Different types of industry-produced and ruminant trans fatty acid intake and risk of type 2 diabetes: findings from the NutriNet-Santé prospective cohort

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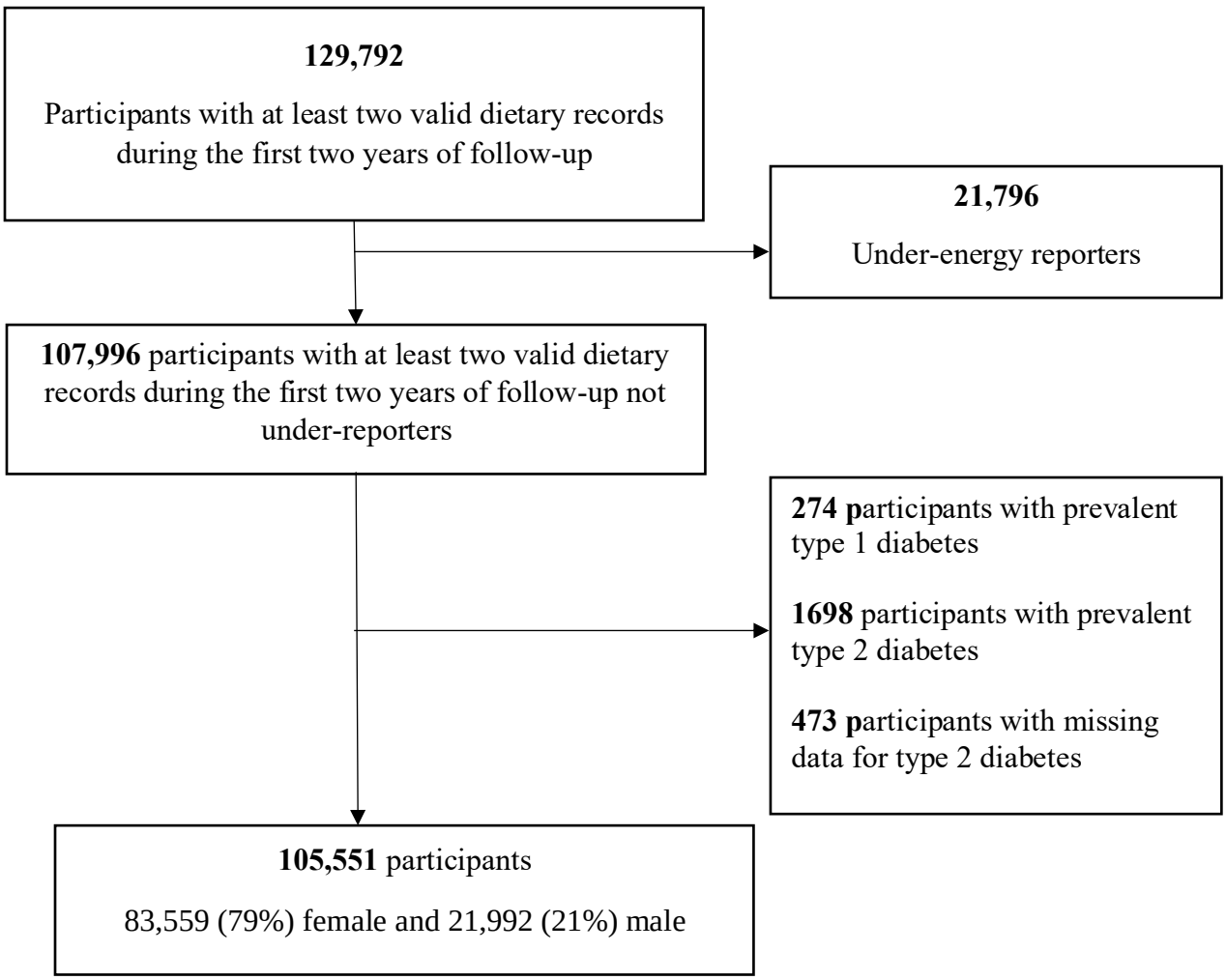
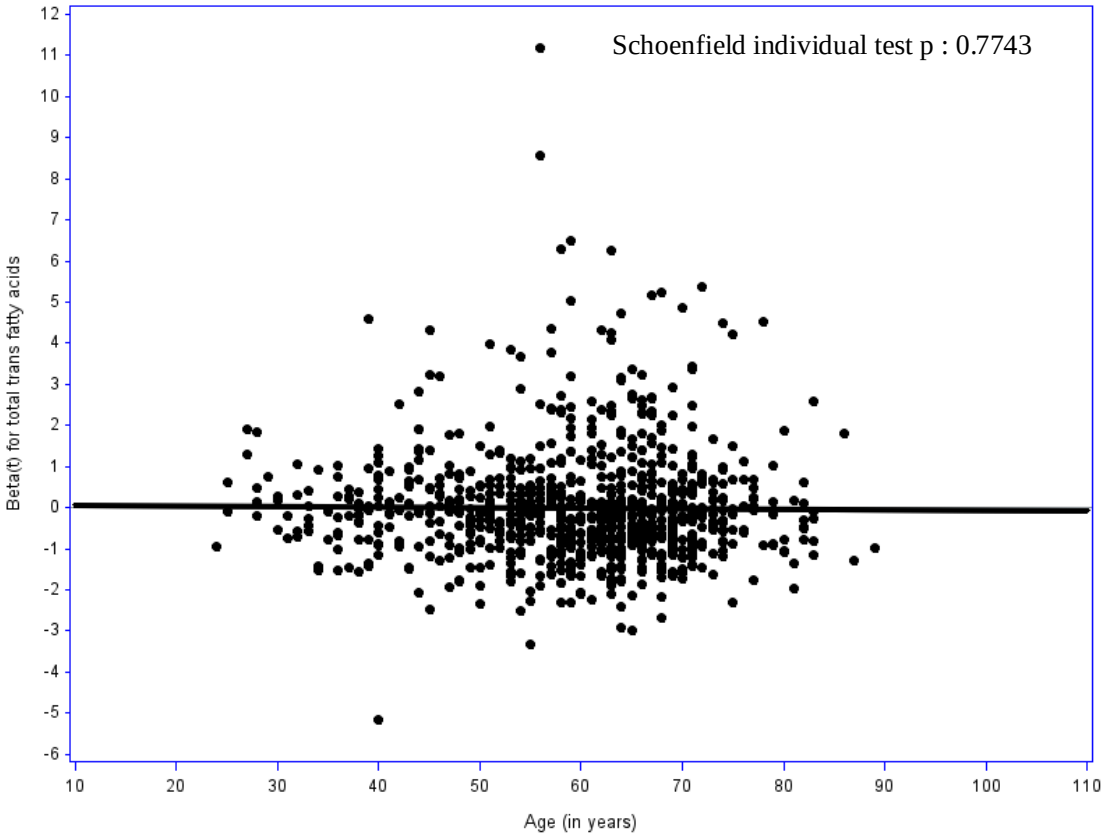
Supplemental Material

Supplemental Figure 1: Flowchart for the selection of the study population, NutriNet-Santé cohort, 2009-2021

