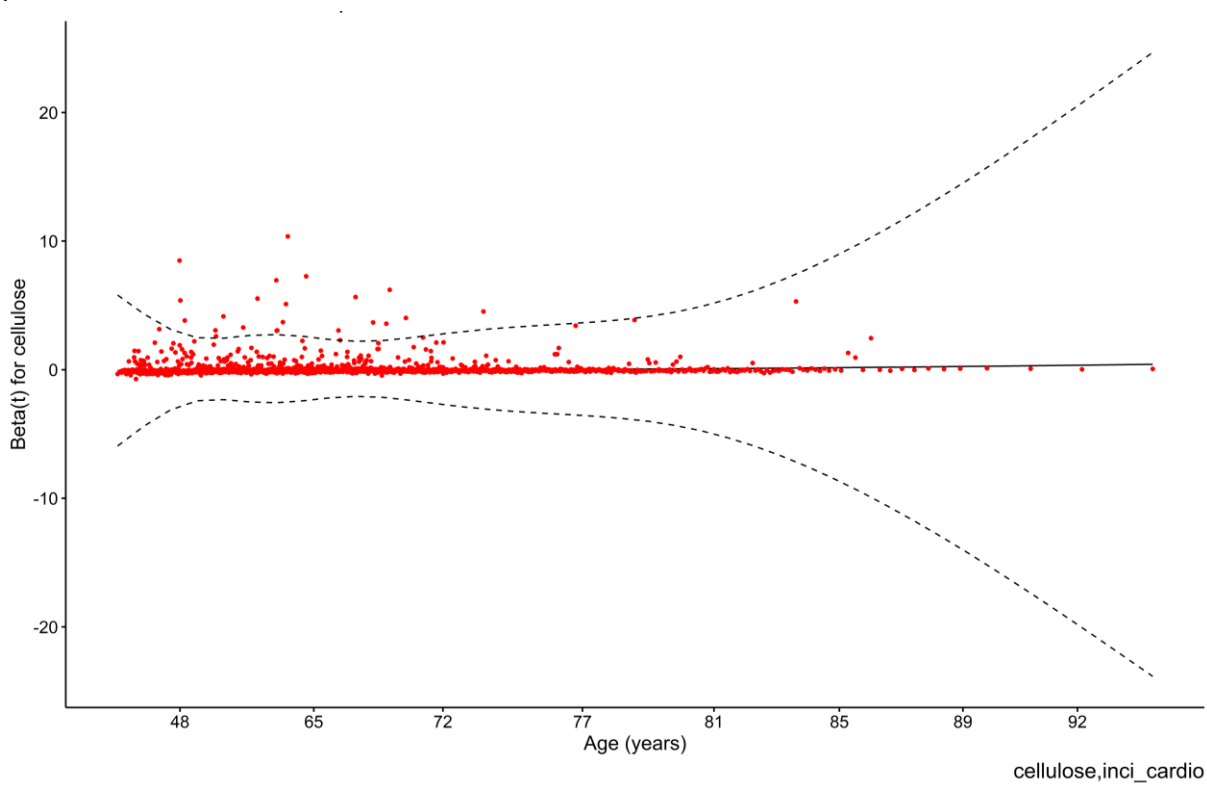
Food categories	Factor loadings	
	Healthy Pattern	Western Pattern
Alcoholic drinks	0,05	0,02
Breakfast cereals	0,02	-0,03
Cakes and biscuits	-0,05	-0,05
Dairy products	0,10	0,05
Eggs	0,12	0,01
Fats and sauces	0,13	0,48
Fish and seafood	0,29	-0,07
Fruit	0,46	-0,04
Meat	-0,08	0,20
Pasta and rice	0,06	0,16
Potatoes and tubers	-0,12	0,55
Poultry	0,04	0,00
Processed meat	0,06	-0,05
Pulses	0,05	0,17
Soups and broths	-0,01	0,53
Sugar and confectionery	0,12	0,03
Sweetened soft drinks	-0,26	0,04
Unsweetened soft drinks	0,53	-0,12
Vegetables	0,44	0,24
Whole grains	0,26	0,02

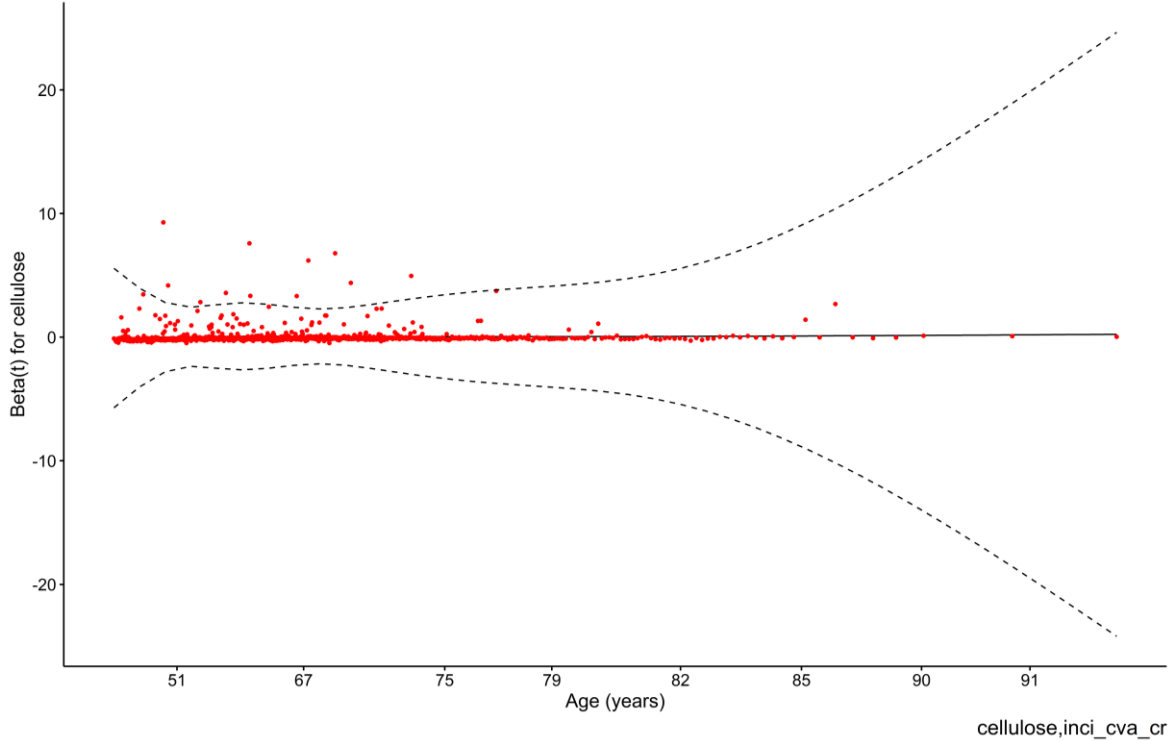
Sellem, Srour et al. 2023 - Food additive emulsifiers and cardiovascular disease risk: results from the prospective NutriNet-Santé cohort – Online supplementary material

eFigure2. Correlations between Schoenfeld residuals and timescale (age, y) from multivariable Cox models between emulsifier intakes and total CVD, CHD, and CVA risks in participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442).

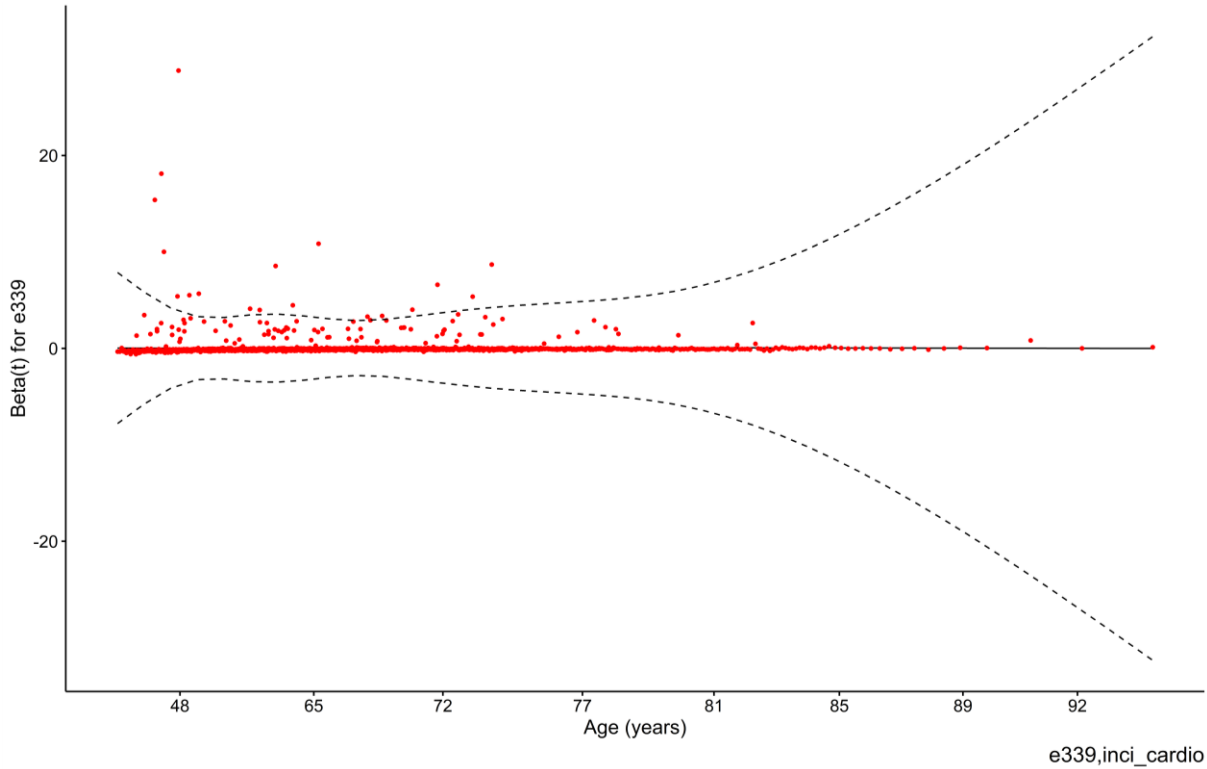
Abbreviations: CHD, coronary heart disease; CVA, cerebrovascular disease; CVD, cardiovascular disease.

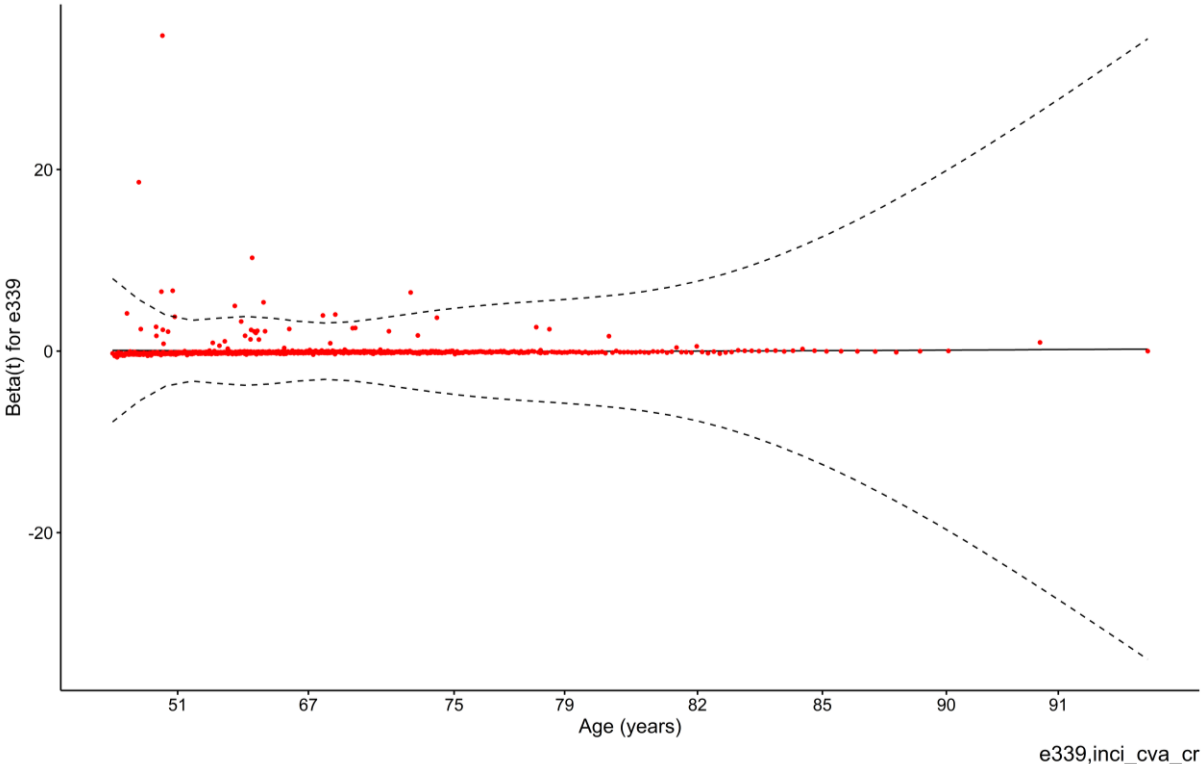
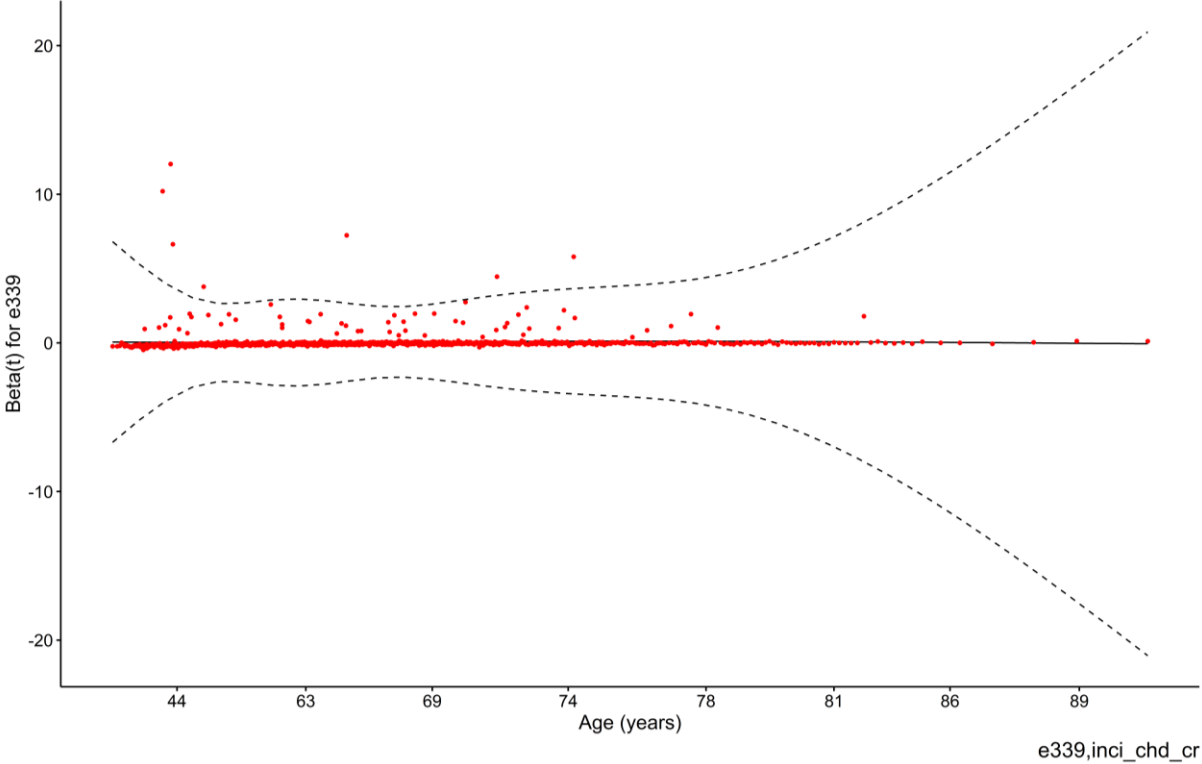
A: Associations between total cellulose intake (E460, E461, E464, E466, E468) and CVD risks



