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 Childhood Energy Intake Is Associated with Nonalcoholic Fatty Liver Disease in Adolescents1–3

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Abstract

Background: Greater adiposity is an important risk factor for nonalcoholic fatty liver disease (NAFLD). Thus, it is likely that dietary intake is involved in the development of the disease. Prospective studies assessing the relation between childhood dietary intake and risk of NAFLD are lacking.

Objective: This study was designed to explore associations between energy, carbohydrate, sugar, starch, protein, monounsaturated fat, polyunsaturated fat, saturated fat, and total fat intake by youth at ages 3, 7, and 13 y and subsequent (mean age: 17.8 y) ultrasound scan (USS)–measured liver fat and stiffness and serum alanine aminotransferase, aspartate aminotransferase, and γ-glutamyltransferase. We assessed whether observed associations were mediated through fat mass at the time of outcome assessment.

Methods: Participants were from the Avon Longitudinal Study of Parents and Children. Trajectories of energy and macronutrient intake from ages 3–13 y were obtained with linear-spline multilevel models. Linear and logistic regression models examined whether energy intake and absolute and energy-adjusted macronutrient intake at ages 3, 7, and 13 y were associated with liver outcomes.

Results: Energy intake at all ages was positively associated with liver outcomes; for example, the odds of having a USS-measured liver fat per 100 kcal increase in energy intake at age 3 y were 1.79 (95% CI: 1.14, 2.79). Associations between absolute macronutrient intake and liver outcomes were inconsistent and attenuated to the null after adjustment for total energy intake. The majority of associations attenuated to the null after adjustment for fat mass at the time liver outcomes were assessed.

Conclusion: Higher childhood and early adolescent energy intake is associated with greater NAFLD risk, and the macronutrients from which energy intake is derived are less important. These associations appear to be mediated, at least in part, by fat mass at the time of outcome assessment. J Nutr 2015;145:983–9.

Keywords: diet, energy intake, childhood, NAFLD, fatty liver

Introduction

Nonalcoholic fatty liver disease (NAFLD)9 is a common cause of chronic liver disease in children and adolescents (1), and is associated with fibrosis, insulin resistance, and dyslipidemia, independently of total body fat (2). Because greater adiposity is a key risk factor for NAFLD (3), it is likely that dietary intake is involved in its development. Greater overall energy intake may increase total body fatness, elevating the risk of fat infiltration into the liver by increasing FFA influx from either the diet or via adipose tissue to the liver, with a consequent increase in insulin resistance.

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2 Author disclosures: LD Howe, A Fraser, C Macdonald-Wallis, and DA Lawlor work in a unit that receives funding from the UK Medical Research Council, and EL Anderson’s studentship is funded by that grant. LD Howe, A Fraser, and C Macdonald-Wallis are funded by UK Medical Research Council postdoctoral research fellowships (MR/M009335/1, G1002375, and MR/J001192/1, respectively).

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3 Supplemental Methods, Supplemental Figure 1, and Supplemental Tables 1–13 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.
9 Abbreviations used: ALSPAC, Avon Longitudinal Study of Parents and Children; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; NAFLD, nonalcoholic fatty liver disease; USS, ultrasound scan.

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were assessed. As a secondary objective, we explored whether
age 17.8 y, and to determine whether any observed associations
overnight, and those attending after lunch, for a minimum of 6 h.
Liver outcomes
would indicate hepatic disease, or were taking medication known to influence
attending the 17–18 y follow-up (Liver USS substudy (2)). No participants
were classified as uncertain. Levels of agreement in
general agreement between the 4 sonographers was 98% or greater,
sonographers using a Siemens Acuson S2000 USS system. Echogenicity was
previously (2). Briefly, upper abdominal USS was completed by 1 of 4 trained
prospective birth cohort from southwest England (14, 15). The study website
The Avon Longitudinal Study of Parents and Children (ALSPAC) is a
prospective birth cohort from southwest England (14, 15). The study website
(www.bris.ac.uk/alspac/researchers/data-access/data-dictionary) (16).
Details of USS assessment in the ALSPAC have been published previ-
ously (2). Briefly, upper abdominal USS was completed by 1 of 4 trained