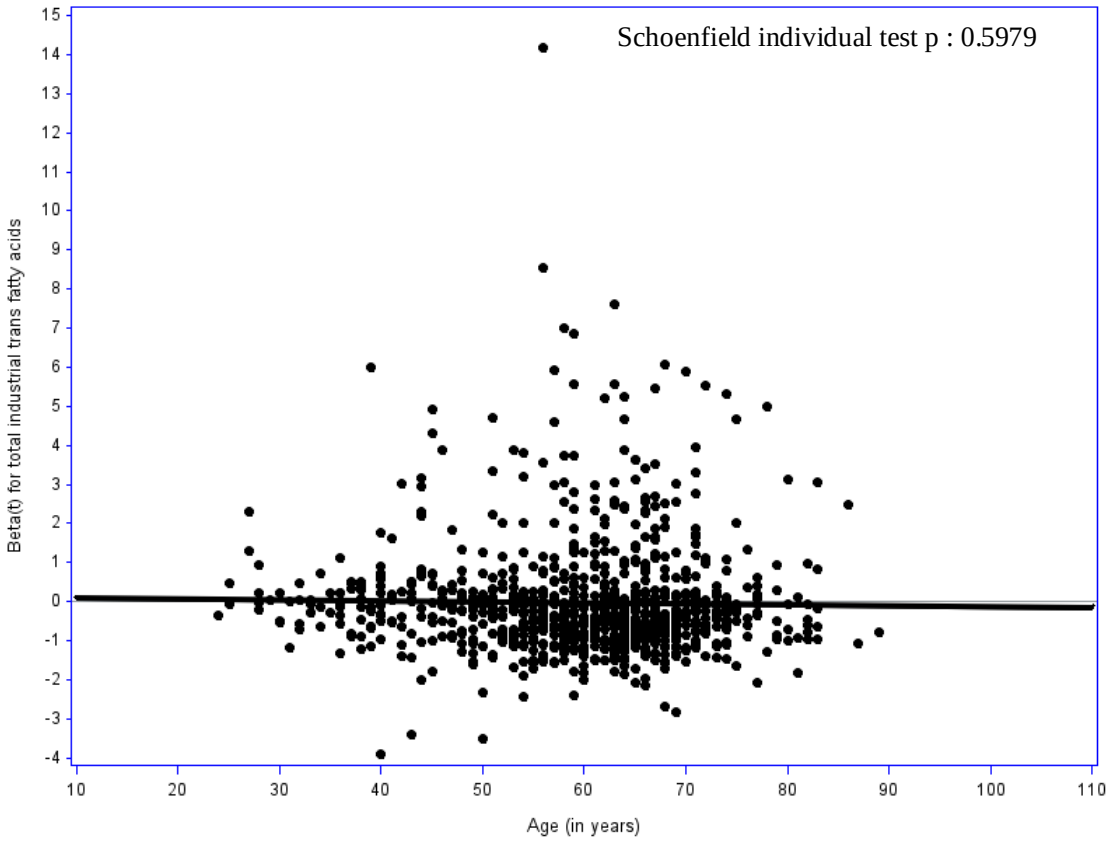


Test of the proportional hazard assumption

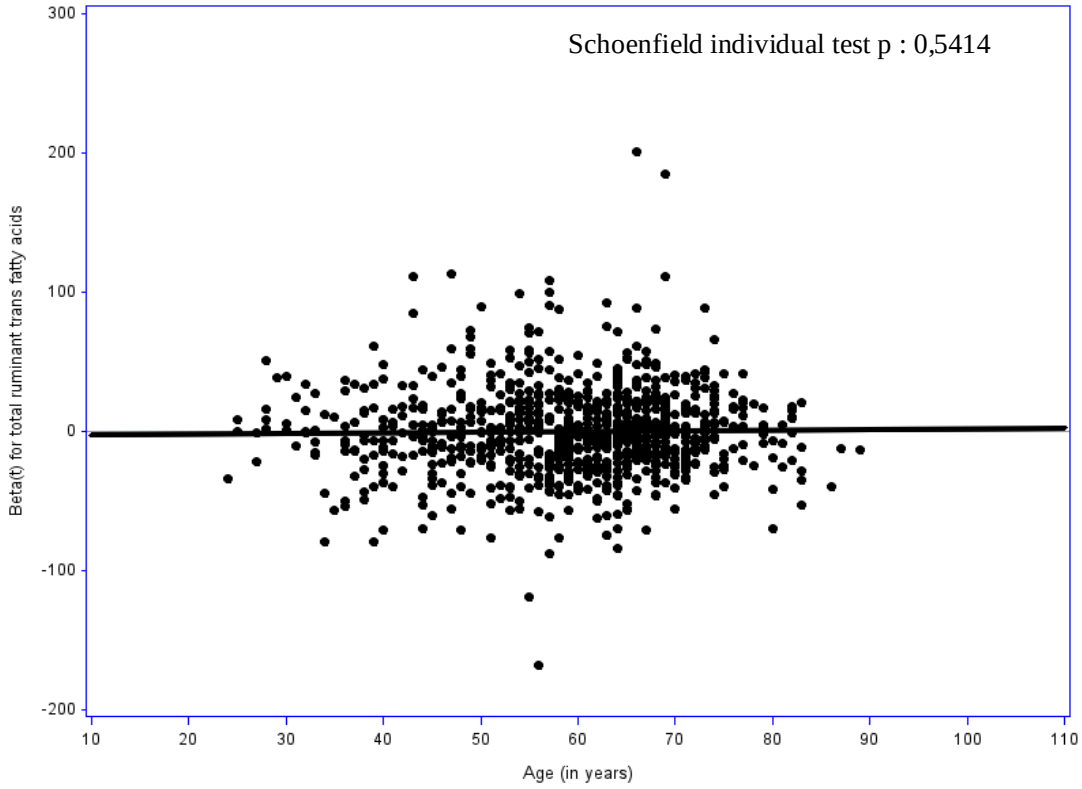
These Figures display Schoenfeld residuals to verify the proportional hazard assumption of the Cox models. Indeed, Cox proportional hazards model implies the verification of several assumptions. Thus, it is important to assess whether a fitted Cox regression model adequately describes the data. The proportional hazards assumption can be checked using statistical tests and graphical diagnostics based on the scaled Schoenfeld residuals. In principle, the Schoenfeld residuals are independent of time. A plot that shows a non-random pattern against time is evidence of violation of the proportional hazards assumption. From the graphical inspection in the figures 2 to 4, there is no pattern with time. The assumption of proportional hazards appears to be supported for total trans fatty acids (Supplemental figure 2-a), total industry-produced trans fatty acids (Supplemental figure 2-b) and total ruminant trans fatty acids (Supplemental figure 2-c).