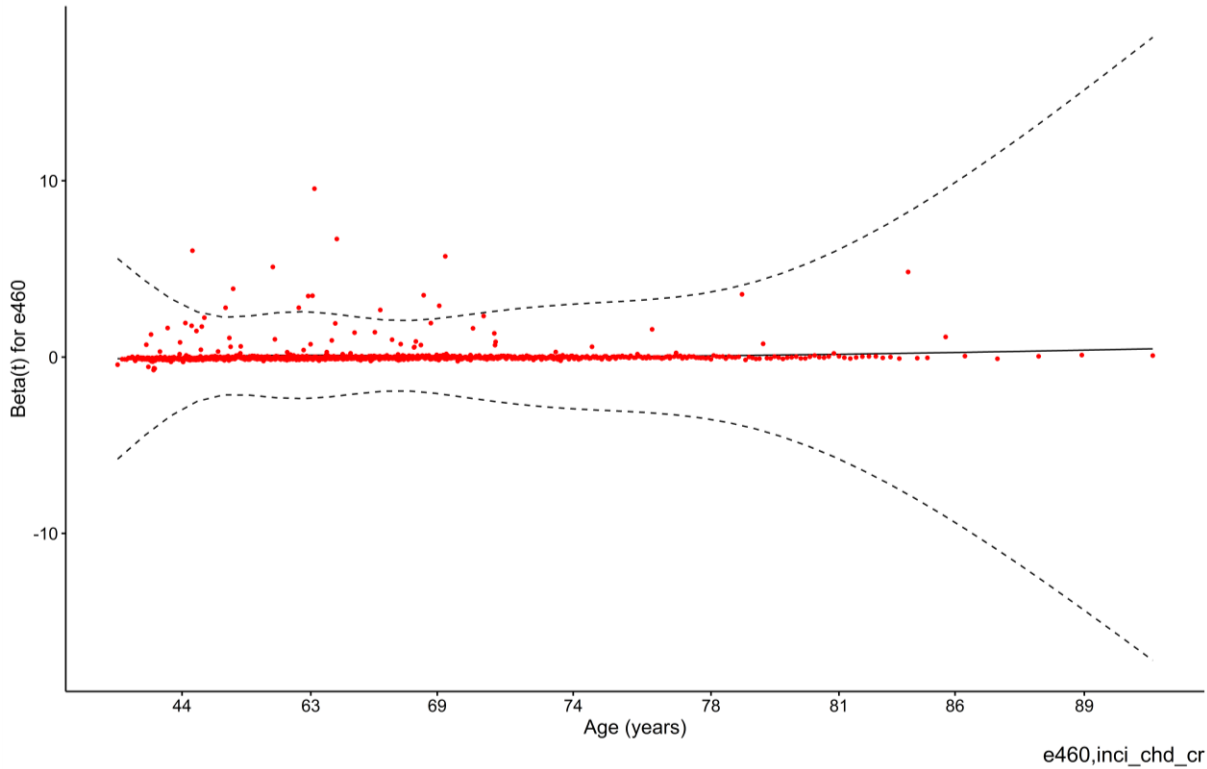
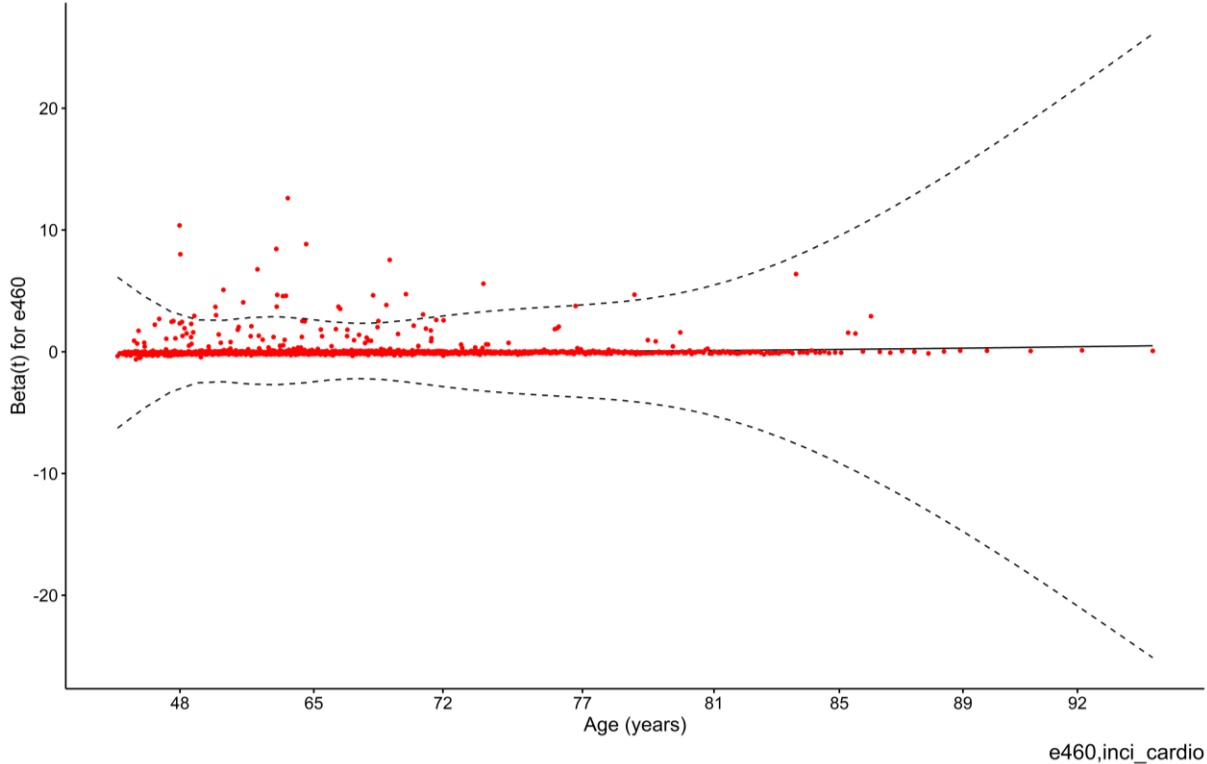


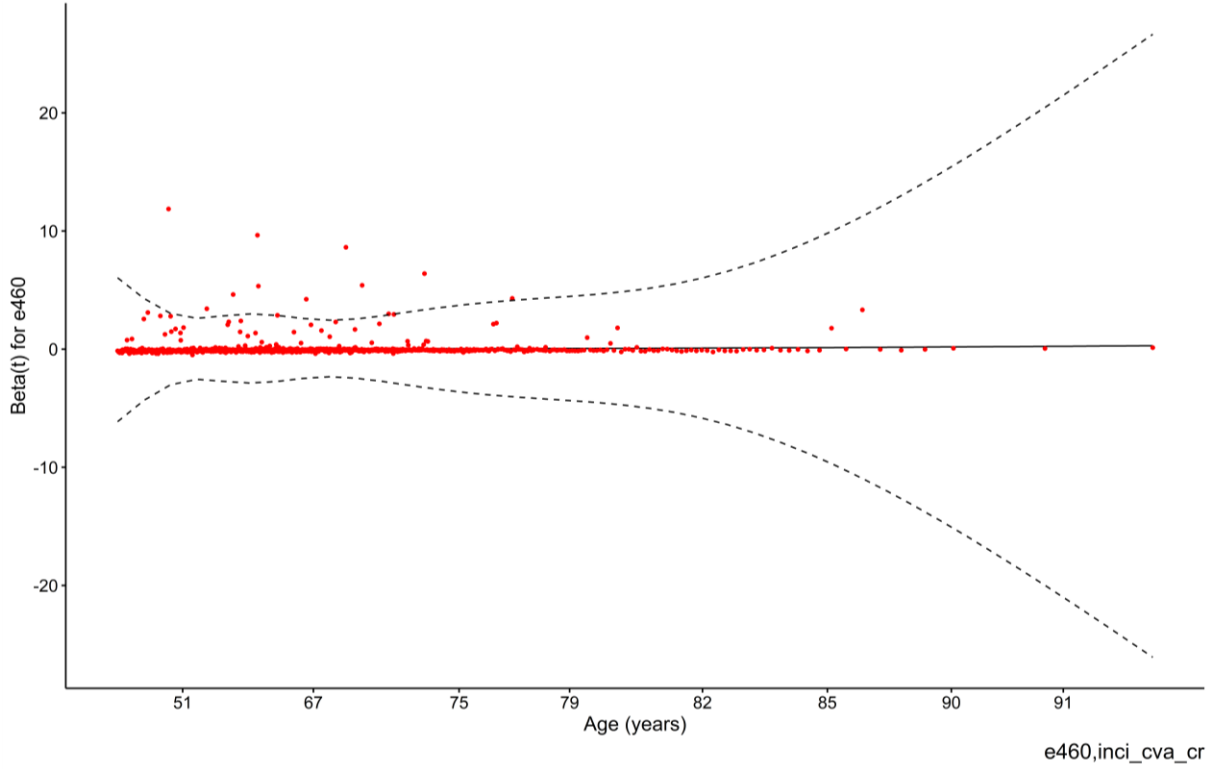
B: Associations between Trisodium phosphate E339 intake and CVD risks