Methods
Study population
The Avon Longitudinal Study of Parents and Children (ALSPAC) is a
prospective birth cohort from southwest England (14, 15). The study website
contains details of all data available through a fully searchable data dictionary
Ethical approval for the study was obtained from the ALSPAC Law and
Ethics Committee and local research ethics committees. A total of 5081
participants attended the 17–18 y follow-up assessment at mean age 17.8 y.
Of these, n = 3188 (62.7%) had data available for ALT, AST, and/or GGT. A
liver USS substudy (n = 1887) was undertaken on a subgroup of participants
inclusion in analyses of USS outcomes, participants had to have valid
participants with blood-based liver data who were classified as hazard-
ous drinkers at both ages were excluded from this study. To be eligible for
inclusion in analyses of USS outcomes, participants had to have valid
data for USS-measured liver fat or liver stiffness and at least one measure
of dietary intake between ages 3 and 13 y (n = 1786). For analyses
of blood-based liver outcomes, participants were eligible for inclusion if
they had data for ALT, AST, or GGT and at least one measure of dietary
intake between ages 3 and 13 y (n = 3059).

Liver outcomes
Participants attending the morning clinic were instructed to fast
overnight, and those attending after lunch, for a minimum of 6 h.
Details of USS assessment in the ALSPAC have been published previ-
ously (2). Briefly, upper abdominal USS was completed by 1 of 4 trained
sonographers using a Siemens Acuson S2000 USS system. Echogenicity was
assessed and recorded as present, absent, or uncertain (17). Only 2 scans
(0.1%) in total were classified as uncertain. Levels of agreement in
identifying echogenicity between the 4 sonographers was 98% or greater,
both immediately after training and at 6 mo intervals throughout data
collection. Acoustic radiation force impulse imaging (acoustic radiation
force impulse measured as shear velocity in meters per second) of the right
lobe of the liver was used to measure liver stiffness (our indicator of liver
fibrosis) with the use of standard protocols (18).

Fasting blood samples were immediately centrifuged and frozen at
−80°C. Measurements were assayed within 3–9 mo after samples were
taken, with no previous freeze-thaw cycles. All assays were completed in
the same laboratory at the University of Glasgow. ALT, GGT, and AST
were measured by Roche Cobas automated analyzers (Roche Diagnos-
tics) with the use of enzymatic methods. All inter- and intra-CVs for these
blood-based assays were <5%.

Dietary intake from ages 3–13 y
Three-day food diaries were mailed to parents when study children were
aged 3.5, 5, 7, 10, and 13 y. Parents recorded their child’s diet until the
child reached age 10 y. At age 10 y, children recorded their own diet with
help from their parents. Diaries were requested for 2 weekdays and
1 weekend day. FFQs were mailed to parents when study children were
aged 3, 4, 7, and 9 y. Full details of dietary intake assessment have been
published previously (19) and are in Supplemental Methods.

Covariables
Potential confounders considered included the following: maternal age
at delivery, parity, education, household social class, and prepregnancy
BMI; and participant’s age, sex, pubertal status, and physical activity
levels. Total fat mass and height at the time of outcome assessment were
considered as potential mediators. A full description of all measures is in
Supplemental Methods.

Eligibility criteria
Participants’ alcohol consumption was assessed at mean ages 16.7 y and
17.8 y with the use of the Alcohol Use Disorders Identification Test (20).
Thirteen participants who completed the USS examination and 29
participants with blood-based liver data who were classified as hazard-
ous drinkers at both ages were excluded from this study. To be eligible for
inclusion in analyses of USS outcomes, participants had to have valid
data for USS-measured liver fat or liver stiffness and at least one measure
of dietary intake between ages 3 and 13 y of age (n = 1786). For analyses
of blood-based liver outcomes, participants were eligible for inclusion if
they had data for ALT, AST, or GGT and at least one measure of dietary
intake between ages 3 and 13 y (n = 3059).

Statistical analysis
Modeling dietary intake trajectories. As described in a previous
publication (21), individual trajectories of energy, total carbohydrate,
sugar, starch, total fat, monounsaturated fat, polyunsaturated fat,
saturated fat and total protein intake from ages 3–13 y were estimated
with the use of linear-spline multilevel models fitted in MLwiN v2.28
with the use of the Stata (StataCorp) command ‘‘runmlwin’’ (22, 23).
They were estimated for participants with at least 1 available food
diary or FFQ, under a missing-at-random assumption. Full model details
are available on request. Trajectories were used to predict the dietary
intake of each participant at ages 3, 7, and 13 y. Energy-adjusted
macronutrient intake was calculated by regressing predicted macronu-
trient intake on predicted energy intake at each age and taking the
residuals from this regression. When assessing associations between
energy-adjusted macronutrient intake and liver outcomes, we further
adjusted for energy intake in all regression models (24).