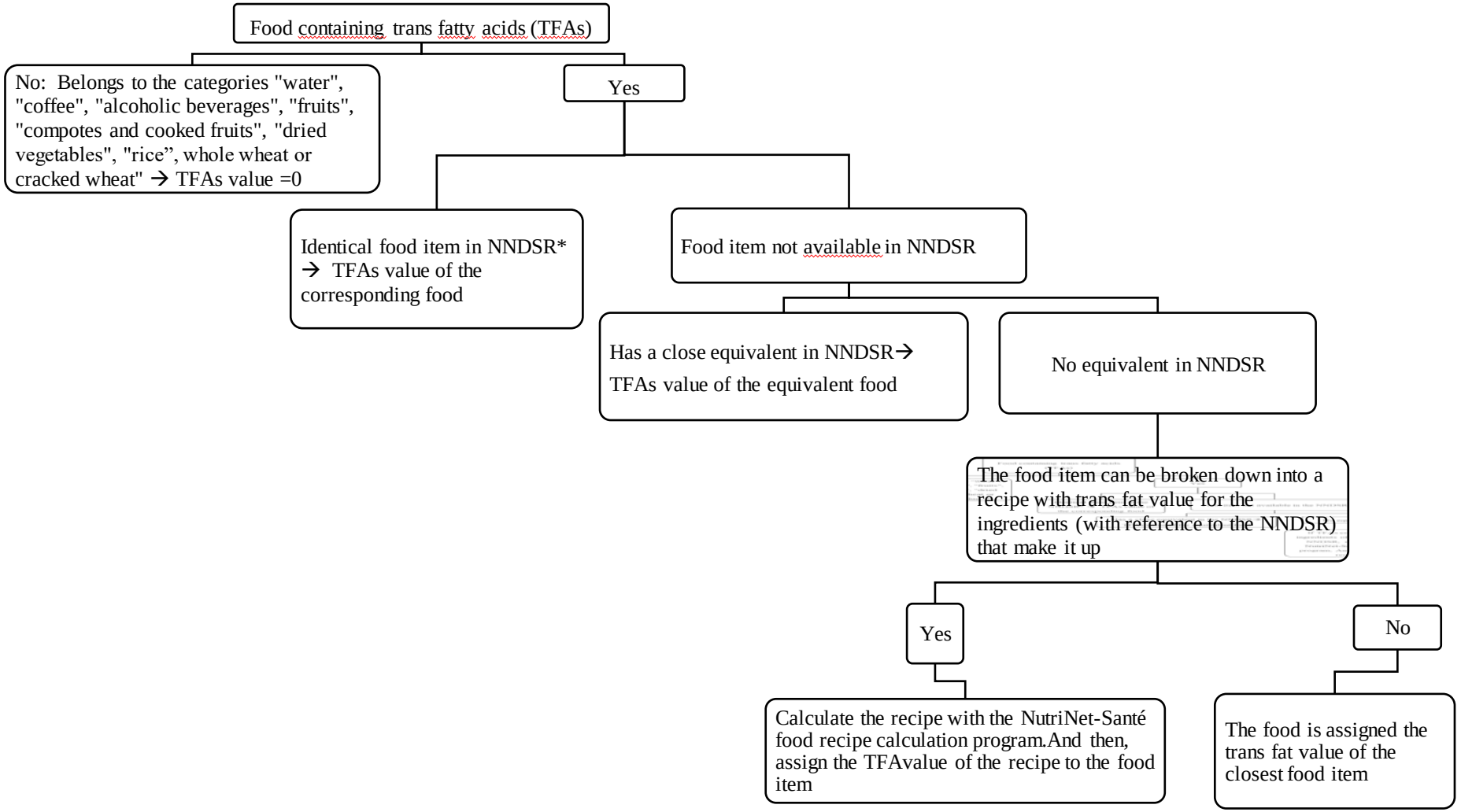
Supplemental Figure 2-a: Proportional hazard assumption testing using rescaled Schoenfeld-type residuals for total TFAs and type 2 diabetes risk



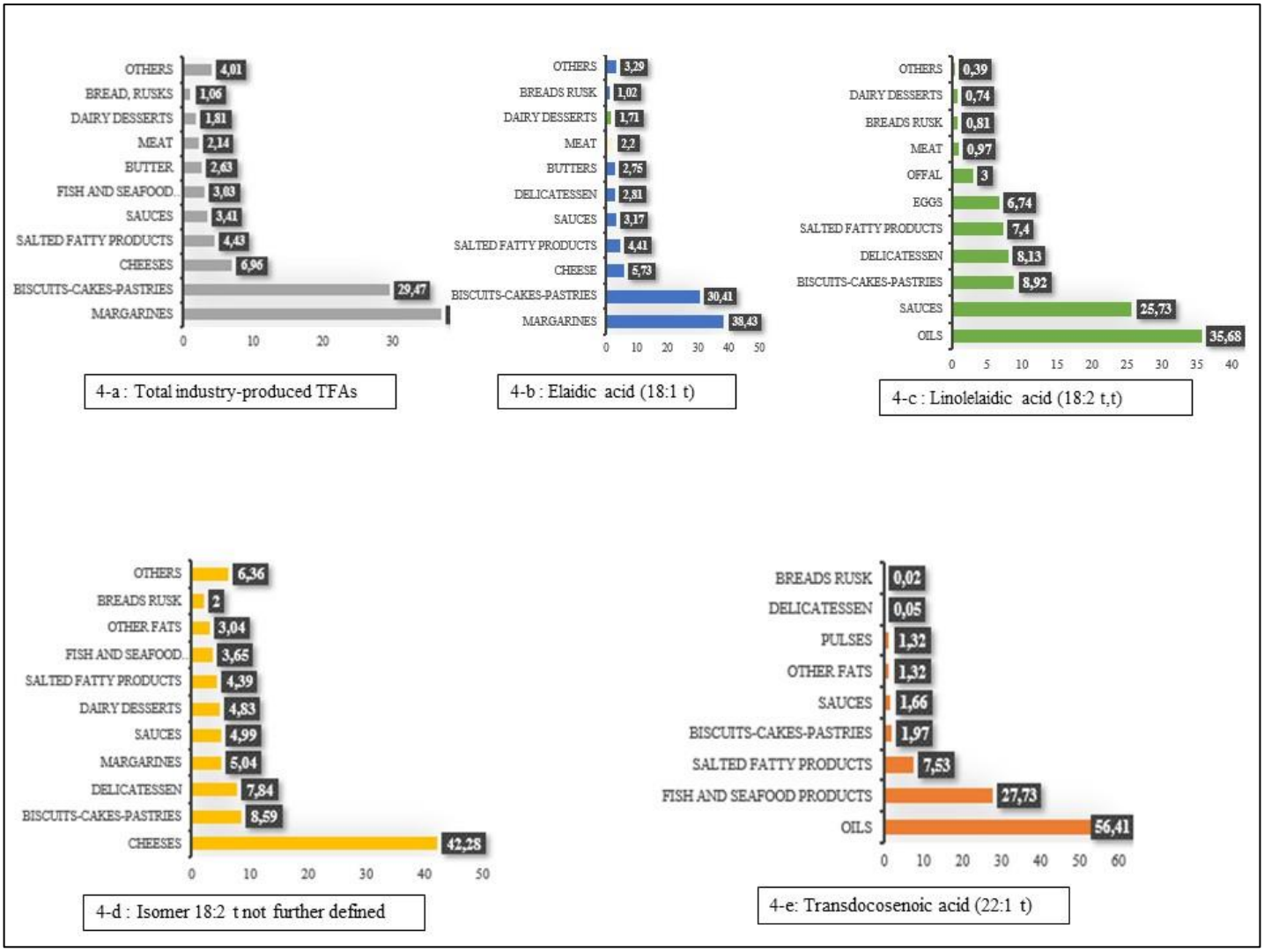
Supplemental Figure 2-b: Proportional hazard assumption testing using rescaled Schoenfeld-type residuals for industry-produced TFAs and type 2 diabetes risk