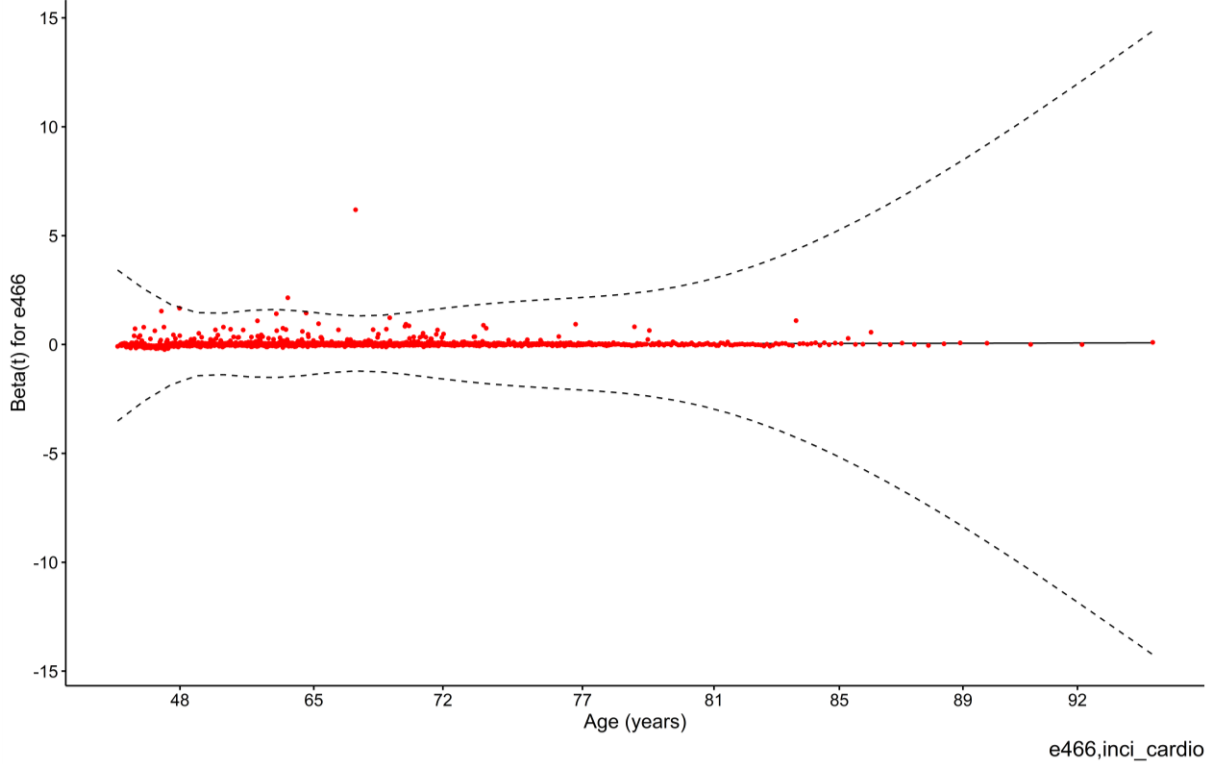


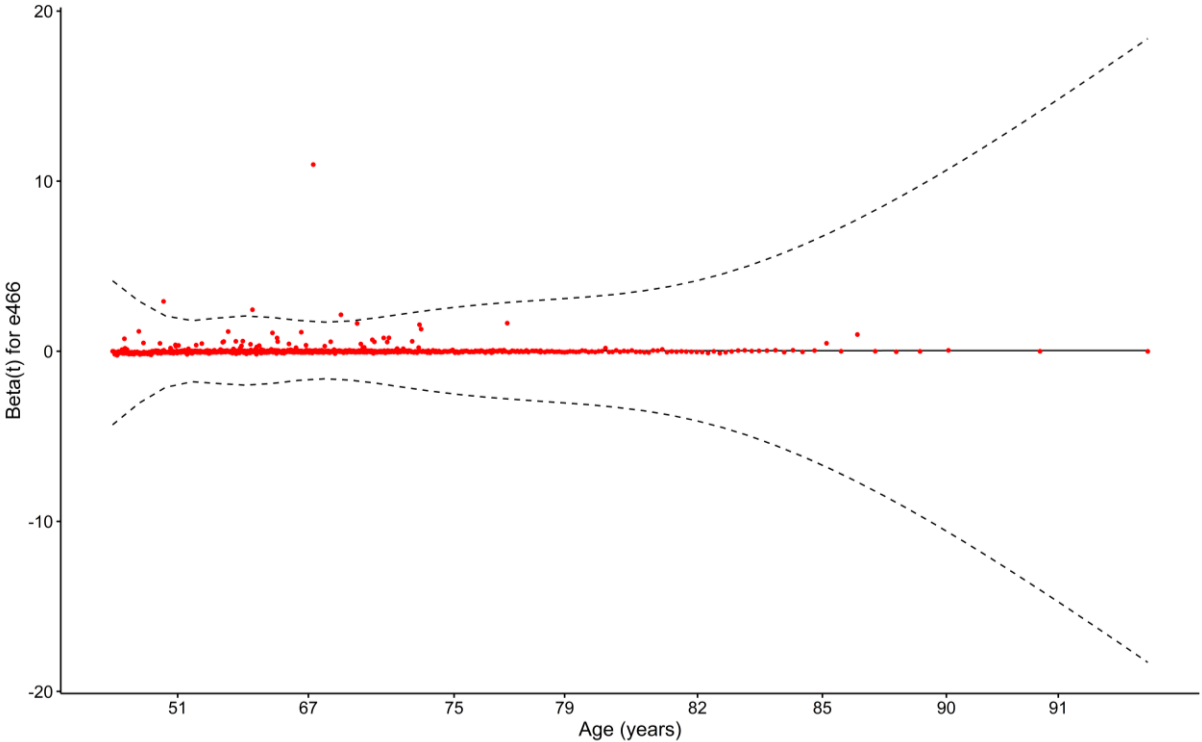
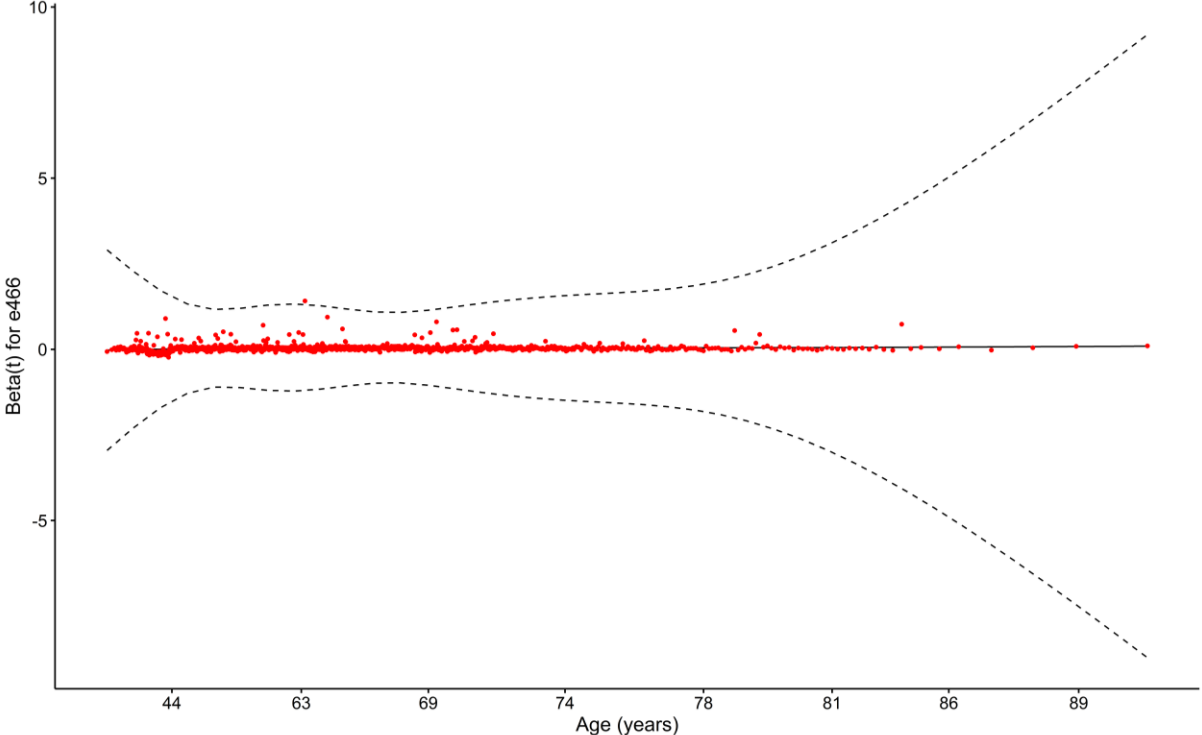
C: Associations between Cellulose E460 intake and CVD risks



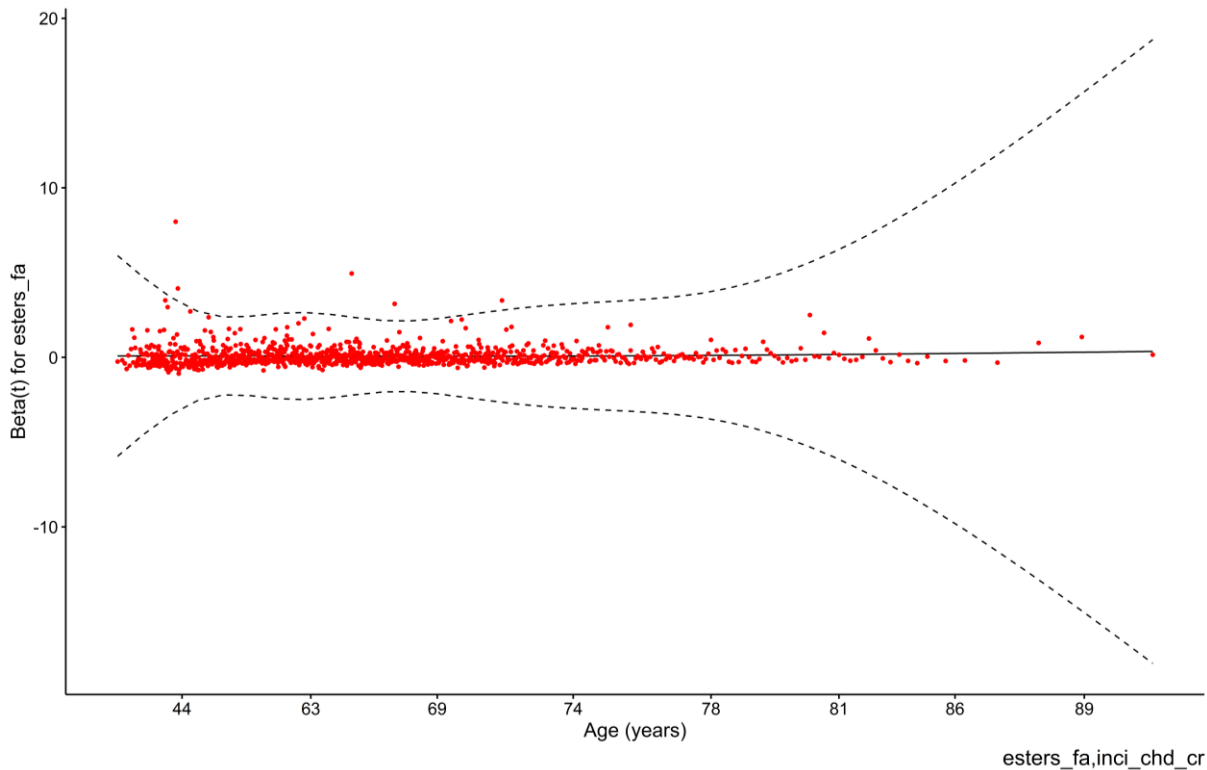
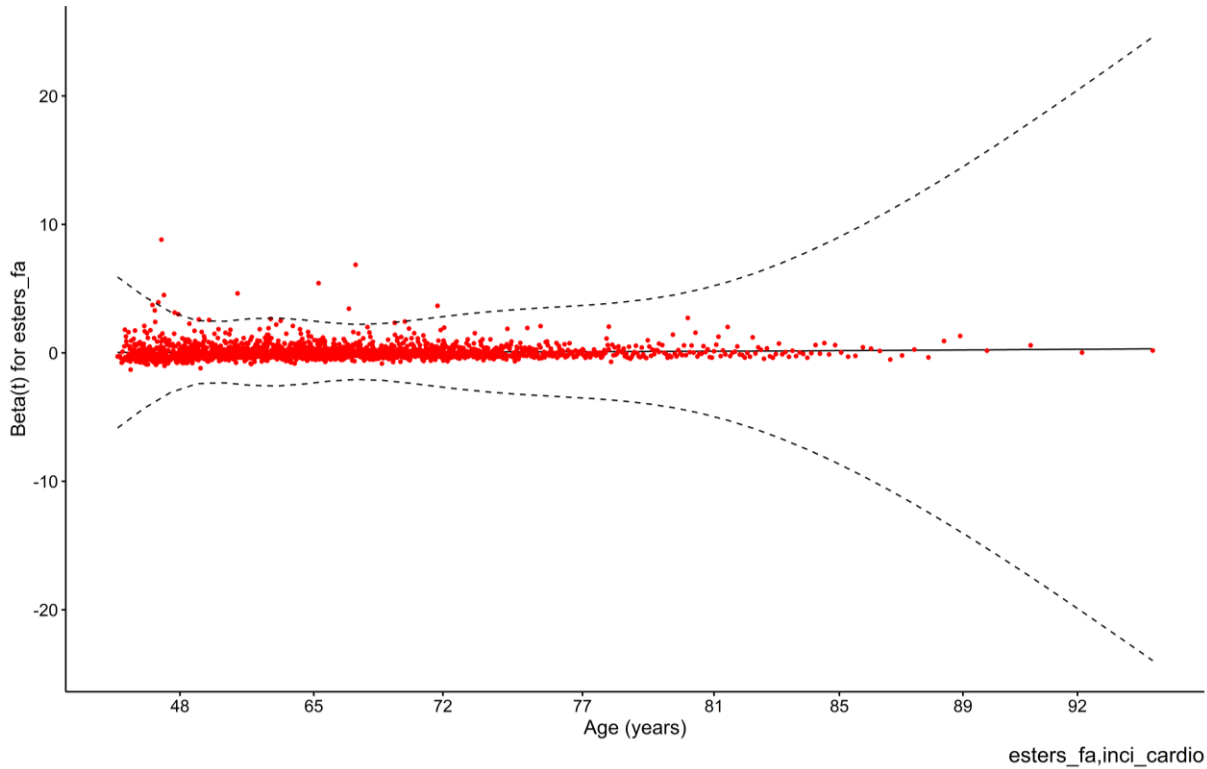


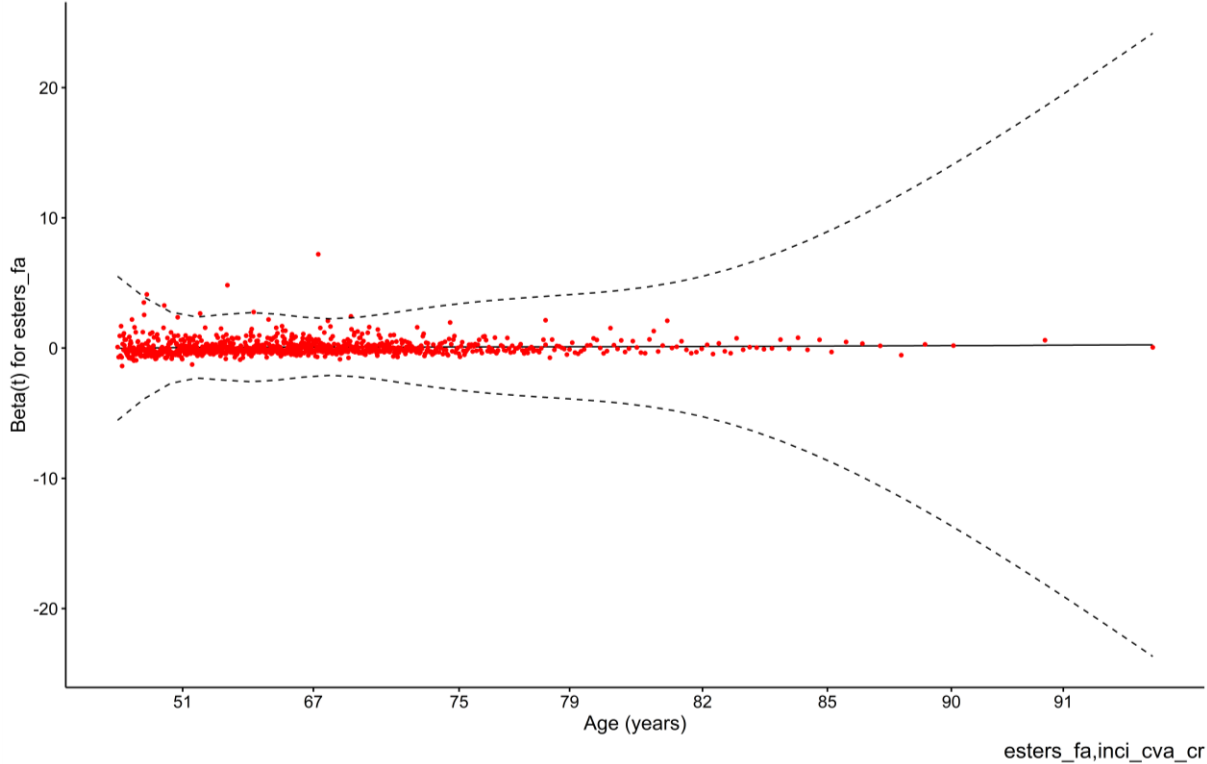
D: Associations between Carboxymethyl cellulose E466 intake and CVD risks