Associations between dietary intake and liver outcomes. Regres-
sion analyses were conducted in Stata v12.0. All continuous outcomes
were positively skewed; their ln values were used in regression analyses
to ensure residuals were normally distributed. Predicted dietary intake at
ages 3, 7, and 13 y were related to continuous outcomes with the use of
linear regression, and to the binary USS-measured liver fat variable with
the use of logistic regression. Coefficients from regression models
including logged variables were back-transformed and are interpreted as
a percentage change.

Associations were examined in the following models: 1) unadjusted,
2) adjusted for potential confounders, and 3) additionally adjusted for
DXA-determined fat mass, height, and height squared at mean age
17.8 y to determine whether this attenuated any observed associations.
Likelihood ratio tests were used to check for gender interactions in all
regression analyses.

984 Anderson et al.
Dealing with missing data and additional analyses. One-third of eligible participants with USS data (594 of 1786), and 27% of eligible participants with blood-based liver outcomes (821 of 3059) had missing data for potential confounders and/or outcomes. Missing data for any one characteristic varied from 0.03–13% (Supplemental Tables 1 and 2). To minimize selection bias and increase efficiency, multivariate multiple imputation was used to impute missing data for potential confounders and outcomes for eligible participants. Full details of this procedure are in Supplemental Methods. Details of a series of sensitivity analyses conducted to verify model assumptions, test the robustness of our findings, and explore whether associations between dietary intake at age 13 y and outcomes might have been confounded by physical activity or pubertal stage are also provided in Supplemental Methods.

Results
The prevalence of USS-measured fatty liver was 2.5% in males and females. An elevated ALT (>40 U/L) was noted in 4.3% of males (63 of 1474) and 1.6% of females (26 of 1585). Variable distributions were similar among imputed and observed datasets (Supplemental Tables 1 and 2).

We present results with sexes combined; sex was adjusted for in all regression models (P values for interaction with sex ≥0.1). Results of the confounder-adjusted model (model 2) are presented in Tables 1–6, with results from other models provided in Supplemental Tables 3–6.

Associations between energy intake at ages 3, 7, and 13 y and liver outcomes. Energy intake at age 3 y was positively associated with USS-measured liver fat, ALT, and GGT. Energy intake at age 7 y was positively associated with all liver outcomes except AST. Energy intake at 13 y was positively associated with ALT, AST, and GGT (Table 1).

Associations between absolute and energy-adjusted macronutrient intake at ages 3, 7, and 13 y and liver outcomes. Associations between absolute and energy-adjusted carbohydrate, sugar, starch, protein, and fat intake at ages 3, 7, and 13 y and USS- and blood- (n = 3059) based liver outcomes are presented in Tables 2–6, respectively. Associations between saturated, monounsaturated and polyunsaturated fat and liver outcomes are in the Supplemental Methods, because they were much the same as those for total fat intake. Although we found evidence of several positive associations between absolute macronutrient intake at 3, 7, and 13 y and each of the USS- and blood-based liver outcomes, there were no consistent patterns, with the exception that energy intake and all absolute macronutrient intake except sugar at ages 3, 7, and 13 y were consistently positively associated with ALT.

After adjusting for energy intake, the majority of the observed positive associations between absolute macronutrient intake and outcomes attenuated to the null (including the consistent positive associations between all macronutrient intake at ages 3, 7, and 13 y and ALT). There were a few exceptions: carbohydrate (Table 2), sugar (Table 3), and fat (Table 6) intake at ages 3, 7, and 13 y all remained positively associated with GGT; carbohydrate and fat intake at age 13 y remained positively associated with AST; and starch (Table 4) and protein (Table 5) intake at age 13 y remained positively associated with ALT.

Mediation by fat mass at the time of liver outcome assessment. After additional adjustment for fat mass at the time liver outcomes were assessed, the majority (49 of 54) of associations between energy intake and absolute macronutrient intake and the USS- and blood-based liver outcomes attenuated toward the null, although some (21) positive associations remained. Most associations between energy-adjusted macronutrient intake and the USS- and blood-based liver outcomes also attenuated toward the null, except that associations between energy-adjusted macronutrients and GGT remained largely unchanged (model 3, Supplemental Tables 3–6).