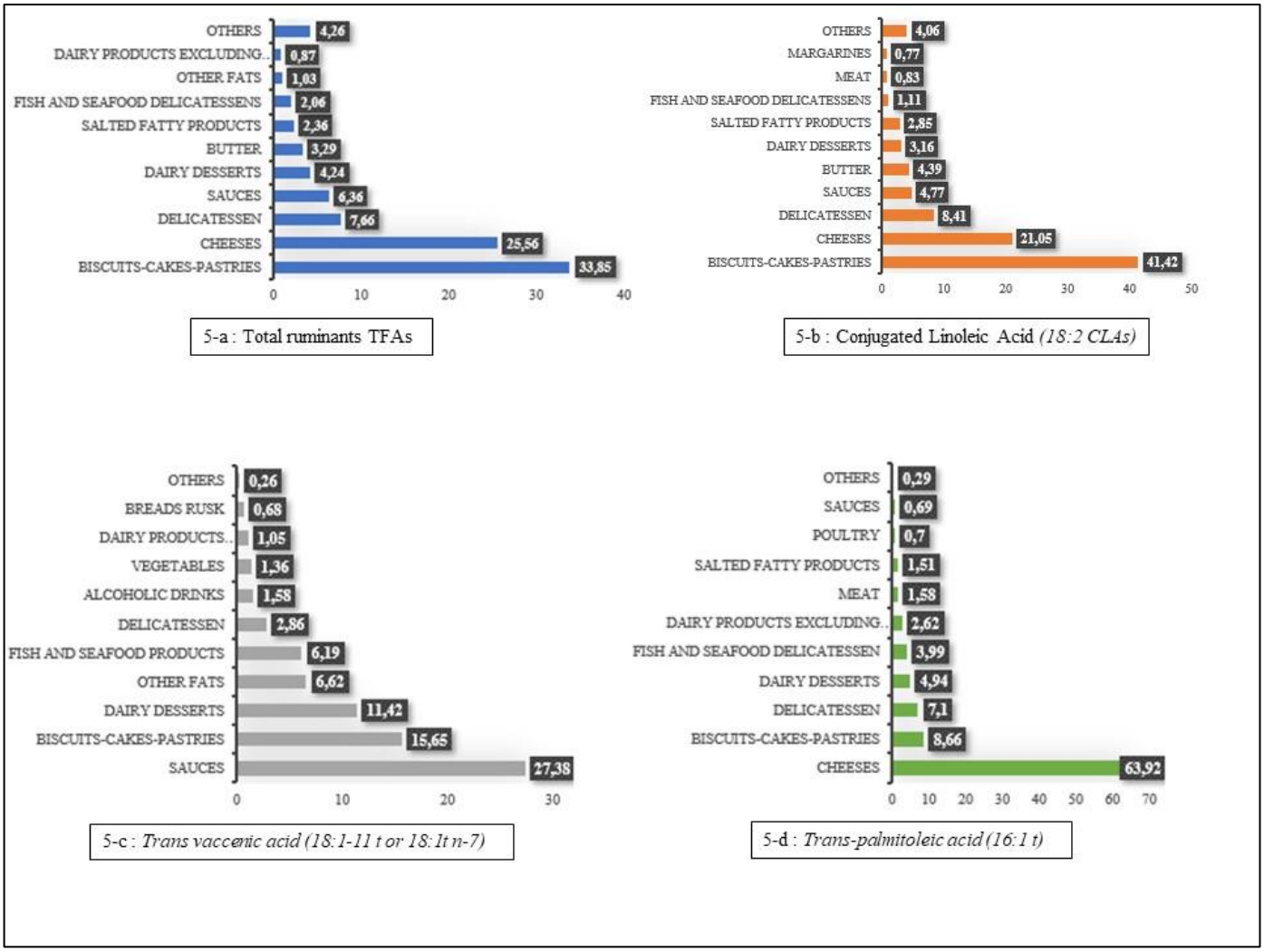
Supplemental Figure 2-c: Proportional hazard assumption testing using rescaled Schoenfeld-type residuals for ruminant TFAs and type 2 diabetes risk



Supplemental Figure 3: Detailed decision tree for TFAs composition assignment with reference to the NNDSR (*National Nutrient Database for Standard Reference of the United States). A TFA composition value was attributed to all food items that were likely to contain some. Indeed, when the exact match with the USDA composition table was not found for a particular food item, the value of the closest food/beverage equivalent was selected. For composite food dishes, the amount of TFAs was estimated using validated French recipes by summing TFA amounts contained in the different ingredients composing the dish.



Supplemental Figures 4-a, 4-b, 4-c, 4-d, 4-e: Contribution (%) of food groups to intake of each type of industry-produced TFAs– NutriNet-Santé cohort, France, 2009-2021 (n=105,551)



Supplemental Figures 5a, 5-b, 5-c, 5-d: Contribution (%) of food groups to intake of each type of TFA from ruminant sources – NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

Supplemental Method 1: Type 2 diabetes case ascertainment *(International Statistical Classification of Diseases and Related Health Problems, Tenth Revision [ICD-10] code E11)*

Participants were asked to declare major health events though the yearly health questionnaire, through a specific health check-up questionnaire every six months, or at any time through a specific interface on the study website. They were also asked to declare all currently taken medications and treatments via the check-up and yearly questionnaires. A search engine with embedded exhaustive Vidal® drug database is used to facilitate medication data entry for the participants. Besides, our research team was the first in France to obtain the authorization by Decree in the Council of State (n°2013-175) to link data from our general population-based cohorts to medico-administrative databases of the National health insurance (SNIIRAM database). Thus, data from the NutriNet-Santé cohort are linked every year to medico-administrative databases of the SNIIRAM, providing detailed information about the reimbursement of medication and medical consultations. Regarding type 2 diabetes specifically: all 969 cases were primarily detected through the declaration by the participants of a type 2 diabetes diagnosed by a physician and/or diabetes medication use, in follow-up questionnaires. The questions were: "Have you been diagnosed with type 2 diabetes (if yes, indicate the date of diagnosis)" and "Are you treated for type 2 diabetes?". ATC codes considered for type 2 diabetes medication were A10AB01, A10AB03, A10AB04, A10AB05, A10AB06, A10AC01, A10AC03, A10AC04, A10AD01, A10AD03, A10AD04, A10AD05, A10AE01, A10AE02, A10AE03, A10AE04, A10AE05, A10AE30, A10BA02, A10BB01, A10BB03, A10BB04, A10BB06, A10BB07, A10BB09, A10BB12, A10BD02, A10BD03, A10BD05, A10BD07, A10BD08, A10BD10, A10BD15, A10BD16, A10BF01, A10BF02, A10BG02, A10BG03, A10BH01, A10BH02, A10BH03, A10BX02, A10BX04, A10BX07, A10BX09, A10BX10, A10BX11, A10BX12.