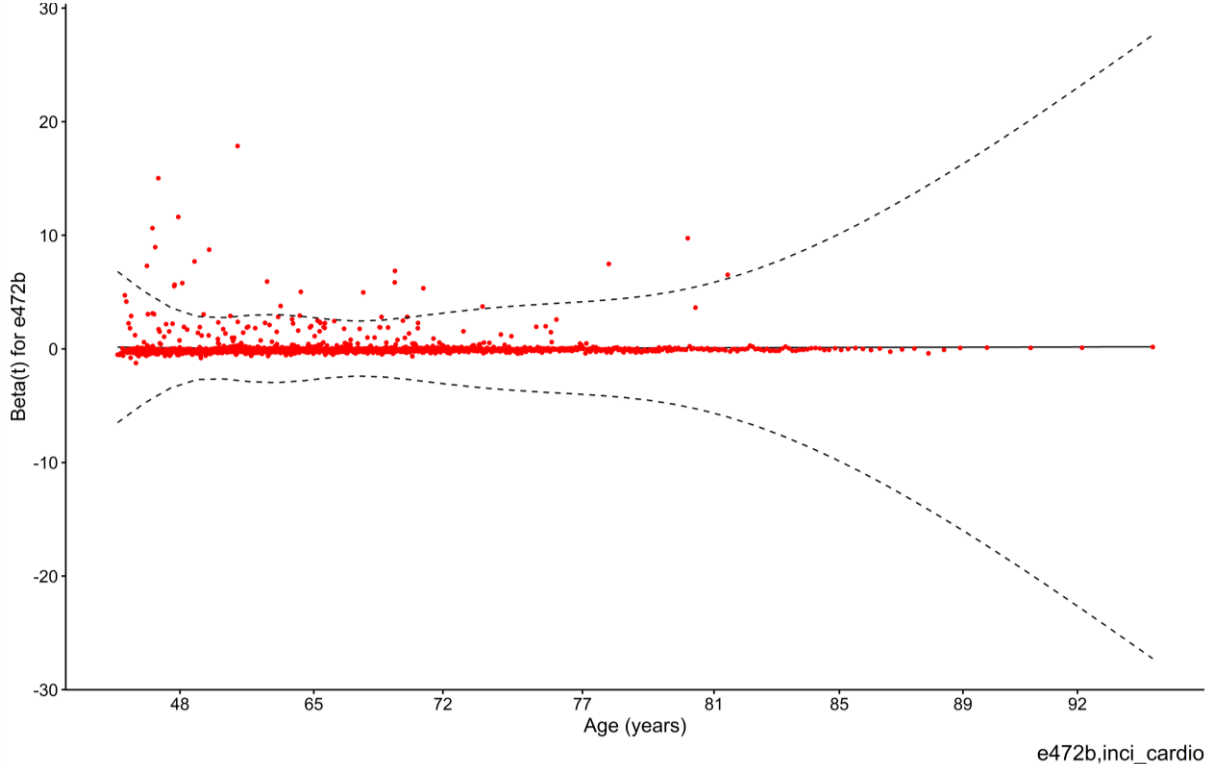


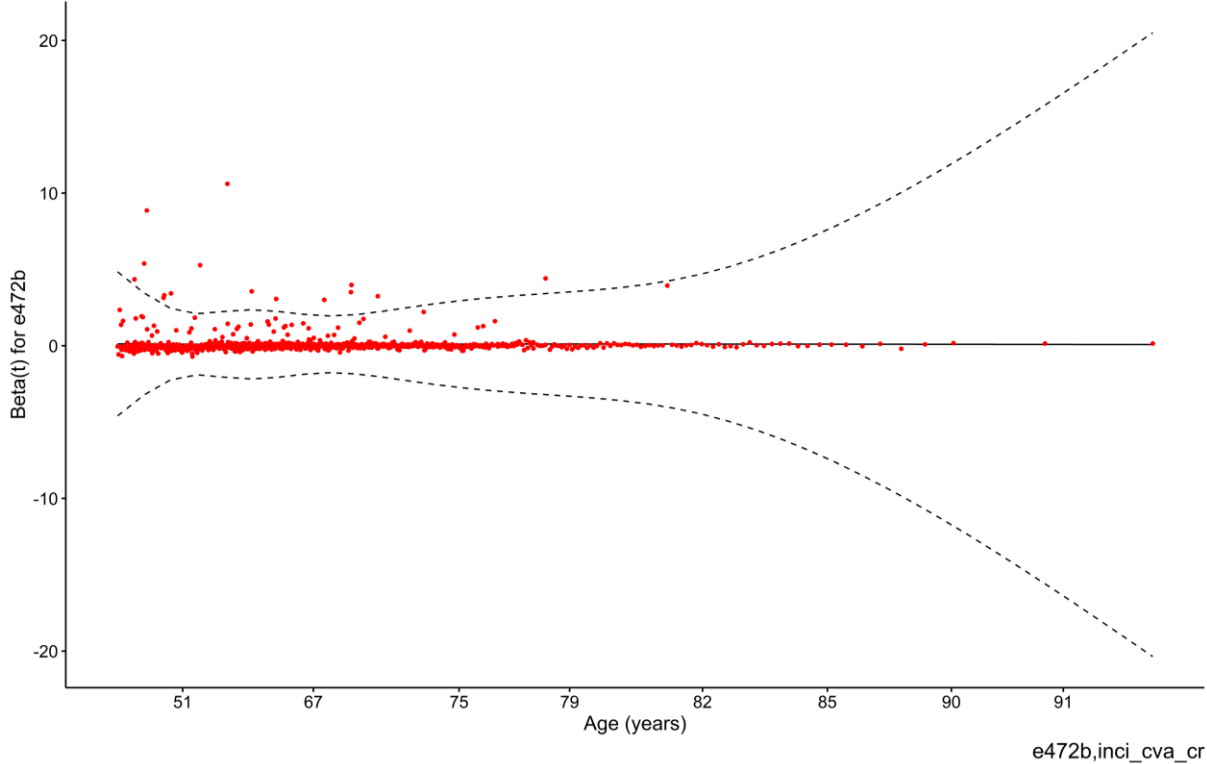
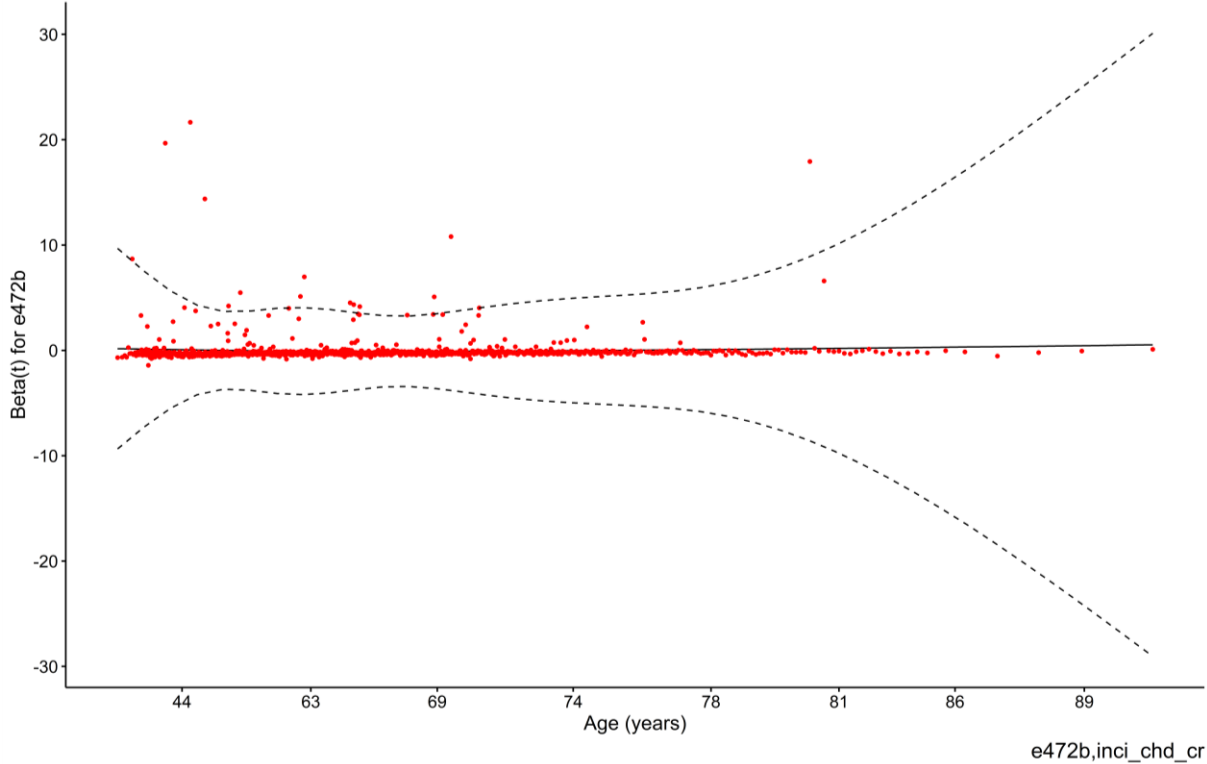
E: Associations between Total mono- and diglycerides of FAs (E471, E472, E472a, E472b, E472c, E472e) intake and CVD risks



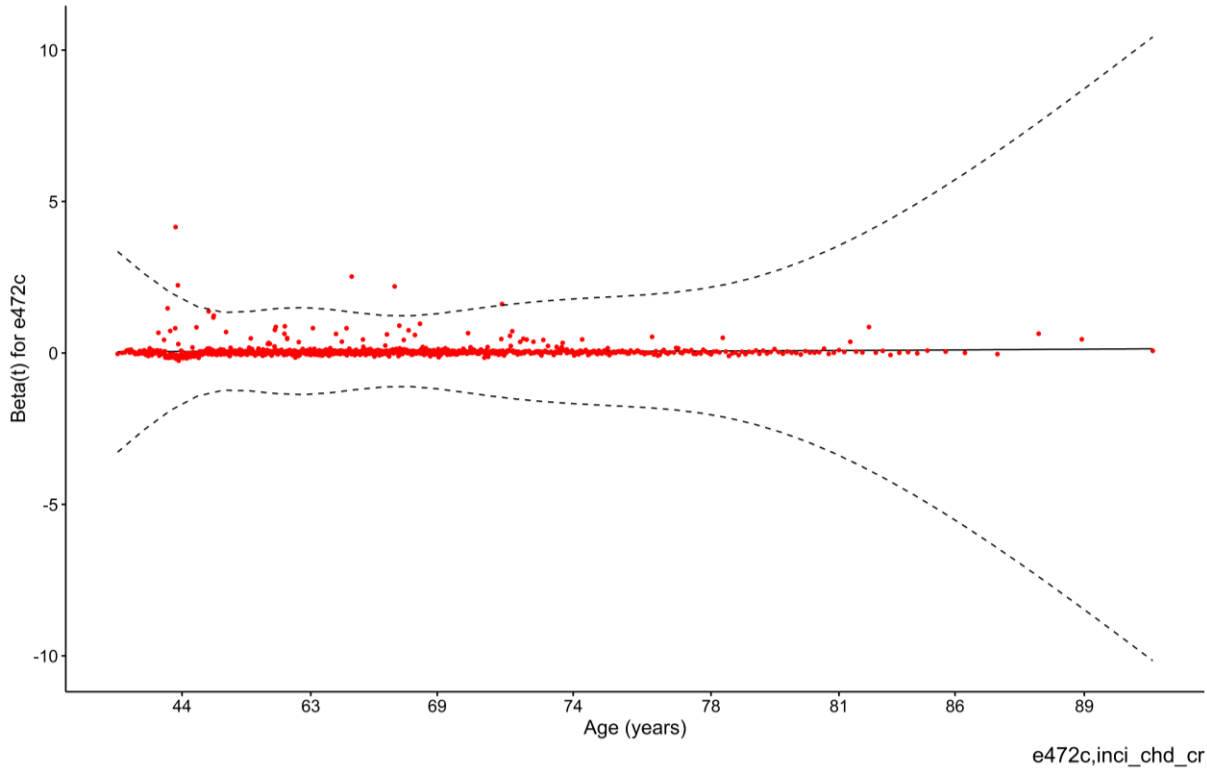
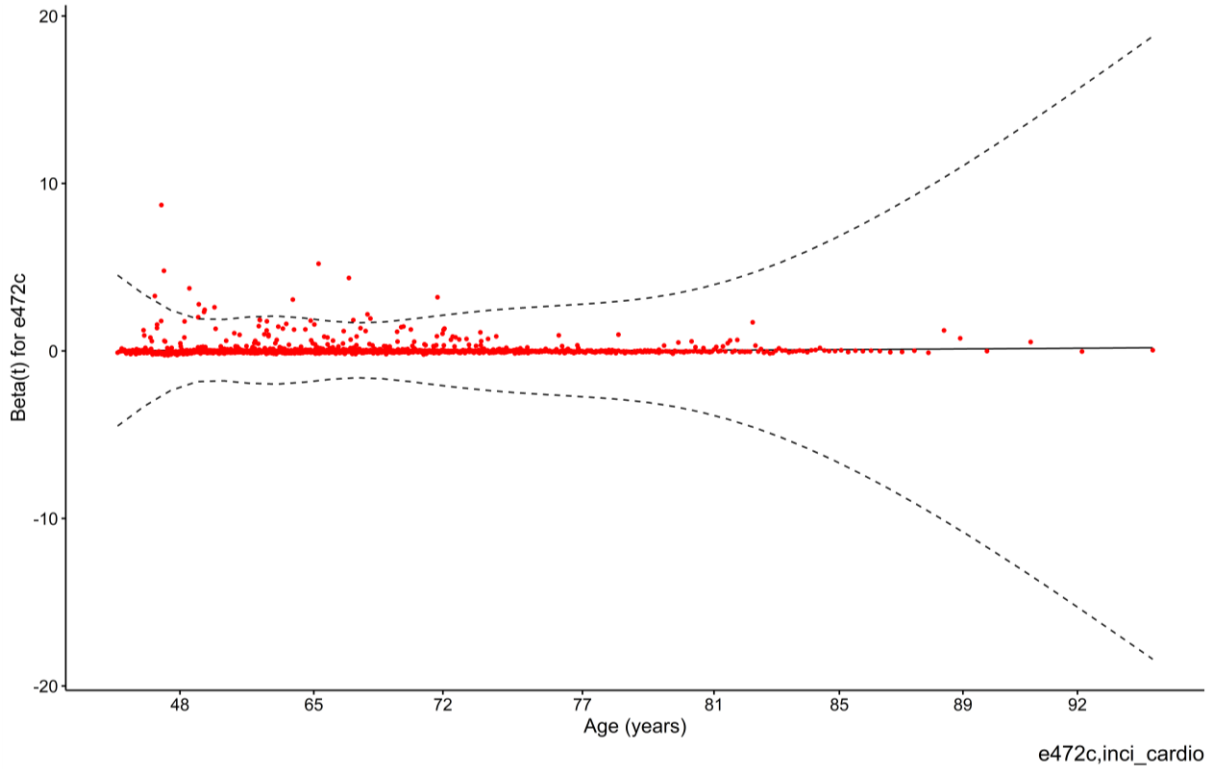


