THE LANCET Diabetes & Endocrinology

# Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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**Online appendix materials**

Appendix Table 1: The distribution of individual saturated fatty acids and groups of fatty acids in the study subcohort by country - EPIC-InterAct study

Appendix Table 2: Sensitivity analyses for the associations between each saturated fatty acid, fatty acid groups and product-to-precursor ratios and type 2 diabetes: EPIC-InterAct Study

Appendix Table 3: Pooled hazard ratio (HR) and 95% CI for associations between quintiles of each saturated fatty acid, fatty acid groups and product-to-precursor ratios and type 2 diabetes: EPIC-InterAct Study

**Appendix Table 1: The distribution of individual saturated fatty acids and groups of fatty acids in the study subcohort by country - EPIC-InterAct study**

| Fatty acids | France N=587 | | Italy N=2006 | | Spain N=3555 | | UK N=1310 | | Netherlands N=1500 | | Germany N=2045 | | Sweden N=2826 | | Denmark N=2090 | | Total N=15919 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | mean | sd | mean | sd | mean | sd | mean | sd | mean | sd | mean | sd | mean | sd | mean | sd | mean | sd |
| Total saturated fatty acids | 47·0 | 1·8 | 45·7 | 1·1 | 45·5 | 1·1 | 46·3 | 1·5 | 46·2 | 1·4 | 45·8 | 0·9 | 46·3 | 1·1 | 46·2 | 1·0 | 46·0 | 1·2 |
| Myristic acid (14:0) | 0·43 | 0·12 | 0·37 | 0·09 | 0·29 | 0·08 | 0·39 | 0·11 | 0·41 | 0·11 | 0·40 | 0·11 | 0·41 | 0·10 | 0·40 | 0·10 | 0·37 | 0·11 |
| Pentadecanoic acid (15:0) | 0·27 | 0·07 | 0·21 | 0·05 | 0·18 | 0·05 | 0·24 | 0·08 | 0·25 | 0·08 | 0·22 | 0·07 | 0·21 | 0·05 | 0·21 | 0·05 | 0·21 | 0·07 |
| Palmitic acid (16:0) | 30·5 | 1·6 | 30·0 | 1·4 | 29·0 | 1·6 | 30·3 | 1·6 | 30·2 | 1·8 | 30·3 | 1·5 | 30·6 | 1·5 | 30·9 | 1·5 | 30·1 | 1·7 |
| Heptadecanoic acid (17:0) | 0·50 | 0·11 | 0·41 | 0·07 | 0·44 | 0·10 | 0·42 | 0·09 | 0·41 | 0·09 | 0·39 | 0·07 | 0·40 | 0·08 | 0·38 | 0·08 | 0·41 | 0·09 |
| Stearic acid (18:0) | 14·4 | 1·5 | 14·0 | 1·2 | 14·8 | 1·2 | 14·0 | 1·4 | 14·0 | 1·6 | 13·8 | 1·3 | 14·0 | 1·1 | 13·7 | 1·2 | 14·1 | 1·3 |
| Arachidic acid (20:0) | 0·14 | 0·03 | 0·13 | 0·03 | 0·13 | 0·03 | 0·16 | 0·05 | 0·14 | 0·05 | 0·13 | 0·03 | 0·13 | 0·03 | 0·12 | 0·03 | 0·13 | 0·04 |
| Behenic acid (22:0) | 0·25 | 0·06 | 0·22 | 0·07 | 0·23 | 0·06 | 0·27 | 0·10 | 0·29 | 0·14 | 0·21 | 0·07 | 0·24 | 0·06 | 0·22 | 0·05 | 0·24 | 0·08 |
| Tricosanoic acid (23:0) | 0·13 | 0·05 | 0·11 | 0·04 | 0·10 | 0·03 | 0·13 | 0·07 | 0·13 | 0·07 | 0·09 | 0·05 | 0·11 | 0·03 | 0·10 | 0·04 | 0·11 | 0·05 |
| Lignoceric acid (24:0) | 0·26 | 0·06 | 0·23 | 0·06 | 0·23 | 0·05 | 0·24 | 0·08 | 0·28 | 0·11 | 0·21 | 0·06 | 0·22 | 0·05 | 0·21 | 0·04 | 0·23 | 0·07 |