In addition to the diagnosis of type 2 diabetesM and/or a medication report, two sources of confirmation were considered. First, linkage with the SNIIRAM database confirmed more than 80% of the cases surveyed (ICD-10 codes E11). Second, among participants who provided a blood sample at the clinical/biological examination, 85.3 % of those with elevated fasting blood glucose (i.e., >1.26 g/L[9]) had consistently reported a diagnosis of type 2 diabetesM and/or medication. However, elevated blood glucose without any declaration of type 2 diabetes diagnosis or treatment was not considered specific enough to classify the participant as a type 2 diabetes case.

Supplemental Method 2: Multiple Imputation by Chained Equations

Missing values for covariates were handled using the Multiple Imputation by Chained Equations (MICE) method[2] (20 imputed datasets) for the following covariates: smoking status (0.07% missing), level of education (0.86%), physical activity (13.81%), occupation (0.86%),

prevalence of dyslipidemia (0.44%), BMI (1.56%), family history of diabetes (1.39% missing), marital status (0.25% missing), prevalence of cardiovascular disease (0.44% missing).

Supplemental Method 3: Method for deriving dietary patterns by Principal Component Analysis and corresponding factor loadings

Dietary patterns were produced from principal-components analysis based on 20 predefined food groups, using the SAS "Proc Factor" procedure. This factor analysis forms linear combinations of the original food groups, grouping together correlated variables. Coefficients defining these linear combinations are called factor loadings. A positive factor loading means that the food group is positively associated with the factor, whereas a negative loading reflects an inverse association with the factor. For interpreting the factor, foods with a coefficient under -0.25 or over 0.25 were considered. Factors were then rotated by orthogonal transformation using the SAS "Varimax" option to maximize the independence (orthogonality) of retained factors and obtain a simpler structure for easier interpretation. In determining the number of factors retain, eigenvalues greater than 1.25, the scree test (with values being retained at the break point between components with large eigenvalues and those with small eigenvalues on the scree plot), and the interpretability of the factors were considered. For each subject, a factor score for each pattern was computed by summing observed consumption from all food groups, weighted by the food group factor loadings. The factor score measures the conformity of an individual's diet to the given pattern. Labeling was descriptive, based on foods most strongly associated with the dietary patterns. The 'Healthy' pattern (explaining 10.7% of the variance) was characterized by higher intakes of fruits, vegetables, soups and broths, unsweetened soft drinks and whole grains. The 'Western' pattern (explaining 7.7% of the variance) was characterized by higher intakes of fat and sauces, alcohol, meat and starchy foods. These patterns were introduced into the models to reflect the overall pattern of food consumption of the participants.

	Factor loadings	
	'Healthy' Pattern	'Western' Pattern
Alcoholic drinks	-0.133277	0.353153
Breakfast cereals	0.116896	-0.243968
Cakes and biscuits	-0.286360	-0.010026
Dairy products	0.079645	-0.012452
Eggs	0.117015	0.059990
Fats and sauces	0.035011	0.667740
Fish and seafood	0.292119	0.125929
Fruit	0.517207	0.046517
Meat	-0.279305	0.404238
Pasta and rice	-0.299307	0.429694
Potatoes and tubers	-0.012724	0.500089
Poultry	-0.055723	0.088790
Processed meat	-0.338193	0.270663
Pulses	0.303690	0.015773
Soups and broths	0.390139	0.291322
Sugar and confectionery	-0.120684	0.126217
Sweetened soft drinks	-0.423675	-0.014394
Unsweetened soft drinks	0.375867	0.180510
Vegetables	0.689052	0.276493
Whole grains	0.561902	-0.072701

Supplemental Table 1: Association between trans fatty acid intake and type 2 diabetes risk excluding cases occurring during the first two years of follow-up (to challenge the potential reverse causality bias), NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	149 / 26,324	156 / 26,326	178 / 26,326	236 / 26,325	
	HR (95% CI)	1	0.91 (0.72-1.14)	1.13 (0.89-1.43)	1.38 (1.07-1.77)	0.001
Trans fatty acids from industry-produced sources	Incident cases / Participants	150 / 26,324	154 / 26,326	179 / 26,326	236 / 26,325	
	HR (95% CI)	1	0.91 (0.72-1.14)	1.16 (0.91-1.47)	1.42 (1.10-1.85)	<0.001
Elaidic acid (18:1 t)	Incident cases / Participants	151 / 26,324	156 / 26,326	178 / 26,326	234 / 26,325	
	HR (95% CI)	1	0.92 (0.73-1.15)	1.10 (0.87-1.41)	1.33 (1.03-1.72)	0.005
Linolelaidic acid (18:2 t,t)	Incident cases / Participants	116 / 26,326	155 / 26,324	215 / 26,326	233 / 26,325	
	HR (95% CI)	1	1.12 (0.87-1.44)	1.31 (1.03-1.67)	1.37 (1.08-1.73)	0.01
Transdocosenoic acid (22:1 t)	Incident cases / Participants	130 / 28,599	188 / 25,582	181 / 25,582	220 / 25,538	
	HR (95% CI)	1	1.14 (0.90-1.45)	1.03 (0.81-1.31)	1.07 (0.85-1.35)	0.9
Isomer 18:2 t not further defined	Incident cases / Participants	129 / 26,324	170 / 26,326	207 / 26,326	213 / 26,325	
	HR (95% CI)	1	1.11 (0.88-1.40)	1.35 (1.07-1.70)	1.37 (1.07-1.75)	0.007
Trans fatty acids from ruminant sources	Incident cases / Participants	146 / 26,324	190 / 26,326	188 / 26,326	195 / 26,325	
	HR (95% CI)	1	1.03 (0.82-1.29)	1.09 (0.85-1.38)	1.16 (0.87-1.56)	0.3
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	154 / 26,324	195 / 26,326	188 / 26,326	182 / 26,325	
	HR (95% CI)	1	1.05 (0.84-1.31)	1.06 (0.83-1.35)	1.01 (0.74-1.37)	0.9
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	126 / 26,325	192 / 26,325	205 / 26,326	196 / 26,325	
	HR (95% CI)	1	1.17 (0.92-1.49)	1.21 (0.95-1.53)	1.20 (0.94-1.54)	0.3
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	150 / 26,324	181 / 26,326	186 / 26,326	202 / 26,325	
	HR (95% CI)	1	1.01 (0.81-1.25)	0.94 (0.75-1.18)	1.15 (0.92-1.44)	0.2

