

## Online appendix 2: Supplementary analyses

This document lists results from all analyses of exposure vs. glycemic regulation – including primary, secondary and sensitivity analyses.

### Abbreviations

On the tables on next pages, we use the following abbreviations:

- AChE = red blood cell acetylcholine esterase
- AChE/Hb = AChE normalized by hemoglobin concentration
- Bootstrap = confidence intervals for estimates were derived using bootstrap procedure (see main text for details)
- FE = fixed effect model (see main text for description of the statistical model)
- Hb = hemoglobin
- HbA<sub>1c</sub> = Glycosylated hemoglobin A
- ME = classic mixed effect model (see main text for details)
- RCM = random coefficient model (a type of mixed effect model; see main text for details)
- RE = random effect (see main text for details)

## Definitions of covariate sets

<b>Random coefficient model</b>		<b>Fixed effect model</b>		
<b>Basic covariate set</b>	<b>Extended covariate set</b>	<b>Basic covariate set</b>	<b>Full covariate set</b>	<b>Comment</b>
Age (continuous) Sex (dichotomous) Alcohol consumption (grams of alcohol in the last week, continuous) MET-minutes per week of physical activity (continuous) Servings of fruit and vegetables consumed per week (continuous) Tobacco smoking (grams of tobacco per day in the last week, continuous)	Basic set + BMI (continuous) Years of full-time education (proxy for socioeconomic status, continuous)	$\Delta$ age $\Delta$ (alcohol consumption) $\Delta$ (MET-minutes) $\Delta$ (consumption of fruit and vegetables) $\Delta$ (tobacco smoking)	Minimal set + $\Delta$ BMI	Sex and education level (as proxy for socioeconomic status) is not included in the fixed effect model, as they are assumed constant.

Consumption of alcohol and tobacco was modelled under the assumption of a linear exposure-response relationship, as the number of people reporting any use of tobacco or alcohol in the last week was relatively low. The remaining continuous variables were modelled using restricted cubic splines to allow non-linear dose-response relationships. The location of spline knots for each independent variable was determined automatically by Stata according to percentiles of the variable, as recommended by Harrell<sup>1</sup> and implemented in Stata's mkspline command. For four knots, the percentiles are 5, 35, 65 and 95. For three knots, they are 10, 50 and 90. For five knots, they are 5, 27.5, 50, 72.5 and 95.<sup>1</sup>

## Overview of statistical models in this appendix

Mixed effect models (planned *a priori*)

Model number	Outcome metric	Statistical model	Assumptions regarding linearity	Handling of interdependent data (family)	Handling of multiple AChE and HbA1c measurement in same phase*	Handling of HbA1c < 4% NGSP	Classification	Covariate set
1	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 4 knots	RE	First measurement used	Imputed	Primary analysis	Basic set
							Primary analysis	Unadjusted
							Sensitivity analysis	Extended set
2	FPG (continuous)	RCM	Cubic splines, 4 knots	RE	First measurement used	N/A	Secondary analysis	Basic set
							Sensitivity analysis	Extended set
							Sensitivity analysis	Unadjusted
3	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 4 knots	RE	First measurement used	Excluded	Sensitivity analysis	Basic set
4	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 4 knots	RE	If two measurements were made, the second one is used	Imputed		
5	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 4 knots	RE + bootstrap	First measurement used	Imputed		
6	HbA <sub>1c</sub> dichotomized into normal ( $\leq 38$ mmol/mol) vs. raised ( $\geq 39$ mmol/l)**	ME (logistic)	Cubic splines, 4 knots	RE	First measurement used	Imputed		
7	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 3 knots	RE	First measurement used	Imputed		
8	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 5 knots	RE	First measurement used	Imputed		
9	[Model described in analysis protocol, but excluded as described below]	N/A	N/A	N/A	N/A	N/A	Sensitivity analysis	Extended set + Hb
10	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 4 knots	RE	First measurement used	Imputed		
11	FPG (continuous) (excluding all observations where the AChE gave a warning that delays had happened during analysis, or temperature at FPG analysis $> 27$ °C)	RCM	Cubic splines, 4 knots	RE	First measurement used	N/A	Sensitivity analysis	Basic set

12	HbA <sub>1c</sub> (continuous) (excluding all observations where the AChE gave a warning that delays had happened)	RCM	Cubic splines, 4 knots	RE	First measurement used	Imputed	Sensitivity analysis	Basic set
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Fixed effect models (planned *a priori*)

Model number	Description	Outcome metric	Assumptions regarding linearity	Handling of interdependent data (family)	Handling of multiple AChE and HbA <sub>1c</sub> measurement in same phase*	Handling of HbA <sub>1c</sub> < 4% NGSP	Classification	Covariate set
13	Secondary model for primary outcome	ΔHbA <sub>1c</sub> (continuous), phase 1+3	Cubic splines, 4 knots	RE	First measurement used	Imputed	Secondary analysis	Basic set
							Secondary analysis	Unadjusted
							Sensitivity analysis	Extended set
14	Sensitivity analysis	ΔHbA <sub>1c</sub> (continuous), phase 1+2	Cubic splines, 4 knots	RE	First measurement used	Imputed	Sensitivity analysis	Basic set
15	Sensitivity analysis	ΔHbA <sub>1c</sub> (continuous), phase 2+3	Cubic splines, 4 knots	RE	First measurement used	Imputed	Sensitivity analysis	Basic set