**Appendix Table 2: Sensitivity analyses for the associations between each saturated fatty acid, fatty acid groups and product-to-precursor ratios and type 2 diabetes: EPIC-InterAct Study**

| Saturated fatty acid | | | | | |
|---|---|---|---|---|---|
| | **Model 2** | **Model 2A** | **Model 2B** | **Model 2C** | **Model 2D** |
| Myristic (14:0) | 1·15 (1·09, 1·22) | 1·16 (1·10, 1·23) | 1·14 (1·07, 1·21) | 1·16 (1·10, 1·22) | 1·15 (1·09· 1·22) |
| Pentadecanoic (15:0) | 0·79 (0·73, 0·85) | 0·80 (0·73, 0·86) | 0·81 (0·75, 0·87) | 0·79 (0·73, 0·86) | 0·79 (0·73, 0·85) |
| Palmitic (16:0) | 1·26 (1·15, 1·37) | 1·26 (1·15, 1·37) | 1·22 (1·12, 1·34) | 1·26 (1·16, 1·37) | 1·26 (1·15, 1·37) |
| Heptadecanoic (17:0) | 0·67 (0·63, 0·71) | 0·67 (0·63, 0·70) | 0·71 (0·67, 0·75) | 0·67 (0·63, 0·71) | 0·67 (0·63, 0·71) |
| Stearic (18:0) | 1·06 (1·00, 1·13) | 1·06 (1·00, 1·13) | 1·05 (0·99, 1·11) | 1·06 (1·00, 1·12) | 1·06 (1·00, 1·13) |
| Arachidic (20:0) | 0·74 (0·65, 0·84) | 0·74 (0·64, 0·84) | 0·74 (0·66, 0·84) | 0·74 (0·65, 0·84) | 0·74 (0·65, 0·84) |
| Behenic (22:0) | 0·79 (0·69, 0·90) | 0·78 (0·68, 0·90) | 0·82 (0·72, 0·93) | 0·79 (0·69, 0·90) | 0·79 (0·69, 0·90) |
| Tricosanoic (23:0) | 0·81 (0·72, 0·92) | 0·81 (0·72, 0·92) | 0·82 (0·72, 0·93) | 0·82 (0·72, 0·92) | 0·81 (0·72, 0·92) |
| Lignoceric (24:0) | 0·72 (0·61, 0·85) | 0·72 (0·61, 0·86) | 0·75 (0·64, 0·88) | 0·72 (0·61, 0·86) | 0·72 (0·61, 0·85) |
| SFA group 1 | 1·43 (1·29, 1·58) | 1·42 (1·28, 1·58) | 1·37 (1·24, 1·53) | 1·43 (1·31, 1·55) | 1·43 (1·29, 1·58) |
| SFA group 2 | 0·70 (0·66, 0·74) | 0·70 (0·65, 0·74) | 0·73 (0·69, 0·77) | 0·70 (0·66, 0·74) | 0·70 (0·66, 0·74) |
| SFA group 3 | 0·70 (0·59, 0·84) | 0·70 (0·58, 0·84) | 0·74 (0·62, 0·87) | 0·70 (0·58, 0·84) | 0·70 (0·59, 0·84) |
| 16:1n7 to 16:0 ratio | 1·22 (1·13, 1·32) | 1·23 (1·14, 1·33) | 1·17 (1·10, 1·25) | 1·22 (1·13, 1·32) | 1·22 (1·13, 1·32) |
| 18:1n9 to 18:0 ratio | 0·99 (0·93, 1·05) | 0·99 (0·93, 1·05) | 0·98 (0·93, 1·03) | 0·99 (0·94, 1·05) | 0·99 (0·93, 1·05) |

Pooled hazard ratios and 95% confidence intervals are per 1 SD difference in plasma phospholipid SFA (12,132 T2D cases and 15,919 sub-cohort, including 755 T2D cases in sub-cohort).

Model 2 is the 2 is the model adjusted for age as underlying timescale, centre, sex, physical activity (inactive, moderately inactive, moderately active, active), smoking (never, former, current), education (none, primary school completed, technical or professional school, secondary school, longer education), total energy intake (continuous, kcal/day), alcohol intake (yes/no), BMI (continuous, $kg/m^2$).
*Models 2A to2C show the HR for sensitivity analyses:*
Model A: additionally adjusted for carbohydrates intake (continuous, g/d)
Model B: additionally adjusted for waist circumference (continuous, cm);
Model C: additionally adjusted for prevalent cardiovascular disease (myocardial infarction or stroke) and prevalent cancer (all yes/no);
Model D: with exclusion of 723 individuals who were likely to be energy mis-reporters.