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalence of cardiovascular disease (categorical: yes, no), prevalence of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 2: Association between trans fatty acid intake and type 2 diabetes further adjusting for dietary patterns ("Healthy" and "Western") instead of fruit, vegetable and meat intakes, NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	199 / 26,359	221 / 26,403	242 / 26,402	307 / 26,387	
	HR (95% CI)	1	0.94 (0.77-1.15)	1.09 (0.88-1.35)	1.29 (1.02-1.62)	0.005
Trans fatty acids from industry-produced sources	Incident cases / Participants	199 / 26,364	218 / 26,401	245 / 26,399	307 / 26,387	
	HR (95% CI)	1	0.96 (0.78-1.17)	1.15 (0.93-1.43)	1.37 (1.08-1.73)	0.001
Elaidic acid (18:1 t)	Incident cases / Participants	202 / 26,367	219 / 26,397	242 / 26,399	306 / 26,388	
	HR (95% CI)	1	0.94 (0.77-1.15)	1.09 (0.88-1.35)	1.27 (1.01-1.60)	0.008
Linolelaidic acid (18:2 t,t)	Incident cases / Participants	157 / 26,344	221 / 26,404	295 / 26,417	296 / 26,386	
	HR (95% CI)	1	1.18 (0.95-1.46)	1.39 (1.13-1.71)	1.34 (1.08-1.64)	0.02
Transdocosenoic acid (22:1 t)	Incident cases / Participants	185 / 28,654	254 / 25,596	237 / 25,687	293 / 25,614	
	HR (95% CI)	1	1.09 (0.88-1.33)	0.96 (0.78-1.18)	1.00 (0.81-1.22)	0.7
Isomer 18:2 t not further defined	Incident cases / Participants	179 / 26,362	230 / 26,397	274 / 26,416	286 / 26,376	
	HR (95% CI)	1	1.06 (0.87-1.30)	1.28 (1.05-1.57)	1.32 (1.07-1.63)	0.005
Trans fatty acids from ruminant sources	Incident cases / Participants	195 / 26,364	256 / 26,394	256 / 26,409	262 / 26,384	
	HR (95% CI)	1	1.05 (0.86-1.28)	1.09 (0.88-1.35)	1.21 (0.93-1.56)	0.1
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	205 / 26,363	260 / 26,399	260 / 26,410	244 / 26,379	
	HR (95% CI)	1	1.06 (0.87-1.29)	1.09 (0.88-1.36)	1.04 (0.79-1.36)	0.8
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	174 / 26,321	256 / 26,416	278 / 26,432	261 / 26,382	
	HR (95% CI)	1	1.11 (0.90-1.36)	1.13 (0.91-1.39)	1.11 (0.89-1.38)	0.5
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	195 / 26,374	232 / 26,393	267 / 26,408	275 / 26,376	
	HR (95% CI)	1	1.01 (0.83-1.23)	1.07 (0.88-1.30)	1.27 (1.05-1.55)	0.006

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalence of cardiovascular disease (categorical: yes, no), prevalence of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 3: Association between trans fatty acid intake and type 2 diabetes risk restricting the study population to participants with at least four 24h-dietary records during the first two years, NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	172 / 15,058	178 / 15,058	193 / 15,058	240 / 15,059	
	HR (95% CI)	1	1.06 (0.85-1.33)	1.09 (0.86-1.37)	1.36 (1.06-1.73)	0.008
Trans fatty acids from industry-produced sources	Incident cases / Participants	175 / 15,058	173 / 15,058	194 / 15,058	241 / 15,059	
	HR (95% CI)	1	1.00 (0.80- 1.26)	1.08 (0.85- 1.36)	1.28 (1.00- 1.65)	0.03
Elaidic acid (18:1 t)	Incident cases / Participants	175 / 15,057	180 / 15,059	188 / 15,058	240 / 15,059	
	HR (95% CI)	1	1.04 (0.84- 1.30)	1.03 (0.82- 1.30)	1.25 (0.97- 1.59)	0.06
Linolelaidic acid (18:2 t,t)	Incident cases / Participants	154 / 15,059	175 / 15,058	215 / 15,057	239 / 15,059	
	HR (95% CI)	1	1.15 (0.92-1.45)	1.38 (1.11-1.71)	1.26 (1.02-1.57)	0.1
Transdocosenoic acid (22:1 t)	Incident cases / Participants	101 / 8,534	226 / 17,233	202 / 17,234	254 / 17,232	
	HR (95% CI)	1	1.14 (0.89-1.47)	1.00 (0.77-1.29)	1.13 (0.88-1.45)	0.5
Isomer 18:2 t not further defined	Incident cases / Participants	154 / 15,057	169 / 15,059	221 / 15,059	239 / 15,058	
	HR (95% CI)	1	0.94 (0.75-1.18)	1.31 (1.05-1.63)	1.37 (1.09-1.72)	<0.001
Trans fatty acids from ruminant sources	Incident cases / Participants	179 / 15,058	197 / 15,059	196 / 15,057	211 / 15,059	
	HR (95% CI)	1	1.20 (0.96-1.50)	1.30 (1.03-1.65)	1.39 (1.05-1.83)	0.02
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	180 / 15,058	209 / 15,058	198 / 15,059	196 / 15,058	
	HR (95% CI)	1	1.30 (1.04-1.61)	1.28 (1.01-1.62)	1.25 (0.93-1.67)	0.2
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	184 / 15,072	189 / 15,044	199 / 15,060	211 / 15,057	
	HR (95% CI)	1	1.03 (0.83-1.27)	0.98 (0.79-1.21)	1.09 (0.87-1.36)	0.5
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	160 / 15,057	187 / 15,059	208 / 15,059	228 / 15,058	
	HR (95% CI)	1	1.20 (0.96-1.48)	1.18 (0.95-1.47)	1.37 (1.10-1.70)	0.007

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalence of cardiovascular disease (categorical: yes, no), prevalence of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 4: Association between trans fatty acid intake and type 2 diabetes, excluding incident cases of type 1 diabetes from the study population NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	199 / 26,365	221 / 26,365	242 / 26,367	307 / 26,366	
	HR (95% CI)	1	0.96 (0.78-1.17)	1.14 (0.93-1.41)	1.38 (1.11-1.73)	<0.001
Trans fatty acids from industry-produced sources	Incident cases / Participants	199 / 26,365	218 / 26,365	245 / 26,367	307 / 26,366	
	HR (95% CI)	1	0.97 (0.79-1.19)	1.20 (0.97-1.49)	1.45 (1.16-1.83)	<0.001
Elaidic acid (18:1 t)	Incident cases / Participants	203 / 26,365	218 / 26,365	242 / 26,367	306 / 26,366	
	HR (95% CI)	1	0.95 (0.77-1.16)	1.14 (0.92-1.41)	1.36 (1.08-1.70)	0.001
Linolelaidic acid (18:2 t,t)	Incident cases / Participants	157 / 26,362	221 / 26,369	295 / 26,367	296 / 26,365	
	HR (95% CI)	1	1.18 (0.95-1.47)	1.37 (1.12-1.69)	1.29 (1.05-1.59)	0.07
Transdocosenoic acid (22:1 t)	Incident cases / Participants	185 / 28,636	254 / 25,619	238 / 25,620	292 / 25,588	
	HR (95% CI)	1	1.08 (0.88-1.32)	0.97 (0.79-1.20)	1.00 (0.82-1.22)	0.8
Isomer 18:2 t not further defined	Incident cases / Participants	179 / 26,364	230 / 26,367	274 / 26,368	286 / 26,364	
	HR (95% CI)	1	1.07 (0.87-1.31)	1.28 (1.05-1.57)	1.31 (1.06-1.62)	0.007
Trans fatty acids from ruminant sources	Incident cases / Participants	195 / 26,365	256 / 26,367	256 / 26,366	262 / 26,365	
	HR (95% CI)	1	1.07 (0.87-1.30)	1.11 (0.90-1.38)	1.24 (0.96-1.61)	0.09
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	205 / 26,365	260 / 26,366	259 / 26,368	245 / 26,364	
	HR (95% CI)	1	1.08 (0.89-1.31)	1.12 (0.91-1.39)	1.10 (0.84-1.44)	0.5
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	174 / 26,367	257 / 26,363	276 / 26,368	262 / 26,365	
	HR (95% CI)	1	1.15 (0.94-1.42)	1.18 (0.96-1.46)	1.19 (0.96-1.48)	0.2
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	195 / 26,364	232 / 26,367	267 / 26,367	275 / 26,365	
	HR (95% CI)	1	1.00 (0.82-1.22)	1.04 (0.86-1.27)	1.20 (0.99-1.46)	0.03