Sensitivity analyses. Results were similar when restricting to plausible reporters of dietary intake (Supplemental Table 7) and when restricting to participants with 1 complete data on all variables (Supplemental Table 8), 2) at least 2 measures of dietary intake from 3–13 y (Supplemental Table 9), and 3) a measure of dietary intake in each linear-spline period (Supplemental Table 10). Results were similar if a bivariate multilevel model was used instead of dietary intake residuals from a univariate multilevel model in regression models (Supplemental Table 11), except that CIs were substantially wider. This is expected, given that the bivariate models account for the individual-level dietary intake residuals’ being estimated and not known. Results were also similar after additional adjustment for Alcohol Use Disorders Identification Test scores (Supplemental Table 12), and pubertal status and physical activity at age 13 y (Supplemental Table 13).

Discussion
In this study we assessed associations between energy intakes and absolute and energy-adjusted total fat, mono- and polyunsaturated fat, saturated fat, total carbohydrate, sugar, starch,

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Associations between energy intake at ages 3, 7, and 13 y and USS- and blood-based liver outcomes at mean age 17.8 y in the imputed data1</th>
</tr>
</thead>
<tbody>
<tr>
<td>USS-measured liver fat</td>
<td>Value</td>
</tr>
<tr>
<td>3 y</td>
<td>1.79 (1.14, 2.79)</td>
</tr>
<tr>
<td>7 y</td>
<td>1.30 (1.06, 1.60)</td>
</tr>
<tr>
<td>13 y</td>
<td>1.12 (0.84, 1.49)</td>
</tr>
<tr>
<td>USS-measured liver stiffness</td>
<td></td>
</tr>
<tr>
<td>3 y</td>
<td>1 (0, 3)</td>
</tr>
<tr>
<td>7 y</td>
<td>1 (0, 1)</td>
</tr>
<tr>
<td>13 y</td>
<td>0 (−1, 1)</td>
</tr>
</tbody>
</table>

1 Values are ORs (95% CIs) for liver fat and % changes (95% CIs) for liver stiffness, ALT, AST, and GGT. n = 1786 for USS-measured liver outcomes at all ages. n = 3059 for blood-based liver outcomes at all ages. Coefficients are per 100 kcal increase in energy intake at ages 3, 7, and 13 y. Adjusted for sex, age at outcome assessment, maternal prepregnancy BMI, maternal age, social class, maternal education, and parity. ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; USS, ultrasound scan.
and total protein intake at ages 3, 7, and 13 y and measures of liver health in late adolescence. Because we excluded participants with hazardous alcohol consumption in the 12 mo before liver assessment, and results did not change with further adjustment for alcohol consumption, and because no participants had known hepatic disorders or were on medications that would affect liver function, the associations observed are likely to reflect those of childhood diet with adolescent NAFLD.

Energy intake in childhood and early adolescence was consistently positively associated with markers of NAFLD, but was not associated with liver stiffness. Associations between absolute macronutrient intakes and liver outcomes were inconsistent. There was no evidence that a particular macronutrient was most strongly associated with liver outcomes, or that intake at a particular age was most strongly associated with liver outcomes. However, all absolute macronutrient intake, as well as energy intake, at ages 3, 7, and 13 y were consistently positively associated with ALT. After adjusting for energy intake, the majority of the observed positive associations between absolute macronutrient intake and ALT (and other liver outcomes with positive associations) attenuated to the null. These results suggest that higher energy intake in childhood and early adolescence is associated with greater NAFLD risk, and that the relative proportions of macronutrients from which energy intake is derived are less important. We found some evidence to suggest that fat mass at the time of liver outcome assessment in part mediates the association between childhood dietary intake and NAFLD, with most associations between energy and absolute macronutrient intakes and liver outcomes attenuating toward the null upon adjustment for fat mass.

In a previous study with the use of data from the same cohort, we found that the proportion of participants classified as under- or over-reporters of energy intake increased from 15% at age 3 y to 63% at age 13 y (21). This is perhaps due to the fact that measurement error in dietary intake increases strongly with age, as children begin completing food diaries themselves and eating away from home more often. We attempted to account for this potential source of bias when modeling the trajectories of dietary intake by adjusting for a plausibility of reporting ratio, which has been described in detail elsewhere (21). We also checked results after restricting analyses to participants classified as plausible reporters at ages 3, 7, and 13 y, and they were similar to the main results. This provides some support that implausible reporting of dietary intake does not substantially bias our main results.

**Comparison with findings from other studies.** We found energy intake in childhood and adolescence to be consistently positively associated with markers of NAFLD, which contradicts findings from studies reporting no associations between energy intake and USS-identified NAFLD (9, 10), ALT, and AST (11). We found absolute fat intake to be positively associated with ALT; however, this was not associated with any other liver outcomes.