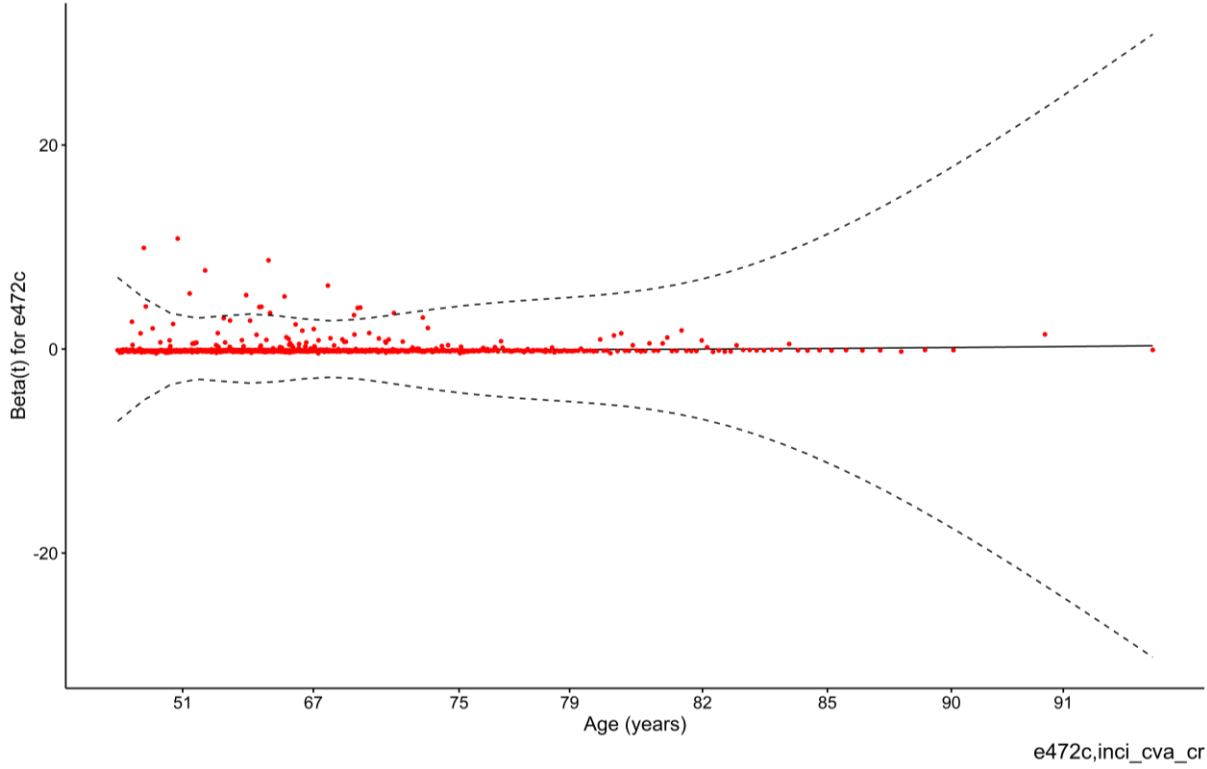
F: Associations of Lactic acid esters of mono- and diglycerides of FAs E472b intake and CVD risks





G: Associations of Citric acid esters of mono- and diglycerides of FAs E472c intake and CVD risks

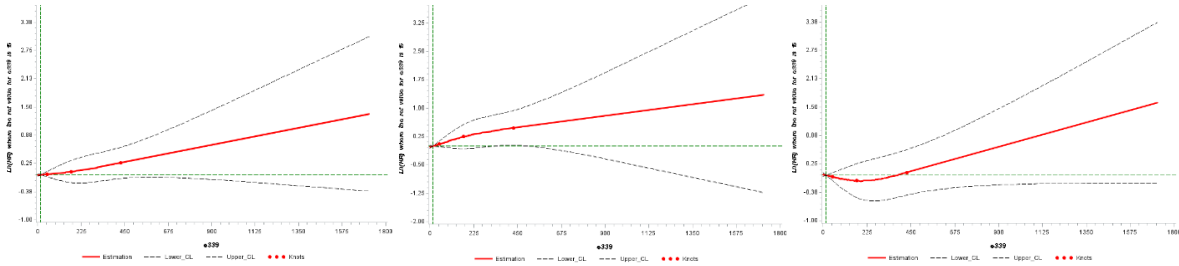




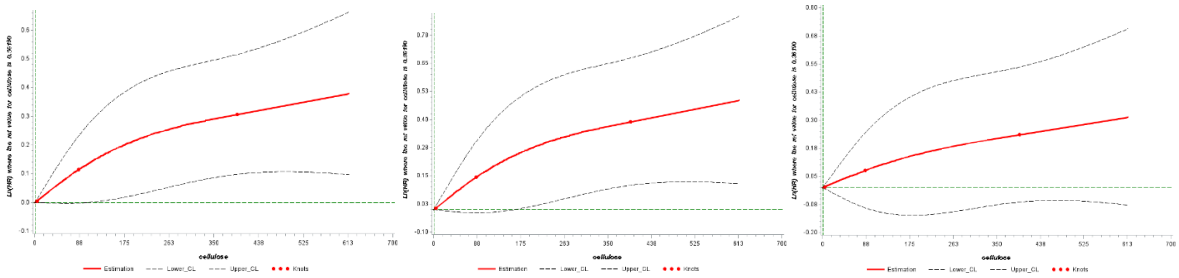
eFigure3. Restricted cubic spline plot for the linearity assumption of the association between emulsifier intakes and total CVD, CHD, and CVA risks in participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442).

Abbreviations: CHD, coronary heart disease; CVA, cerebrovascular disease; CVD, cardiovascular disease.

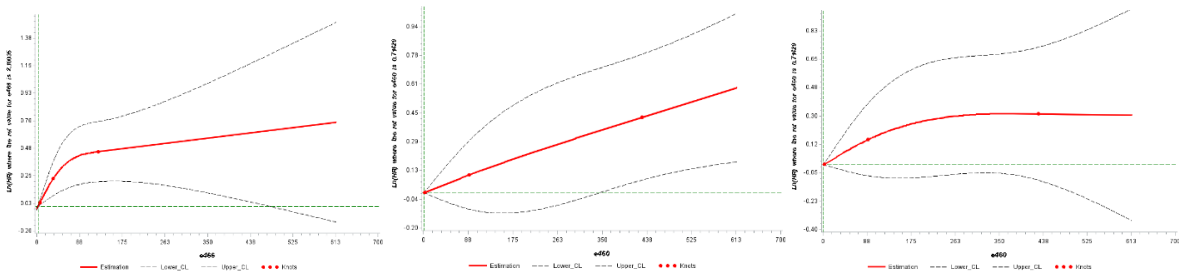
A: Associations between Trisodium phosphate intake (E339) and CVD, CHD, and CVA risk.



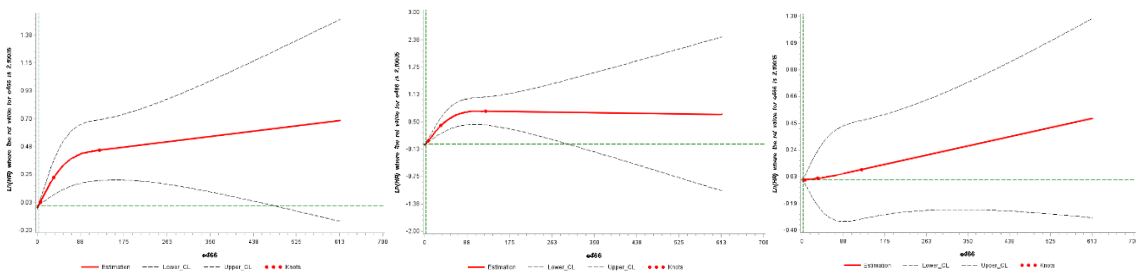
B: Associations between total cellulose intake (E460, E461, E464, E466, E468) and CVD, CHD, and CVA risk.



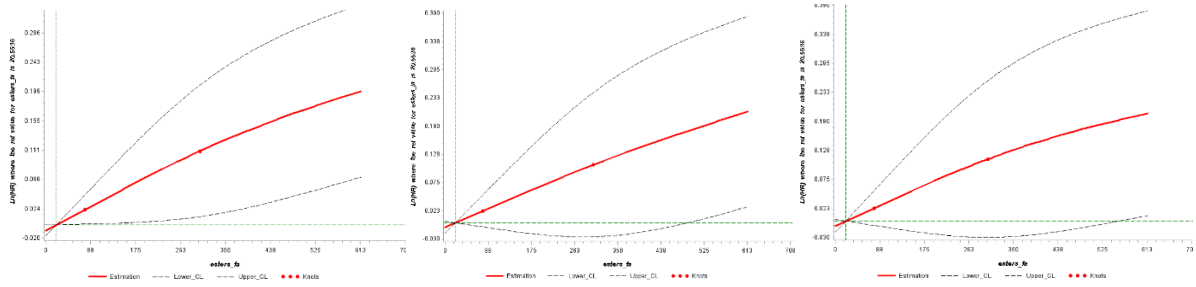
C: Associations between cellulose intake (E460) and CVD, CHD, and CVA risk.



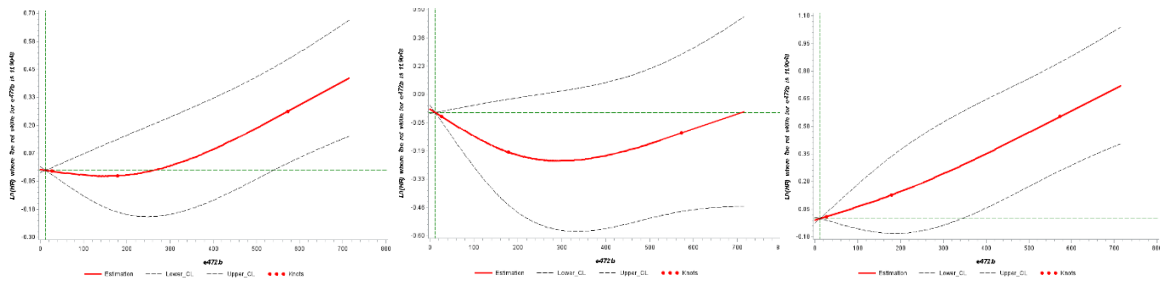
D: Associations between carboxymethylcellulose intake (E466) and CVD, CHD, and CVA risk.



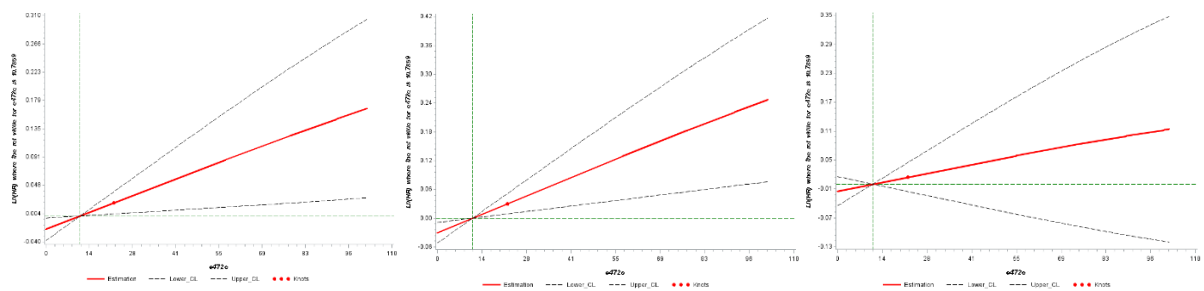
E: Associations between total mono- and diglycerides of fatty acid intake (E471, E472, E472a, E472b, E472c, E472e) and CVD, CHD, and CVA risk.