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalence of cardiovascular disease (categorical: yes, no), prevalence of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 5: Association between trans fatty acid intake and type 2 diabetes further adjusting for fiber instead of whole-grain intake, NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	199 / 26,359	221 / 26,403	242 / 26,402	307 / 26,387	
	HR (95% CI)	1	0.95 (0.78-1.17)	1.14 (0.92-1.41)	1.38 (1.10-1.73)	<0.001
Trans fatty acids from industry-produced sources	Incident cases / Participants	199 / 26,364	218 / 26,401	245 / 26,399	307 / 26,387	
	HR (95% CI)	1	0.97 (0.79-1.19)	1.20 (0.96-1.48)	1.44 (1.15-1.82)	<0.001
Elaidic acid (18:1 t)	Incident cases / Participants	202 / 26,367	219 / 26,397	242 / 26,399	306 / 26,388	
	HR (95% CI)	1	0.96 (0.78-1.17)	1.14 (0.93-1.41)	1.36 (1.09-1.71)	0.001
Linolelaidic acid (18:2 t,t)	Incident cases / Participants	157 / 26,344	221 / 26,404	295 / 26,417	296 / 26,386	
	HR (95% CI)	1	1.18 (0.95-1.46)	1.37 (1.11-1.68)	1.28 (1.04-1.58)	0.08
Transdocosenoic acid (22:1 t)	Incident cases / Participants	185 / 28,654	254 / 25,596	237 / 25,687	293 / 25,614	
	HR (95% CI)	1	1.08 (0.88-1.33)	0.97 (0.79-1.19)	1.00 (0.82-1.22)	0.7
Isomer 18:2 t not further defined	Incident cases / Participants	179 / 26,362	230 / 26,397	274 / 26,416	286 / 26,376	
	HR (95% CI)	1	1.07 (0.87-1.31)	1.28 (1.05-1.57)	1.31 (1.06-1.62)	0.007
Trans fatty acids from ruminant sources	Incident cases / Participants	195 / 26,364	256 / 26,394	256 / 26,409	262 / 26,384	
	HR (95% CI)	1	1.06 (0.87-1.29)	1.11 (0.90-1.37)	1.24 (0.96-1.61)	0.09
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	205 / 26,363	260 / 26,399	260 / 26,410	244 / 26,379	
	HR (95% CI)	1	1.08 (0.89-1.31)	1.12 (0.90-1.39)	1.09 (0.83-1.42)	0.6
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	174 / 26,321	256 / 26,416	278 / 26,432	261 / 26,382	
	HR (95% CI)	1	1.15 (0.93-1.41)	1.18 (0.96-1.46)	1.19 (0.96-1.47)	0.2
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	195 / 26,374	232 / 26,393	267 / 26,408	275 / 26,376	
	HR (95% CI)	1	0.99 (0.82-1.21)	1.04 (0.85-1.26)	1.19 (0.98-1.45)	0.04

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalent of cardiovascular disease (categorical: yes, no), prevalent of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 6: Association between trans fatty acid intake and type 2 diabetes further adjusting for the proportion of ultra-processed food (in weight, percentage of grams per day) in the total diet, NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	199 / 26,359	221 / 26,403	242 / 26,402	307 / 26,387	
	HR (95% CI)	1	0.97 (0.79- 1.19)	1.16 (0.93- 1.43)	1.39 (1.11- 1.75)	<0.001
Trans fatty acids from industry-produced sources	Incident cases / Participants	199 / 26,364	218 / 26,401	245 / 26,399	307 / 26,387	
	HR (95% CI)	1	0.99 (0.81- 1.21)	1.23 (0.99- 1.52)	1.48 (1.18- 1.87)	<0.001
Elaidic acid (18:1 t)	Incident cases / Participants	202 / 26,367	219 / 26,397	242 / 26,399	306 / 26,388	
	HR (95% CI)	1	0.98 (0.80- 1.20)	1.17 (0.95- 1.45)	1.40 (1.12- 1.76)	<0.001
Octadecadienoic acid (18:2 t,t)	Incident cases / Participants	157 / 26,344	221 / 26,404	295 / 26,417	296 / 26,386	
	HR (95% CI)	1	1.18 (0.95- 1.46)	1.37 (1.11- 1.69)	1.29 (1.05- 1.59)	0.06
Transdocosenoic acid (22:1 t)	Incident cases / Participants	185 / 28,654	254 / 25,596	237 / 25,687	293 / 25,614	
	HR (95% CI)	1	1.08 (0.88- 1.33)	0.97 (0.79- 1.20)	1.01 (0.82- 1.23)	0.8
Isomer 18:2 t not further defined	Incident cases / Participants	179 / 26,362	230 / 26,397	274 / 26,416	286 / 26,376	
	HR (95% CI)	1	1.06 (0.86- 1.30)	1.26 (1.03- 1.54)	1.26 (1.01- 1.56)	0.02
Trans fatty acids from ruminant sources	Incident cases / Participants	195 / 26,364	256 / 26,394	256 / 26,409	262 / 26,384	
	HR (95% CI)	1	1.06 (0.87- 1.29)	1.10 (0.89- 1.36)	1.21 (0.94- 1.57)	0.1
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	205 / 26,363	260 / 26,399	260 / 26,410	244 / 26,379	
	HR (95% CI)	1	1.08 (0.89- 1.32)	1.12 (0.90- 1.39)	1.08 (0.83- 1.42)	0.6
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	174 / 26,321	256 / 26,416	278 / 26,432	261 / 26,382	
	HR (95% CI)	1	1.12 (0.91- 1.37)	1.13 (0.92- 1.39)	1.11 (0.90- 1.38)	0.5
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	195 / 26,374	232 / 26,393	267 / 26,408	275 / 26,376	
	HR (95% CI)	1	1.00 (0.82- 1.22)	1.05 (0.86- 1.27)	1.19 (0.98- 1.45)	0.04