**TABLE 2** Associations between absolute and energy-adjusted carbohydrate intake at ages 3, 7, and 13 y and USS- and blood-based liver outcomes at mean age 17.8 y in the imputed data.

<table>
<thead>
<tr>
<th>USS-measured</th>
<th>Absolute carbohydrate intake</th>
<th>Energy-adjusted carbohydrate intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver fat</td>
<td>Value</td>
<td>P</td>
</tr>
<tr>
<td>3 y</td>
<td>1.38 (1.06, 1.80)</td>
<td>0.02</td>
</tr>
<tr>
<td>7 y</td>
<td>1.21 (1.04, 1.41)</td>
<td>0.01</td>
</tr>
<tr>
<td>13 y</td>
<td>0.96 (0.82, 1.13)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

**TABLE 3** Associations between absolute and energy-adjusted sugar intake at ages 3, 7, and 13 y and USS- and blood-based liver outcomes at mean age 17.8 y in the imputed data.

<table>
<thead>
<tr>
<th>USS-measured</th>
<th>Absolute sugar intake</th>
<th>Energy-adjusted sugar intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver fat</td>
<td>Value</td>
<td>P</td>
</tr>
<tr>
<td>3 y</td>
<td>1.44 (1.02, 2.04)</td>
<td>0.04</td>
</tr>
<tr>
<td>7 y</td>
<td>1.23 (0.99, 1.53)</td>
<td>0.06</td>
</tr>
<tr>
<td>13 y</td>
<td>0.96 (0.79, 1.17)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

1 Values are ORs (95% CIs) for liver fat and % changes (95% CIs) for liver stiffness, ALT, AST, and GGT. n = 1786 for USS-measured liver outcomes at all ages. n = 3059 for blood-based liver outcomes at all ages. Coefficients are per 100 kcal increase in energy intake at ages 3, 7, and 13 y. Adjusted for sex, age at outcome assessment, maternal prepregnancy BMI, maternal age, social class, maternal education, and parity. ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; USS, ultrasound scan.
outcomes and the associations attenuated to the null after adjustment for energy intake. Consistent with this finding, 2 cross-sectional studies found absolute fat intake to be similar in children with absent, mild, and moderate to severe NAFLD (9, 10), 1 study found no difference in percentage fat intake by ALT status (11), and another study reported no significant differences between children with steatosis compared with steatohepatitis for fraction of energy from fat (12). Published results for subgroups of the prevalence for the more moderate to severe end of the disease spectrum and consequently our results may be underestimated. Important, recently a meta-analysis including 49 different studies to date have observed associations between protein intake (absolute or percentage) and liver outcomes. Further large prospective studies are required to clarify associations between macronutrient intake and risk of NAFLD.

 Whereas energy intake at all ages was positively associated with most markers of NAFLD, this was not the case for liver stiffness. This could indicate that childhood energy intake affects the likelihood of liver fat accumulation but not liver fibrosis, or that our measure of liver stiffness is not variable enough for us to clearly detect associations in this study. Although we are not aware of other studies with the detailed data that we have to explore this, it is necessary to assess these associations in additional large prospective studies to see if they confirm our findings.

**Strengths and limitations.** Although power for the binary outcome of USS-measured liver fat was limited because of the small number of cases, we looked at a range of related outcomes including ALT. The USS has a reported sensitivity of 85–90% and specificity of 70–85% for detecting liver fat of at least 10% but lower sensitivity and specificity for lower concentrations of fat (9). Thus, our prevalence estimate most likely reflects the prevalence for the more moderate to severe end of the disease spectrum and consequently our results may be underestimated.

**TABLE 4** Associations between absolute and energy-adjusted starch intake at ages 3, 7, and 13 y and USS- and blood-based liver outcomes at mean age 17.8 y in the imputed data

<table>
<thead>
<tr>
<th>USS-measured</th>
<th>Absolute starch intake</th>
<th>Energy-adjusted starch intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver fat</td>
<td>Value</td>
<td>P</td>
</tr>
<tr>
<td>3 y</td>
<td>1.24 (0.88, 1.8)</td>
<td>0.25</td>
</tr>
<tr>
<td>7 y</td>
<td>1.14 (0.90, 1.43)</td>
<td>0.28</td>
</tr>
<tr>
<td>13 y</td>
<td>1.06 (0.79, 1.43)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