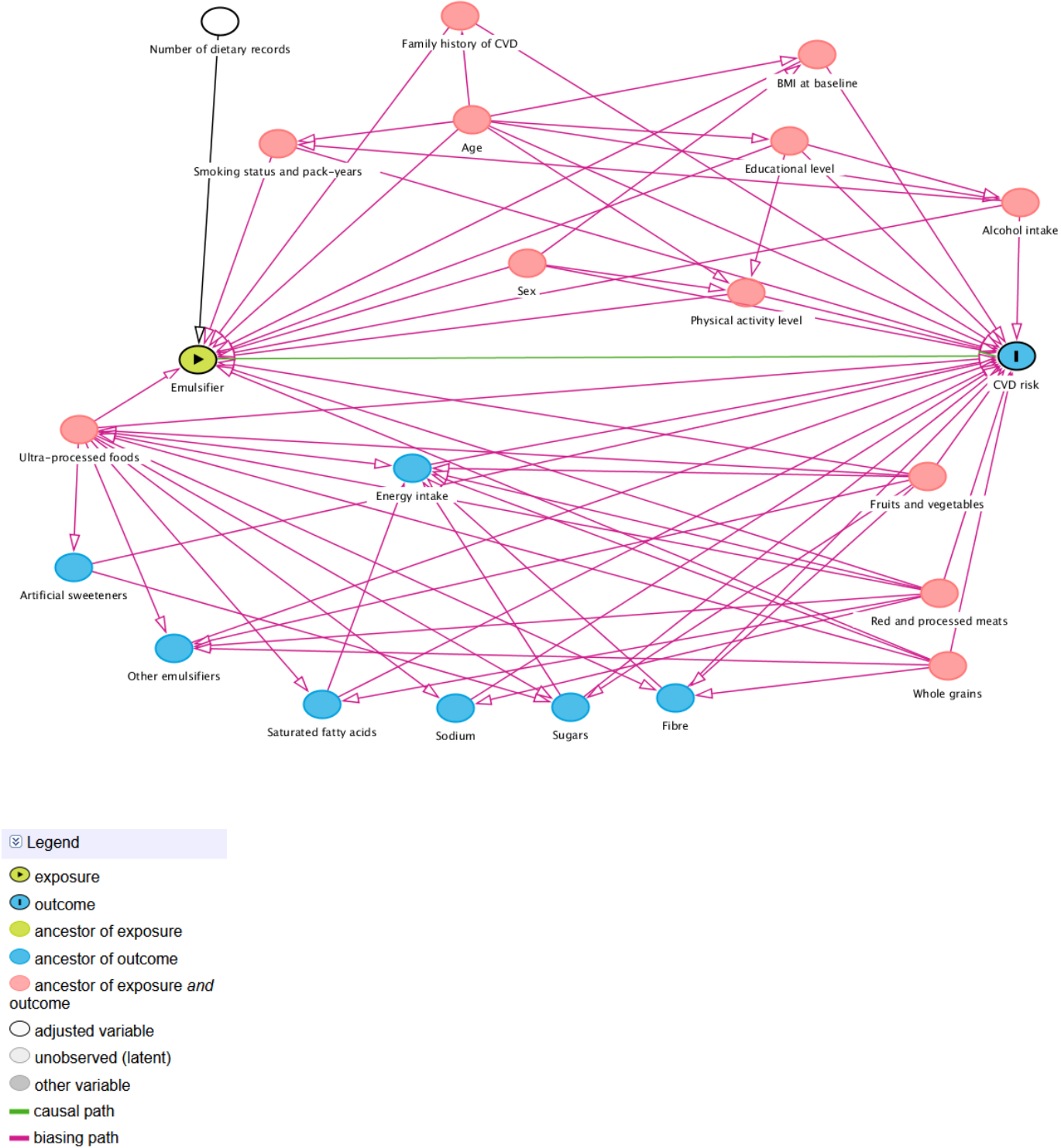
F: Associations between lactic acid ester of mono- and diglycerides of fatty acid intake (E472b) and CVD, CHD, and CVA risk.



G: Associations between Citric acid esters of mono- and diglycerides of FAs intakes (E472c) and CVD risk.

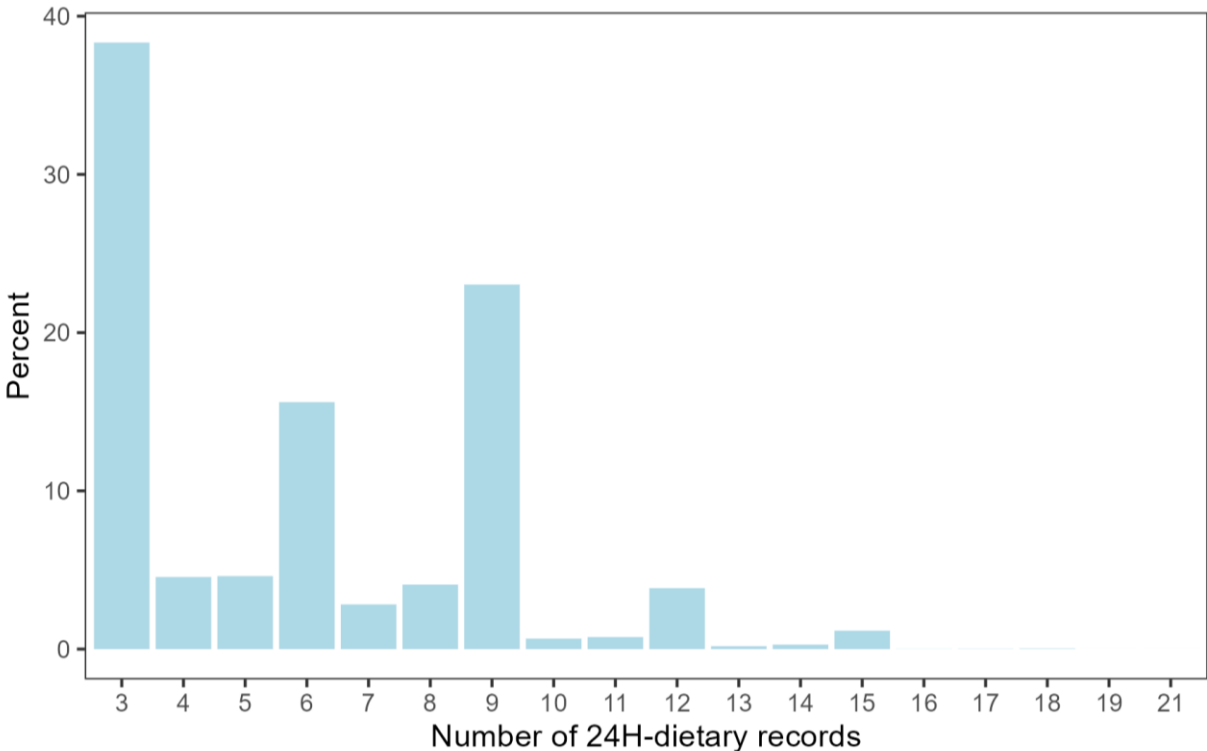


eFigure4. Directed acyclic graphs showing the conceptual framework of the adjustment strategy for the association between emulsifier intakes and CVD risk in participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442).



For readability purposes, no links were plotted between the top and bottom set of variables (including the links would not change the adjustment strategy).

eFigure5. Distribution of the number of 24h-dietary records per participant during their first two years of follow-up, NutriNet-Santé cohort, 2009-2021 (n=95,442)



Note for the interpretation of the graphs: Only two dietary records at baseline were mandatory to be included in the study (three in this specific paper). Other records were optional. Besides, the recruitment in the NutriNet-Santé cohort is open and still ongoing, therefore some participants have only been included for three years for instance (and not from 2009), median follow-up time: 9.0 y.

eResults

eTable1. Detailed contributions of 24 food groups to emulsifier intakes among participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442).^a

Food groups	Total emulsifiers	Total modified starches	Total phosphates	Total lactylates	Total polyglycerol esters of FAs	Total mono- and diglycerides of FAs	Total celluloses	Total carrageenans	Total alginates
	Food group contribution (%)								
Processed fruits and vegetables	18.8	28.1	3.7	1.3	0.0	2.1	11.4	1.7	1.4
Processed potatoes and tubers	4.4	5.4	0.9	0.0	0.0	3.1	20.1	0.1	0.01
Refined grains and cereals	5.3	5.4	6.9	14.3	0.0	7.4	5.2	1.6	0.8
Whole grains and cereals	0.4	0.1	0.04	5.8	0.0	4.7	0.1	0.01	0.0
Processed pulses and legumes	0.4	0.4	0.6	0.0	0.0	0.01	1.3	0.04	0.7
Nuts, seeds and dried fruits	0.03	0.01	0.05	0.0	0.0	0.001	0.0	0.0001	0.0
Dairy products	9.9	8.9	7.4	0.2	0.0	3.1	0.5	17.0	2.2
Dairy desserts	7.3	7.9	0.8	0.0	0.0	2.6	0.5	30.5	17.7
Processed red meat and offals	1.9	2.3	1.6	0.4	0.0	0.1	0.2	0.04	0.7
Processed poultry	1.2	1.3	1.5	0.1	0.0	0.2	1.0	0.4	0.7
Other processed meat	1.7	1.5	4.3	0.3	0.0	2.1	0.2	1.2	1.7
Processed eggs	1.3	0.8	3.3	0.02	0.0	0.7	0.1	0.1	0.8
Processed fish and seafood	1.6	1.5	0.8	0.01	0.0	0.2	0.02	1.5	0.1
Fats and sauces	9.6	10.9	2.5	0.4	11.1	22.5	11.0	11.3	5.7
Broths	7.6	13.7	0.8	0.0	0.0	0.1	0.0	0.1	0.0
Breakfast cereals	0.4	0.01	1.0	0.0	0.6	1.3	0.4	0.0005	0.2
Confectionery	6.1	1.0	0.04	0.0	9.4	10.6	0.4	13.7	4.2
Cakes and biscuits	14.7	6.6	56.9	2.4	19.0	22.0	43.4	14.1	51.0
Pastries	1.7	0.2	0.4	74.5	59.9	14.4	2.9	1.9	0.2
Unsweetened soft drinks	2.1	0.3	2.6	0.0	0.0	0.01	0.8	2.6	0.1
Sweetened soft drinks	0.7	0.03	0.5	0.0	0.0	0.1	0.01	0.5	0.0
Alcoholic drinks	0.0005	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.003
Meal replacements	0.6	0.9	0.049	0.0	0.0	0.003	0.0	0.6	0.0
Others	2.3	2.5	3.4	0.3	0.0	2.8	0.5	0.9	11.9
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Abbreviations: FAs, fatty acids.

^a Groups of emulsifiers were defined as follows (European codes): total phosphates (E339, E340, E341, E343, E450, E451, E452), total lactylates (E481, E482), total polyglycerol esters of FAs (E475, E476), total mono and diglycerides of FAs (E471, E472, E472a, E472b, E472c, E472e), total celluloses (E460, E461, E464, E466, E468), total carrageenans (E407, E407a), total alginates (E400, E401, E402, E404, E405), and total modified starches (E14xx).

eTable2. Associations between emulsifier intakes and CVD risk among study participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442)^a

Emulsifier ^b	HR per additional SD of intake (95%CI) ^c	p-value
Total cardiovascular diseases (n=1,995 incident cases)		
Total emulsifiers	0.98 (0.93-1.04)	0.5
Total alginates	1.01 (0.96-1.06)	0.6
Sodium alginate E401	1.02 (0.97-1.07)	0.6
Total carrageenans	0.99 (0.94-1.04)	0.7
Carrageenan E407	0.99 (0.94-1.04)	0.7
Processed Euchema Seaweed E407a	0.99 (0.94-1.04)	0.7
Total phosphates	0.99 (0.93-1.04)	0.6
Trisodium phosphate E339	1.04 (0.99-1.09)	0.1
Tripotassium phosphate E340	1.01 (0.95-1.07)	0.8
Tricalcium phosphate E341	0.95 (0.87-1.03)	0.2
Diphosphates E450	0.99 (0.93-1.04)	0.6
Triphosphates E451	1.02 (0.97-1.07)	0.4
Polyphosphates E452	1.01 (0.96-1.07)	0.6
Total celluloses	1.05 (1.02-1.09)	0.004
Cellulose E460	1.05 (1.01-1.09)	0.007
Hydroxypropylmethyl cellulose E464	0.99 (0.94-1.05)	0.8
Carboxymethyl cellulose E466	1.03 (1.01-1.05)	0.004
Total mono- and diglycerides of FAs	1.07 (1.04-1.11)	<0.001
Mono- and diglycerides of FAs E471	1.03 (0.98-1.09)	0.2
Lactic acid esters of mono- and diglycerides of FAs E472b	1.06 (1.02-1.10)	0.004
Citric acid esters of mono- and diglycerides of FAs E472c	1.04 (1.02-1.07)	0.002
Acetyl tartaric acid esters of mono- and diglycerides of FAs E472e	1.03 (0.99-1.07)	0.2
Total polyglycerol esters of FAs	1.03 (0.98-1.08)	0.3
Polyglycerol esters of FAs E475	1.02 (0.96-1.08)	0.5
Polyglycerol esters of interesterified ricinoleic acid E476	1.02 (0.99-1.06)	0.2
Total lactylates	0.99 (0.94-1.05)	0.8
Sodium stearyl-2-lactylate E481	0.99 (0.93-1.05)	0.7
Total modified starches	0.99 (0.94-1.03)	0.6
Lecithins E322	1.01 (0.95-1.08)	0.7
Sodium citrate E331	1.04 (0.99-1.10)	0.1
Carob bean gum E410	1.03 (0.98-1.08)	0.2
Guar gum E412	0.99 (0.94-1.04)	0.7
Gum arabic E414	0.99 (0.92-1.07)	0.8
Gum Xanthan Gum E415	0.98 (0.93-1.03)	0.4
Pectins E440	0.98 (0.93-1.03)	0.4
Ammonium salts of phosphatidic acid E442	1.02 (0.97-1.07)	0.5
Sodium bicarbonate E500	0.97 (0.92-1.03)	0.4
Beeswax E901	1.01 (0.96-1.06)	0.8
Coronary heart diseases (n=1,044 incident cases)		
Total emulsifiers	0.97 (0.90-1.05)	0.5
Total alginates	0.99 (0.91-1.07)	0.7
Sodium alginate E401	0.98 (0.91-1.06)	0.6
Total carrageenans	0.96 (0.89-1.03)	0.2
Carrageenan E407	0.95 (0.88-1.02)	0.2