SFA group 1: sum of 14:0, 16:0 and 18:0
SFA group 2: sum of 15:0 and 17:0
SFA group 3: sum of 20:0, 22:0, 23:0 and 24:0

**Appendix Table 3: Pooled hazard ratio (HR) and 95% CI for associations between quintiles of each saturated fatty acid, fatty acid groups and product-to-precursor ratios and type 2 diabetes: EPIC-InterAct Study**

| | Q2 vs Q1 | | | Q3 vs Q1 | | | Q4 vs Q1 | | | Q5 vs Q1 | | | Per quintile | | | *p* value for |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HR | Lower | Upper | HR | Lower | Upper | HR | Lower | Upper | HR | Lower | Upper | HR | Lower | Upper | trend |
| Model 1 | | | | | | | | | | | | | | | | |
| Myristic acid (14:0) | 1·30 | 1·16 | 1·45 | 1·53 | 1·38 | 1·69 | 1·74 | 1·53 | 1·99 | 1·64 | 1·47 | 1·83 | 1·14 | 1·11 | 1·18 | <0·0001 |
| Pentadecanoic acid (15:0) | 0·86 | 0·79 | 0·93 | 0·74 | 0·68 | 0·81 | 0·62 | 0·54 | 0·71 | 0·46 | 0·37 | 0·56 | 0·82 | 0·78 | 0·86 | <0·0001 |
| Palmitic acid (16:0) | 1·19 | 1·05 | 1·34 | 1·39 | 1·16 | 1·66 | 1·58 | 1·26 | 1·97 | 1·75 | 1·35 | 2·27 | 1·16 | 1·09 | 1·23 | <0·0001 |
| Heptadecanoic acid (17:0) | 0·65 | 0·57 | 0·75 | 0·41 | 0·33 | 0·51 | 0·30 | 0·24 | 0·37 | 0·24 | 0·20 | 0·30 | 0·68 | 0·64 | 0·71 | <0·0001 |
| Stearic acid (18:0) | 1·04 | 0·96 | 1·14 | 1·15 | 0·99 | 1·33 | 1·47 | 1·23 | 1·75 | 1·75 | 1·46 | 2·09 | 1·16 | 1·12 | 1·21 | <0·0001 |
| Arachidic acid (20:0) | 0·65 | 0·56 | 0·76 | 0·55 | 0·47 | 0·64 | 0·48 | 0·40 | 0·56 | 0·42 | 0·33 | 0·53 | 0·80 | 0·76 | 0·85 | <0·0001 |
| Behenic acid (22:0) | 0·81 | 0·73 | 0·90 | 0·69 | 0·58 | 0·82 | 0·62 | 0·50 | 0·76 | 0·59 | 0·46 | 0·77 | 0·87 | 0·81 | 0·93 | <0·0001 |
| Tricosanoic acid (23:0) | 0·82 | 0·67 | 1·01 | 0·66 | 0·54 | 0·82 | 0·67 | 0·53 | 0·84 | 0·56 | 0·48 | 0·66 | 0·86 | 0·82 | 0·90 | <0·0001 |
| Lignoceric acid (24:0) | 0·63 | 0·55 | 0·72 | 0·56 | 0·46 | 0·68 | 0·49 | 0·41 | 0·59 | 0·42 | 0·34 | 0·51 | 0·80 | 0·75 | 0·85 | <0·0001 |
| Cis-16:1 to cis-16:0 ratio | 1·46 | 1·32 | 1·61 | 1·85 | 1·67 | 2·05 | 2·50 | 2·25 | 2·78 | 3·37 | 2·82 | 4·03 | 1·35 | 1·30 | 1·41 | <0·0001 |
| Cis-18:1n9c to cis-18:0 ratio | 0·85 | 0·78 | 0·92 | 0·83 | 0·74 | 0·93 | 0·73 | 0·63 | 0·83 | 0·68 | 0·55 | 0·86 | 0·91 | 0·87 | 0·96 | <0·0001 |
| SFA group 1 | 1·75 | 1·44 | 2·13 | 2·66 | 2·07 | 3·41 | 4·07 | 2·99 | 5·54 | 5·63 | 4·24 | 7·47 | 1·52 | 1·43 | 1·62 | <0·0001 |
| SFA group 2 | 0·70 | 0·62 | 0·79 | 0·50 | 0·44 | 0·56 | 0·37 | 0·31 | 0·44 | 0·27 | 0·23 | 0·32 | 0·72 | 0·68 | 0·75 | <0·0001 |
| SFA group 3 | 0·71 | 0·61 | 0·81 | 0·52 | 0·43 | 0·64 | 0·48 | 0·39 | 0·59 | 0·45 | 0·37 | 0·55 | 0·80 | 0·75 | 0·85 | <0·0001 |
| Model 2 | | | | | | | | | | | | | | | | |