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalent of cardiovascular disease (categorical: yes, no), prevalent of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 7: Association between trans fatty acid intake and type 2 diabetes in ex and non-smokers, NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	190 / 22,556	204 / 22,602	227 / 22,595	277 / 22,583	
	HR (95% CI)	1	0.96 (0.78-1.18)	1.17 (0.94-1.45)	1.37 (1.09-1.73)	0.001
Trans fatty acids from industry-produced sources	Incident cases / Participants	185 / 22,562	210 / 22,598	225 / 22,592	278 / 22,584	
	HR (95% CI)	1	1.03 (0.83-1.27)	1.24 (0.99-1.54)	1.47 (1.16-1.87)	<0.001
Elaidic acid (18:1 t)	Incident cases / Participants	193 / 22,561	203 / 22,597	223 / 22,590	279 / 22,588	
	HR (95% CI)	1	0.95 (0.77-1.17)	1.14 (0.92-1.42)	1.35 (1.07-1.70)	0.002
Octadecadienoic acid (18:2 t,t)	Incident cases / Participants	144 / 22,565	213 / 22,591	277 / 22,604	264 / 22,576	
	HR (95% CI)	1	1.28 (1.03-1.61)	1.46 (1.17-1.81)	1.33 (1.07-1.65)	0.1
Transdocosenoic acid (22:1 t)	Incident cases / Participants	162 / 23,421	241 / 22,297	224 / 22,311	271 / 22,307	
	HR (95% CI)	1	1.13 (0.91-1.40)	1.03 (0.82-1.28)	1.04 (0.84-1.29)	0.8
Isomer 18:2 t not further defined	Incident cases / Participants	169 / 22,568	219 / 22,591	248 / 22,602	262 / 22,575	
	HR (95% CI)	1	1.12 (0.91-1.38)	1.28 (1.04-1.58)	1.31 (1.05-1.64)	0.01
Trans fatty acids from ruminant sources	Incident cases / Participants	187 / 22,562	240 / 22,593	233 / 22,599	238 / 22,582	
	HR (95% CI)	1	1.15 (0.94-1.41)	1.13 (0.91-1.42)	1.29 (0.99-1.69)	0.09
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	190 / 22,559	247 / 22,599	238 / 22,595	223 / 22,583	
	HR (95% CI)	1	1.12 (0.92-1.37)	1.14 (0.91-1.42)	1.12 (0.84-1.48)	0.5
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	171 / 22,520	232 / 22,664	256 / 22,578	239 / 22,574	
	HR (95% CI)	1	1.07 (0.87-1.33)	1.16 (0.94-1.43)	1.13 (0.90-1.41)	0.3
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	186 / 22,572	220 / 22,590	241 / 22,597	251 / 22,577	
	HR (95% CI)	1	1.03 (0.84-1.26)	1.04 (0.85-1.28)	1.21 (0.98-1.48)	0.05

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalent of cardiovascular disease (categorical: yes, no), prevalent of dislipidemia (categorical: yes, no), marital status (categorical: married, in a relationship, divorced, widowed, single), baseline intakes of energy without alcohol (continuous, kcal/d), alcohol (continuous, g/d), sodium (continuous, g/d), saturated fatty acids (continuous, g/d), sugar (continuous, g/d), whole-grain foods (continuous, g/d), red and processed meat (continuous, g/d), fruits and vegetables (continuous, g/d).

Supplemental Table 8: Association between trans fatty acid intake and type 2 diabetes adjusted for clinical factors, NutriNet-Santé cohort, France, 2009-2021 (n=105,551)

		Sex-specific quartiles				
		1	2	3	4	P-trend
Total trans fatty acids	Incident cases / Participants	199 / 26,359	221 / 26,403	242 / 26,402	307 / 26,387	
	HR (95% CI)	1	0.93 (0.76-1.13)	1.09 (0.90-1.34)	1.29 (1.06-1.59)	0.002
Trans fatty acids from industry-produced sources	Incident cases / Participants	199 / 26,364	218 / 26,401	245 / 26,399	307 / 26,387	
	HR (95% CI)	1	0.97 (0.79-1.18)	1.20 (0.97-1.48)	1.43 (1.14-1.80)	<0.001
Elaidic acid (18:1 t)	Incident cases / Participants	202 / 26,367	219 / 26,397	242 / 26,399	306 / 26,388	
	HR (95% CI)	1	0.93 (0.76-1.13)	1.11 (0.90-1.36)	1.28 (1.03-1.59)	0.005
Linolelaidic acid (18:2 t,t)	Incident cases / Participants	157 / 26,344	221 / 26,404	295 / 26,417	296 / 26,386	
	HR (95% CI)	1	1.21 (0.97-1.50)	1.44 (1.17-1.77)	1.43 (1.16-1.76)	0.003
Isomer 18:2 t not further defined	Incident cases / Participants	179 / 26,362	230 / 26,397	274 / 26,416	286 / 26,376	
	HR (95% CI)	1	1.10 (0.90-1.35)	1.36 (1.11-1.66)	1.41 (1.14-1.74)	<0.001
Transdocosenoic acid (22:1 t)	Incident cases / Participants	185 / 28,654	254 / 25,596	237 / 25,687	293 / 25,614	
	HR (95% CI)	1	1.10 (0.89-1.35)	0.96 (0.78-1.19)	0.99 (0.81-1.21)	0.6
Trans fatty acids from ruminant sources	Incident cases / Participants	195 / 26,364	256 / 26,394	256 / 26,409	262 / 26,384	
	HR (95% CI)	1	1.04 (0.86-1.26)	1.09 (0.89-1.33)	1.18 (0.94-1.48)	0.1
Conjugated linoleic acid (18:2 CLAs)	Incident cases / Participants	205 / 26,363	260 / 26,399	260 / 26,410	244 / 26,379	
	HR (95% CI)	1	1.06 (0.88-1.29)	1.13 (0.92-1.37)	1.07 (0.85-1.35)	0.5
Trans vaccenic acid (18:1-11 t or 18:1t n-7)	Incident cases / Participants	174 / 26,321	256 / 26,416	278 / 26,432	261 / 26,382	
	HR (95% CI)	1	1.10 (0.89-1.35)	1.13 (0.92-1.38)	1.09 (0.88-1.35)	0.6
Trans-palmitoleic acid (16:1 t)	Incident cases / Participants	195 / 26,374	232 / 26,393	267 / 26,408	275 / 26,376	
	HR (95% CI)	1	1.01 (0.83-1.23)	1.04 (0.85-1.26)	1.23 (1.01-1.49)	0.02

HR: Cause-specific hazard ratios, CI: Confidence Interval. Multivariable Cox proportional hazard model were adjusted for (=main model) age (time scale), sex, body mass index (continuous, kg/m^2), physical activity (categorical IPAQ variable: high, moderate, low), smoking status (categorical: never, former, current smokers), educational level (categorical: less than high school degree, less than two years after high school degree, two and more years after high school degree), number of 24-hour dietary records (continuous), family history of type 2 diabetes (categorical: yes, no), prevalent of cardiovascular disease (categorical: yes, no), prevalent of dislipidemia (categorical: yes, no) and marital status (categorical: married, in a relationship, divorced, widowed, single).

References

1. Desquilbet L, Mariotti F. Dose-response analyses using restricted cubic spline functions in public health research. *Stat Med*. 2010;29(9):1037-1057. doi:10.1002/sim.3841

2. Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338:b2393.