Processed Euchema Seaweed E407a	1.03 (0.97-1.09)	0.3
Total phosphates	0.98 (0.90-1.06)	0.5
Trisodium phosphate E339	1.06 (1.00-1.12)	0.03
Tripotassium phosphate E340	1.00 (0.91-1.11)	0.9
Tricalcium phosphate E341	0.96 (0.87-1.07)	0.5
Diphosphates E450	0.96 (0.89-1.04)	0.4
Triphosphates E451	1.01 (0.95-1.08)	0.7
Polyphosphates E452	1.02 (0.95-1.09)	0.6
Total celluloses	1.07 (1.02-1.12)	0.004
Cellulose E460	1.07 (1.02-1.12)	0.005
Hydroxypropylmethyl cellulose E464	0.97 (0.88-1.06)	0.5
Carboxymethyl cellulose E466	1.04 (1.02-1.06)	0.001
Total mono- and diglycerides of FAs	1.08 (1.03-1.14)	0.001
Mono- and diglycerides of FAs E471	1.03 (0.96-1.11)	0.4
Lactic acid esters of mono- and diglycerides of FAs E472b	0.99 (0.91-1.06)	0.7
Citric acid esters of mono- and diglycerides of FAs E472c	1.06 (1.03-1.09)	<0.001
Acetyl tartaric acid esters of mono- and diglycerides of FAs E472e	1.03 (0.98-1.09)	0.3
Total polyglycerol esters of FAs	1.02 (0.94-1.10)	0.6
Polyglycerol esters of FAs E475	1.00 (0.91-1.09)	0.9
Polyglycerol esters of interesterified ricinoleic acid E476	1.03 (0.99-1.08)	0.1
Total lactylates	0.97 (0.89-1.05)	0.4
Sodium stearoyl-2-lactylate E481	0.96 (0.88-1.05)	0.4
Total modified starches	1.01 (0.95-1.08)	0.7
Lecithins E322	1.00 (0.91-1.10)	0.99
Sodium citrate E331	1.07 (1.00-1.14)	0.06
Carob bean gum E410	1.01 (0.95-1.08)	0.6
Guar gum E412	0.98 (0.92-1.05)	0.6
Gum arabic E414	0.98 (0.87-1.11)	0.7
Gum Xanthan Gum E415	1.00 (0.93-1.07)	0.98
Pectins E440	0.98 (0.92-1.05)	0.6
Ammonium salts of phosphatidic acid E442	0.97 (0.88-1.06)	0.4
Sodium bicarbonate E500	0.94 (0.87-1.02)	0.1
Beeswax E901	0.99 (0.90-1.08)	0.8
Cerebrovascular diseases (n=974 incident cases)		
Total emulsifiers	1.00 (0.92-1.08)	0.97
Total alginates	1.03 (0.97-1.10)	0.3
Sodium alginate E401	1.04 (0.98-1.11)	0.2
Total carrageenans	1.02 (0.95-1.10)	0.5
Carrageenan E407	1.03 (0.96-1.11)	0.3
Processed Euchema Seaweed E407a	0.93 (0.84-1.02)	0.1
Total phosphates	1.00 (0.92-1.08)	0.9
Trisodium phosphate E339	1.02 (0.95-1.10)	0.5
Tripotassium phosphate E340	1.02 (0.95-1.09)	0.6
Tricalcium phosphate E341	0.92 (0.80-1.06)	0.3
Diphosphates E450	1.01 (0.93-1.09)	0.9
Triphosphates E451	1.03 (0.96-1.10)	0.4
Polyphosphates E452	1.00 (0.93-1.08)	0.9
Total celluloses	1.04 (0.99-1.10)	0.1
Cellulose E460	1.04 (0.98-1.11)	0.1
Hydroxypropylmethyl cellulose E464	1.01 (0.95-1.07)	0.8
Carboxymethyl cellulose E466	1.02 (0.98-1.07)	0.3
Total mono- and diglycerides of FAs	1.07 (1.01-1.13)	0.02

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Mono- and diglycerides of FAs E471	1.03 (0.96-1.11)	0.4
Lactic acid esters of mono- and diglycerides of FAs E472b	1.11 (1.06-1.16)	<0.001
Citric acid esters of mono- and diglycerides of FAs E472c	1.01 (0.95-1.08)	0.7
Acetyl tartaric acid esters of mono- and diglycerides of FAs E472e	1.03 (0.97-1.09)	0.4
Total polyglycerol esters of FAs	1.04 (0.97-1.11)	0.3
Polyglycerol esters of FAs E475	1.03 (0.96-1.11)	0.4
Polyglycerol esters of interesterified ricinoleic acid E476	1.01 (0.96-1.07)	0.6
Total lactylates	1.01 (0.94-1.09)	0.8
Sodium stearoyl-2-lactylate E481	1.01 (0.94-1.09)	0.8
Total modified starches	0.96 (0.89-1.03)	0.2
Lecithins E322	1.01 (0.92-1.11)	0.8
Sodium citrate E331	1.01 (0.93-1.10)	0.7
Carob bean gum E410	1.05 (0.98-1.11)	0.2
Guar gum E412	1.00 (0.93-1.07)	0.9
Gum arabic E414	1.00 (0.91-1.10)	0.99
Gum Xanthan Gum E415	0.95 (0.88-1.03)	0.2
Pectins E440	0.98 (0.91-1.05)	0.5
Ammonium salts of phosphatidic acid E442	1.05 (1.00-1.11)	0.06
Sodium bicarbonate E500	1.02 (0.94-1.10)	0.7
Beeswax E901	1.02 (0.96-1.09)	0.5

^a Multivariable Cox proportional hazard models were adjusted for age (time-scale), sex, BMI (continuous, kg/m²), physical activity (categorical IPAQ variable: high, moderate, low), smoking status, (never smoked, former smoker, occasional smoker, regular smoker), number of smoked cigarettes in pack-years (continuous), educational level (less than high school degree, <2 y after high school degree, ≥2 y after high school degree), number of dietary records (continuous), family history of CVD (yes/no), energy intake without alcohol (continuous, kcal/d), daily intakes of alcohol (continuous, g/d), saturated fatty acids (continuous, g/d), sodium (continuous, mg/d), total fibre (continuous, g/d), sugars (continuous, g/d), fruits and vegetables (continuous, g/d), red and processed meats (continuous, g/d), whole grains (continuous, g/d), proportion of ultra-processed food consumed in the diet, in weight (continuous, %).

^b Groups of emulsifiers were calculated as the sum of individual emulsifiers and defined as follows: total phosphates (E339, E340, E341, E343, E450, E452), total lactylates (E481, E482), total polyglycerol esters of FAs (E475, E476), total mono and diglycerides of FAs (E471, E472, E472a, E472b, E472c, E472e), total celluloses (E460, E461, E464, E466, E468), total carrageenans (E407, E407a), total alginates (E400, E401, E402, E404, E405), total modified starches (E14xx).

^c SD of emulsifier intakes (in mg/d) were: 3170.8 for total emulsifiers, 52.0 for total alginates, 35.3 for E401, 75.7 for total carrageenans, 73.2 for E407, 14.1 for E407a, 502.6 for total phosphates, 58.4 for E339, 96.5 for E340, 227.2 for E341, 349.7 for E450, 122.3 for E451, 86.2 for E452, 93.4 for total celluloses, 69.4 for E460, 32.8 for E464, 32.0 for E466, 287.5 for total mono- and diglycerides of FAs, 208.6 for E471, 103.7 for E472b, 57.6 for E472c, 28.3 for E472e, 63.5 for total polyglycerol esters of FAs, 61.5 for E475, 15.7 for E476, 23.1 for total lactylates, 22.7 for E481, 1147.1 for total modified starches, 78.3 for E322, 280.5 for E331, 69.7 for E410, 233.8 for E412, 428.1 for E414, 221.1 for E415, 310.6 for E440, 42.6 for E442, 2116.7 for E500, and 0.6 for E901.

eTable3. Sensitivity analyses for the associations between emulsifier intakes and CVD risk among study participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442)^a

Emulsifiers ^b	Sensitivity model	Incident cases /Participants	HR per additional SD of intake (95%CI) ^c	p-value
Total cardiovascular diseases				
Trisodium phosphate E339	model 1	1995 / 95442	1.04 (0.99-1.09)	0.09
	model 2	1995 / 95442	1.04 (0.99-1.09)	0.1
	model 3	1995 / 95442	1.04 (0.99-1.09)	0.1
	model 4	1551 / 94998	1.05 (1.00-1.10)	0.07
	model 5	1995 / 95442	1.03 (0.98-1.09)	0.2
	model 6	1995 / 95442	1.04 (0.99-1.09)	0.1
Total celluloses	model 1	1995 / 95442	1.05 (1.02-1.09)	0.004
	model 2	1995 / 95442	1.05 (1.01-1.09)	0.006
	model 3	1995 / 95442	1.05 (1.02-1.09)	0.004
	model 4	1551 / 94998	1.06 (1.02-1.10)	0.001
	model 5	1995 / 95442	1.05 (1.01-1.08)	0.008
	model 6	1995 / 95442	1.05 (1.02-1.09)	0.003
Cellulose E460	model 1	1995 / 95442	1.05 (1.01-1.09)	0.009
	model 2	1995 / 95442	1.05 (1.01-1.09)	0.01
	model 3	1995 / 95442	1.05 (1.01-1.09)	0.007
	model 4	1551 / 94998	1.06 (1.02-1.10)	0.004
	model 5	1995 / 95442	1.07 (1.03-1.10)	0.0004
	model 6	1995 / 95442	1.06 (1.02-1.10)	0.005
Carboxymethyl cellulose E466	model 1	1995 / 95442	1.03 (1.01-1.05)	0.003
	model 2	1995 / 95442	1.03 (1.01-1.05)	0.004
	model 3	1995 / 95442	1.03 (1.01-1.05)	0.004
	model 4	1551 / 94998	1.03 (1.01-1.06)	0.001
	model 5	1995 / 95442	1.02 (0.99-1.05)	0.1
	model 6	1995 / 95442	1.03 (1.01-1.05)	0.005
Total mono- and diglycerides of FAs	model 1	1995 / 95442	1.07 (1.03-1.11)	<0.001
	model 2	1995 / 95442	1.07 (1.03-1.11)	<0.001
	model 3	1995 / 95442	1.07 (1.04-1.11)	<0.001
	model 4	1551 / 94998	1.07 (1.02-1.12)	0.005
	model 5	1995 / 95442	1.13 (1.08-1.19)	<0.001
	model 6	1995 / 95442	1.08 (1.04-1.12)	<0.001
Lactic acid esters of mono- and diglycerides of FAs E472b	model 1	1995 / 95442	1.06 (1.02-1.11)	0.004

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	model 2	1995 / 95442	1.06 (1.02-1.11)	0.003
	model 3	1995 / 95442	1.06 (1.02-1.10)	0.004
	model 4	1551 / 94998	1.07 (1.02-1.12)	0.006
	model 5	1995 / 95442	1.07 (1.02-1.11)	0.003
	model 6	1995 / 95442	1.06 (1.02-1.11)	0.004
Citric acid esters of mono- and diglycerides of FAs E472c	model 1	1995 / 95442	1.04 (1.02-1.07)	0.002
	model 2	1995 / 95442	1.04 (1.02-1.07)	0.002
	model 3	1995 / 95442	1.04 (1.02-1.07)	0.002
	model 4	1551 / 94998	1.04 (1.01-1.08)	0.008
	model 5	1995 / 95442	1.05 (1.02-1.08)	0.0005
	model 6	1995 / 95442	1.05 (1.02-1.08)	0.002
Coronary heart diseases				
Trisodium phosphate E339	model 1	1044 / 95442	1.07 (1.01-1.12)	0.02
	model 2	1044 / 95442	1.06 (1.01-1.12)	0.03
	model 3	1044 / 95442	1.06 (1.00-1.12)	0.03
	model 4	768 / 95166	1.07 (1.01-1.14)	0.02
	model 5	1044 / 95442	1.06 (1.00-1.12)	0.06
	model 6	1044 / 95442	1.06 (1.01-1.12)	0.03
Total celluloses	model 1	1044 / 95442	1.07 (1.02-1.12)	0.005
	model 2	1044 / 95442	1.07 (1.02-1.12)	0.007
	model 3	1044 / 95442	1.07 (1.02-1.12)	0.004
	model 4	768 / 95166	1.08 (1.04-1.13)	<0.001
	model 5	1044 / 95442	1.05 (1.00-1.10)	0.03
	model 6	1044 / 95442	1.07 (1.02-1.12)	0.003
Cellulose E460	model 1	1044 / 95442	1.07 (1.02-1.12)	0.007
	model 2	1044 / 95442	1.06 (1.01-1.11)	0.01
	model 3	1044 / 95442	1.07 (1.02-1.12)	0.005
	model 4	768 / 95166	1.09 (1.04-1.13)	<0.001
	model 5	1044 / 95442	1.07 (1.03-1.12)	0.001
	model 6	1044 / 95442	1.07 (1.02-1.12)	0.004
Carboxymethyl cellulose E466	model 1	1044 / 95442	1.04 (1.02-1.06)	0.001
	model 2	1044 / 95442	1.04 (1.02-1.07)	0.001
	model 3	1044 / 95442	1.04 (1.02-1.06)	0.001
	model 4	768 / 95166	1.04 (1.02-1.07)	<0.001
	model 5	1044 / 95442	1.03 (1.00-1.06)	0.06