**TABLE 5** Associations between absolute and energy-adjusted protein intake at ages 3, 7, and 13 y and USS- and blood-based liver outcomes at mean age 17.8 y in the imputed data

<table>
<thead>
<tr>
<th>USS-measured</th>
<th>Absolute protein intake</th>
<th>Energy-adjusted protein intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver fat</td>
<td>Value</td>
<td>P</td>
</tr>
<tr>
<td>3 y</td>
<td>2.60 (1.18, 5.73)</td>
<td>0.02</td>
</tr>
<tr>
<td>7 y</td>
<td>1.75 (1.12, 2.75)</td>
<td>0.02</td>
</tr>
<tr>
<td>13 y</td>
<td>1.68 (1.02, 2.77)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

1 Values are ORs (95% CIs) for liver fat and % changes (95% CIs) for liver stiffness, ALT, AST, and GGT. n = 1796 for USS-measured liver outcomes at all ages. n = 3059 for blood-based liver outcomes at all ages. Coefficients are per 100 kcal increase in energy intake at ages 3, 7, and 13 y. Adjusted for sex, age at outcome assessment, maternal prepregnancy BMI, maternal age, social class, maternal education, and parity. ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; USS, ultrasound scan.
TABLE 6  Associations between absolute and energy-adjusted fat intake at ages 3, 7, and 13 y and USS- and blood-based liver outcomes at mean age 17.8 y in the imputed data

<table>
<thead>
<tr>
<th></th>
<th>Absolute fat intake</th>
<th>Energy-adjusted fat intake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>Value (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>USS-measured</td>
<td></td>
<td></td>
</tr>
<tr>
<td>liver fat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 y</td>
<td>1.05 (0.96, 1.15)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>0.55 (0.15, 1.99)</td>
<td>0.36</td>
</tr>
<tr>
<td>7 y</td>
<td>1.02 (0.98, 1.07)</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>0.60 (0.27, 1.35)</td>
<td>0.22</td>
</tr>
<tr>
<td>13 y</td>
<td>1.01 (0.95, 1.06)</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>0.93 (0.43, 1.99)</td>
<td>0.85</td>
</tr>
<tr>
<td>USS-measured</td>
<td></td>
<td></td>
</tr>
<tr>
<td>liver stiffness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 y</td>
<td>0 (0, 0)</td>
<td>0.44</td>
</tr>
<tr>
<td></td>
<td>0 (−3, 4)</td>
<td>0.85</td>
</tr>
<tr>
<td>7 y</td>
<td>0 (0, 0)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>0 (−2, 2)</td>
<td>0.97</td>
</tr>
<tr>
<td>13 y</td>
<td>0 (0, 0)</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>−1 (−3, 1)</td>
<td>0.29</td>
</tr>
<tr>
<td>ALT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 y</td>
<td>1 (0, 1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>0 (−3, 4)</td>
<td>0.85</td>
</tr>
<tr>
<td>7 y</td>
<td>0 (0, 1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>0 (−2, 2)</td>
<td>0.97</td>
</tr>
<tr>
<td>13 y</td>
<td>0 (0, 1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>−1 (−3, 1)</td>
<td>0.29</td>
</tr>
<tr>
<td>AST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 y</td>
<td>0 (0, 0)</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>−1 (−5, 3)</td>
<td>0.54</td>
</tr>
<tr>
<td>7 y</td>
<td>0 (0, 0)</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>−2 (−5, 1)</td>
<td>0.14</td>
</tr>
<tr>
<td>13 y</td>
<td>0 (0, 0)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>−4 (−6, −1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>GST</td>
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<td></td>
</tr>
<tr>
<td>3 y</td>
<td>0 (0, 0)</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>−6 (−11, −1)</td>
<td>0.03</td>
</tr>
<tr>
<td>7 y</td>
<td>0 (0, 0)</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>−5 (−8, −2)</td>
<td>&lt;0.01</td>
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<tr>
<td>13 y</td>
<td>0 (0, 0)</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>−6 (−9, −4)</td>
<td>&lt;0.01</td>
</tr>
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</table>

1 Values are ORs (95% CIs) for liver fat and % changes (95% CIs) for liver stiffness, ALT, AST, and GGT. n = 1786 for USS-measured liver outcomes at all ages. n = 3059 for blood-based liver outcomes at all ages. Coefficients are per 100 kcal increase in USS-measured ALT, AST, and GGT.

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References