| Myristic acid (14:0) | 1·22 | 1·07 | 1·38 | 1·35 | 1·18 | 1·54 | 1·51 | 1·29 | 1·77 | 1·48 | 1·26 | 1·73 | 1·12 | 1·08 | 1·17 | <0·0001 |
| Pentadecanoic acid (15:0) | 0·91 | 0·79 | 1·04 | 0·77 | 0·69 | 0·86 | 0·67 | 0·58 | 0·77 | 0·53 | 0·44 | 0·64 | 0·85 | 0·82 | 0·89 | <0·0001 |
| Palmitic acid (16:0) | 1·21 | 1·03 | 1·43 | 1·50 | 1·21 | 1·85 | 1·68 | 1·30 | 2·16 | 1·91 | 1·43 | 2·56 | 1·19 | 1·11 | 1·27 | <0·0001 |
| Heptadecanoic acid (17:0) | 0·74 | 0·68 | 0·82 | 0·51 | 0·45 | 0·57 | 0·39 | 0·34 | 0·46 | 0·34 | 0·28 | 0·42 | 0·74 | 0·71 | 0·77 | <0·0001 |
| Stearic acid (18:0) | 0·96 | 0·85 | 1·09 | 0·95 | 0·83 | 1·08 | 1·15 | 0·99 | 1·33 | 1·12 | 0·95 | 1·33 | 1·04 | 1·01 | 1·08 | 0·009 |
| Arachidic acid (20:0) | 0·71 | 0·60 | 0·86 | 0·60 | 0·48 | 0·73 | 0·50 | 0·41 | 0·62 | 0·48 | 0·35 | 0·65 | 0·82 | 0·76 | 0·88 | <0·0001 |
| Behenic acid (22:0) | 0·78 | 0·69 | 0·87 | 0·69 | 0·58 | 0·82 | 0·59 | 0·47 | 0·72 | 0·56 | 0·43 | 0·74 | 0·85 | 0·80 | 0·91 | <0·0001 |
| Tricosanoic acid (23:0) | 0·75 | 0·64 | 0·88 | 0·65 | 0·52 | 0·82 | 0·66 | 0·53 | 0·83 | 0·54 | 0·43 | 0·67 | 0·86 | 0·81 | 0·91 | <0·0001 |
| Lignoceric acid (24:0) | 0·64 | 0·54 | 0·76 | 0·60 | 0·47 | 0·76 | 0·56 | 0·47 | 0·67 | 0·47 | 0·37 | 0·60 | 0·83 | 0·78 | 0·89 | <0·0001 |
| Cis-16:1 to cis-16:0 ratio | 1·41 | 1·26 | 1·57 | 1·66 | 1·48 | 1·86 | 2·06 | 1·80 | 2·36 | 2·35 | 2·02 | 2·74 | 1·24 | 1·19 | 1·29 | <0·0001 |
| Cis-18:1n9c to cis-18:0 ratio | 0·94 | 0·83 | 1·05 | 0·92 | 0·83 | 1·02 | 0·89 | 0·78 | 1·02 | 0·92 | 0·77 | 1·09 | 0·98 | 0·94 | 1·02 | 0·333 |
| SFA group 1 | 1·50 | 1·28 | 1·76 | 2·00 | 1·62 | 2·48 | 2·94 | 2·26 | 3·84 | 3·66 | 2·75 | 4·87 | 1·38 | 1·29 | 1·48 | <0·0001 |
| SFA group 2 | 0·75 | 0·68 | 0·82 | 0·57 | 0·52 | 0·63 | 0·44 | 0·38 | 0·51 | 0·37 | 0·32 | 0·42 | 0·77 | 0·74 | 0·79 | <0·0001 |
| SFA group 3 | 0·73 | 0·60 | 0·89 | 0·54 | 0·43 | 0·69 | 0·51 | 0·40 | 0·65 | 0·47 | 0·35 | 0·63 | 0·81 | 0·75 | 0·87 | <0·0001 |

Hazard Ratios (HRs) compare quintiles (Q) Q2-Q5 with Q1, where Q1-Q5 were defined by values which divide the distribution of the fatty acid in the overall sub-cohort into fifths.

Model 1: Age as underlying time variable, and adjusted for centre, sex, physical activity (inactive, moderately inactive, moderately active, active), smoking (never, former, current), education level (none, primary school completed, technical or professional school, secondary school, longer education)..

Model 2: Adjusted as in model 1 + total energy intake (continuous, kcal/day), alcohol (yes/no), BMI (continuous, kg/m$^2$).

SFA group 1: sum of 14:0, 16:0 and 18:0

SFA group 2: sum of 15:0 and 17:0

SFA group 3: sum of 20:0, 22:0, 23:0 and 24:0