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	model 6	1044 / 95442	1.04 (1.01-1.06)	0.001
Total mono- and diglycerides of FAs	model 1	1044 / 95442	1.08 (1.03-1.14)	0.001
	model 2	1044 / 95442	1.08 (1.03-1.14)	0.002
	model 3	1044 / 95442	1.08 (1.03-1.14)	0.001
	model 4	768 / 95166	1.08 (1.01-1.15)	0.03
	model 5	1044 / 95442	1.11 (1.04-1.19)	0.001
	model 6	1044 / 95442	1.09 (1.04-1.14)	<0.001
Lactic acid esters of mono- and diglycerides of FAs E472b	model 1	1044 / 95442	0.99 (0.91-1.06)	0.7
	model 2	1044 / 95442	0.99 (0.92-1.07)	0.8
	model 3	1044 / 95442	0.99 (0.91-1.06)	0.7
	model 4	768 / 95166	0.99 (0.90-1.08)	0.8
	model 5	1044 / 95442	0.99 (0.91-1.08)	0.9
	model 6	1044 / 95442	0.99 (0.92-1.07)	0.7
Citric acid esters of mono- and diglycerides of FAs E472c	model 1	1044 / 95442	1.06 (1.03-1.09)	<0.001
	model 2	1044 / 95442	1.06 (1.03-1.09)	<0.001
	model 3	1044 / 95442	1.06 (1.03-1.09)	<0.001
	model 4	768 / 95166	1.06 (1.03-1.10)	<0.001
	model 5	1044 / 95442	1.07 (1.04-1.10)	<0.001
	model 6	1044 / 95442	1.06 (1.03-1.09)	<0.001
Cerebrovascular diseases				
Trisodium phosphate E339	model 1	974 / 95442	1.02 (0.95-1.10)	0.5
	model 2	974 / 95442	1.02 (0.95-1.10)	0.5
	model 3	974 / 95442	1.02 (0.95-1.10)	0.5
	model 4	788 / 95256	1.01 (0.93-1.11)	0.8
	model 5	974 / 95442	1.02 (0.94-1.11)	0.6
	model 6	974 / 95442	1.02 (0.95-1.10)	0.6
Total celluloses	model 1	974 / 95442	1.05 (0.99-1.10)	0.1
	model 2	974 / 95442	1.04 (0.99-1.10)	0.1
	model 3	974 / 95442	1.04 (0.99-1.10)	0.1
	model 4	788 / 95256	1.04 (0.98-1.11)	0.2
	model 5	974 / 95442	1.04 (0.99-1.09)	0.09
	model 6	974 / 95442	1.04 (0.99-1.10)	0.1
Cellulose E460	model 1	974 / 95442	1.04 (0.98-1.11)	0.1
	model 2	974 / 95442	1.04 (0.98-1.10)	0.2
	model 3	974 / 95442	1.04 (0.98-1.11)	0.1

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	model 4	788 / 95256	1.03 (0.96-1.11)	0.4
	model 5	974 / 95442	1.06 (1.00-1.12)	0.04
	model 6	974 / 95442	1.04 (0.98-1.11)	0.1
Carboxymethyl cellulose E466	model 1	974 / 95442	1.02 (0.98-1.07)	0.3
	model 2	974 / 95442	1.02 (0.98-1.07)	0.3
	model 3	974 / 95442	1.02 (0.98-1.07)	0.3
	model 4	788 / 95256	1.03 (0.98-1.07)	0.2
	model 5	974 / 95442	1.01 (0.95-1.07)	0.8
	model 6	974 / 95442	1.02 (0.98-1.06)	0.3
Total mono- and diglycerides of FAs	model 1	974 / 95442	1.07 (1.01-1.13)	0.01
	model 2	974 / 95442	1.07 (1.01-1.13)	0.02
	model 3	974 / 95442	1.07 (1.01-1.13)	0.02
	model 4	788 / 95256	1.07 (1.00-1.13)	0.048
	model 5	974 / 95442	1.15 (1.08-1.23)	<0.001
	model 6	974 / 95442	1.07 (1.01-1.13)	0.02
Lactic acid esters of mono- and diglycerides of FAs E472b	model 1	974 / 95442	1.11 (1.06-1.16)	<0.001
	model 2	974 / 95442	1.11 (1.06-1.16)	<0.001
	model 3	974 / 95442	1.11 (1.06-1.16)	<0.001
	model 4	788 / 95256	1.11 (1.06-1.17)	<0.001
	model 5	974 / 95442	1.11 (1.06-1.16)	<0.001
	model 6	974 / 95442	1.11 (1.06-1.16)	<0.001
Citric acid esters of mono- and diglycerides of FAs E472c	model 1	974 / 95442	1.01 (0.95-1.08)	0.7
	model 2	974 / 95442	1.01 (0.95-1.08)	0.7
	model 3	974 / 95442	1.01 (0.95-1.08)	0.7
	model 4	788 / 95256	1.00 (0.92-1.09)	0.99
	model 5	974 / 95442	1.02 (0.95-1.09)	0.6
	model 6	974 / 95442	1.01 (0.95-1.08)	0.7

^a Multivariable Cox proportional hazard models were adjusted for age (time-scale), sex, BMI (continuous, kg/m²), physical activity (categorical IPAQ variable: high, moderate, low), smoking status, (never smoked, former smoker, occasional smoker, regular smoker), number of smoked cigarettes in pack-years (continuous), educational level (less than high school degree, <2 y after high school degree, ≥2 y after high school degree), number of dietary records (continuous), family history of CVD (yes/no), energy intake without alcohol (continuous, kcal/d), daily intakes of alcohol (continuous, g/d), saturated fatty acids (continuous, g/d), sodium (continuous, mg/d), total fibre (continuous, g/d), sugars (continuous, g/d), fruits and vegetables (continuous, g/d), red and processed meats (continuous, g/d), whole grains (continuous, g/d), proportion of ultra-processed food consumed in the diet, in weight (continuous, %). Model 1 was further adjusted for Healthy and Western dietary patterns derived by principle component analyses. Model 2 was based on the main model and further adjusted for the diagnosis and/or treatment for at least one prevalent metabolic disorder (i.e. type 2 diabetes, hypertriglyceridemia, hypertension). Model 3 was based on the main model and further adjusted for the percentage of weight change from baseline. Model 4 was based on the main model and excluded participants diagnosed with CVD during the first two years of follow-up. Model 5 was based on the main model, using the average of all available 24h dietary records throughout the follow-up of each participant

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(up to 62 records per participant) instead of averaged values on their first two years of follow-up. Model 6 was based on the main model and further adjusted for the intakes of other emulsifiers than the one studied in the model, and for total artificial sweeteners.

^b Groups of emulsifiers were calculated as the sum of individual emulsifiers and defined as follows: total phosphates (E339, E340, E341, E343, E450, E452), total lactylates (E481,E482), total polyglycerol esters of FAs (E475,E476), total mono and diglycerides of FAs (E471, E472, E472a, E472b, E472c, E472e), total celluloses (E460, E461, E464, E466, E468), total carrageenans (E407, E407a), total alginates (E400, E401, E402, E404, E405), total modified starches (E14xx).

^c SD of emulsifier intakes (in mg/d) were: 3170.8 for total emulsifiers, 52.0 for total alginates, 35.3 for E401, 75.7 for total carrageenans, 73.2 for E407, 14.1 for E407a, 502.6 for total phosphates, 58.4 for E339, 96.5 for E340, 227.2 for E341, 349.7 for E450, 122.3 for E451, 86.2 for E452, 93.4 for total celluloses, 69.4 for E460, 32.8 for E464, 32.0 for E466, 287.5 for total mono- and diglycerides of FAs, 208.6 for E471, 103.7 for E472b, 57.6 for E472c, 28.3 for E472e, 63.5 for total polyglycerol esters of FAs, 61.5 for E475, 15.7 for E476, 23.1 for total lactylates, 22.7 for E481, 1147.1 for total modified starches, 78.3 for E322, 280.5 for E331, 69.7 for E410, 233.8 for E412, 428.1 for E414, 221.1 for E415, 310.6 for E440, 42.6 for E442, 2116.7 for E500, and 0.6 for E901.

eTable4. Analyses for the associations between emulsifier intakes and risk of CVD subtypes among study participants from the NutriNet-Santé cohort, 2009-2021 (n=95,442).^a

Emulsifiers ^b	Sensitivity model	Incident cases /Participants	HR per additional SD of intake (95%CI) ^c	p-value
Total cardiovascular diseases				
Trisodium phosphate E339	Stroke	267 / 95442	1.03 (0.89- 1.19)	0.7
	MI	178 / 95442	1.06 (0.93-1.20)	0.4
	Angioplasty	686 / 95442	1.06 (0.97- 1.15)	0.2
	ACS	112 / 95442	0.90 (0.60- 1.35)	0.6
	TIA	781 / 95442	1.01 (0.92-1.10)	0.9
	Angina	499 / 95442	1.07 (1.01- 1.13)	0.02
	Severe CVD	1056 / 95442	1.06 (0.99-1.12)	0.09
Total celluloses	Stroke	267 / 95442	1.01 (0.87- 1.16)	0.9
	MI	178 / 95442	0.97 (0.80-1.19)	0.8
	Angioplasty	686 / 95442	1.09 (1.04- 1.14)	<0.001
	ACS	112 / 95442	1.12 (1.01- 1.23)	0.04
	TIA	781 / 95442	1.05 (0.99-1.11)	0.1
	Angina	499 / 95442	1.05 (0.98- 1.13)	0.2
	Severe CVD	1056 / 95442	1.07 (1.03-1.12)	0.002
Cellulose E460	Stroke	267 / 95442	0.99 (0.85- 1.16)	0.9
	MI	178 / 95442	0.98 (0.81-1.19)	0.8
	Angioplasty	686 / 95442	1.09 (1.04- 1.15)	<0.001
	ACS	112 / 95442	1.12 (0.99- 1.26)	0.07
	TIA	781 / 95442	1.05 (0.99-1.11)	0.1
	Angina	499 / 95442	1.05 (0.97- 1.13)	0.2
	Severe CVD	1056 / 95442	1.07 (1.02-1.13)	0.004
Carboxymethyl cellulose E466	Stroke	267 / 95442	0.70 (0.45- 1.11)	0.1
	MI	178 / 95442	0.99 (0.78-1.25)	0.9
	Angioplasty	686 / 95442	1.05 (1.02- 1.08)	0.003
	ACS	112 / 95442	1.06 (1.00- 1.12)	0.06
	TIA	781 / 95442	1.03 (0.99-1.06)	0.1
	Angina	499 / 95442	1.04 (1.01- 1.07)	0.02
	Severe CVD	1056 / 95442	1.04 (1.00-1.07)	0.03
Total mono- and diglycerides of FAs	Stroke	267 / 95442	1.10 (1.02- 1.18)	0.01
	MI	178 / 95442	0.92 (0.76- 1.12)	0.4
	Angioplasty	686 / 95442	1.09 (1.03- 1.16)	0.006
	ACS	112 / 95442	1.10 (0.95- 1.28)	0.2
	TIA	781 / 95442	1.04 (0.97-1.12)	0.3
	Angina	499 / 95442	1.10 (1.06- 1.15)	<0.001
	Severe CVD	1056 / 95442	1.08 (1.02-1.14)	0.004
Lactic acid esters of mono- and diglycerides of FAs E472b	Stroke	267 / 95442	1.16 (1.08- 1.24)	<0.001
	MI	178 / 95442	0.84 (0.64-1.12)	0.2
	Angioplasty	686 / 95442	1.01 (0.92- 1.10)	0.9
	ACS	112 / 95442	1.08 (0.92- 1.26)	0.4
	TIA	781 / 95442	1.07 (1.01-1.14)	0.02
	Angina	499 / 95442	1.03 (0.95- 1.13)	0.5

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	Severe CVD	1056 / 95442	1.07 (1.01-1.13)	0.02
Citric acid esters of mono- and diglycerides of FAs E472c	Stroke	267 / 95442	1.01 (0.89- 1.16)	0.8
	MI	178 / 95442	0.96 (0.78-1.17)	0.7
	Angioplasty	686 / 95442	1.06 (1.02- 1.10)	0.004
	ACS	112 / 95442	1.05 (0.92- 1.20)	0.4
	TIA	781 / 95442	1.00 (0.92-1.09)	1
	Angina	499 / 95442	1.06 (1.03- 1.10)	<0.001
	Severe CVD	1056 / 95442	1.05 (1.01-1.09)	0.006

MI: Myocardial infarction; ACS: acute coronary syndrome; TIA: transient ischemic attack.

Severe CVD encompass all individual outcomes except for TIA and Angina.

^a Multivariable Cox proportional hazard models were adjusted for age (time-scale), sex, BMI (continuous, kg/m²), physical activity (categorical IPAQ variable: high, moderate, low), smoking status, (never smoked, former smoker, occasional smoker, regular smoker), number of smoked cigarettes in pack-years (continuous), educational level (less than high school degree, <2 y after high school degree, ≥2 y after high school degree), number of dietary records (continuous), family history of CVD (yes/no), energy intake without alcohol (continuous, kcal/d), daily intakes of alcohol (continuous, g/d), saturated fatty acids (continuous, g/d), sodium (continuous, mg/d), total fibre (continuous, g/d), sugars (continuous, g/d), fruits and vegetables (continuous, g/d), red and processed meats (continuous, g/d), whole grains (continuous, g/d), proportion of ultra-processed food consumed in the diet, in weight (continuous, %).

^b Groups of emulsifiers were calculated as the sum of individual emulsifiers and defined as follows: total phosphates (E339, E340, E341, E343, E450, E452), total lactylates (E481, E482), total polyglycerol esters of FAs (E475, E476), total mono and diglycerides of FAs (E471, E472, E472a, E472b, E472c, E472e), total celluloses (E460, E461, E464, E466, E468), total carrageenans (E407, E407a), total alginates (E400, E401, E402, E404, E405), total modified starches (E14xx).

^c SD of emulsifier intakes (in mg/d) were: 3170.8 for total emulsifiers, 52.0 for total alginates, 35.3 for E401, 75.7 for total carrageenans, 73.2 for E407, 14.1 for E407a, 502.6 for total phosphates, 58.4 for E339, 96.5 for E340, 227.2 for E341, 349.7 for E450, 122.3 for E451, 86.2 for E452, 93.4 for total celluloses, 69.4 for E460, 32.8 for E464, 32.0 for E466, 287.5 for total mono- and diglycerides of FAs, 208.6 for E471, 103.7 for E472b, 57.6 for E472c, 28.3 for E472e, 63.5 for total polyglycerol esters of FAs, 61.5 for E475, 15.7 for E476, 23.1 for total lactylates, 22.7 for E481, 1147.1 for total modified starches, 78.3 for E322, 280.5 for E331, 69.7 for E410, 233.8 for E412, 428.1 for E414, 221.1 for E415, 310.6 for E440, 42.6 for E442, 2116.7 for E500, and 0.6 for E901.

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