Mixed effect models (*post hoc*)

Model number	Description	Outcome metric	Statistical model	Assumptions regarding linearity	Handling of interdependent data (family)	Handling of multiple AChE measurements in same phase*	Handling of HbA <sub>1c</sub> < 4% NGSP	Covariate set
16	Sensitivity analysis	HbA <sub>1c</sub> (continuous)	RCM	Cubic splines, 4 knots	RE	First measurement used	Imputed	Basic set + project phase
								Extended set + project phase

\* Handling of multiple AChE measurements in same phase: Each participant had his/her AChE measured in each phase. In some cases, the primary investigator suspected that an error had occurred during analysis (e.g., due to very low or very high measured hemoglobin values), and a second measurement was therefore made. Both results were saved. The decision to re-do the AChE analysis or not may have been biased unintentionally. Therefore, in the primary analyses we always used the first measurement, as measurement errors are assumed to happen at random. In some sensitivity analyses, we instead used the result from the second measurement.

\*\* The cutoff 39 mmol/mol was chosen *a priori*, because HbA<sub>1c</sub> ≥ 39 mmol/mol is categorized as raised by the American Diabetes Association.<sup>2</sup>

### Changes from analysis protocol

Before the analyses were carried out, an analysis protocol was published online.<sup>3</sup> During analysis, a few modifications were made to the models. The changes are listed point-by-point below.

- Due to the clear trend in AChE/Hb across study phases (see Table 2 in the main text), we decided to exclude project phase as a predictor in the random coefficient models. We deemed that because of the temporal trend in AChE/Hb, adjusting for phase would likely lead to bias towards the null hypothesis. As a sensitivity analysis, we re-included phase in model 16.
- Our plan was to calculate confidence intervals in model 5 using a random coefficient model with random effects for family, and with bootstrapping. To allow each iteration of the regression to complete in finite time, we wanted to model all predictor under the assumption of linearity (i.e., we would not use splines). However, we discovered that the processing time for the bootstrapped RCM model was still unfeasibly long, so we decided to instead bootstrap a classical mixed effect model, i.e.

$$y = \beta_0 + \beta_b \times b + \left( \sum_i \beta_{c,i} \times c_i \right) + \alpha + \tau + \varepsilon$$

Where  $y$  is outcome,  $\beta_0$  is the intercept,  $\beta_b$  is a fixed effect for exposure  $b$ ,  $\beta_{c,i}$  is a fixed effect for the  $i^{th}$  confounder  $c_i$ ,  $\alpha$  is a random term for family,  $\tau$  is a random term for person, and  $\varepsilon$  is an error term. In this model, all participants have the same  $\beta_b$  (contrary to the RCM).

The classical mixed effect model ran much faster than the random coefficient model, meaning that bootstrapping became feasible. To make it easier to compare results across models, we decided to also use splines in the revised model 5.

- For model 6, the original plan was to analyze the dichotomized HbA<sub>1c</sub> variable in a logistic random coefficient model, i.e. a model of the following structure:

$$\log \left( \text{odds}(HbA_{1c} \geq 39 \text{ mmol/mol}) \right) = \beta_0 + \beta_b \times b + \left( \sum_i \beta_{c,i} \times c_i \right) + \alpha + \tau + \varepsilon$$

where all terms on the right-hand side of the equation have the same meaning as in model 1. I.e., each participant would have her/his own  $\beta_b$ , and  $\beta_b$  would be normally distributed. However, Stata could not fit this model within a reasonable amount of time. Hence, the model was changed so that all participants had the same  $\beta_b$ . This latter model ran without issues.

- Our analysis protocol included a model (model 9) where we wanted to re-calculate AChE/Hb after adjusting hemoglobin to take into account that the Test-mate ChE device might underestimate hemoglobin. However, extra quality control with different Test-Mate devices indicated that when hemoglobin is negatively biased, so is AChE, and by approximately the same fraction, meaning that AChE/Hb is relatively unaffected (results not shown). Hence, we decided that adjusting hemoglobin and recalculating AChE/Hb was more likely to bias our results than to correct any biases. This analysis was therefore not carried out.

### Notes on figures and tables in this appendix

Plots of outcomes vs. predictors modelled using splines show the effect estimates with 95% confidence intervals, relative to the predicted outcome at the median value of the predictor. The black points on the trend curves show the location of the knots for the restricted cubic splines (see page 2). For reference purposes, a histogram of the predictor is overlaid on each figure.

Tables of results for predictors modeled using splines show effect estimates with 95% confidence intervals at the location of the spline knots (see page 2), relative to the median value of the predictor. For predictors modelled categorically or under the assumption of linearity, tables show regression coefficients.

Please note that the covariate sets in adjusted analyses were selected based on Directed Acyclic Graphs with the purpose of obtaining an unbiased estimate of the effect of AChE/Hb on glycemic regulation. No attempt was made to select covariates to provide unbiased estimates of the effects of other predictors (such as age). Hence, regression results for other predictors could potentially be biased and are only listed to provide context for the main results (AChE/Hb vs. glycemic regulation).

### References for this appendix

- 1 Harrell FE. *Regression Modeling Strategies : With Applications to Linear Models, Logistic Regression, and Survival Analysis*. New York, UNITED STATES: Springer New York, 2001.
- 2 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019;42:S13-S28.
- 3 Hansen MRH, Jørs E, Sandbæk A et al. Protocol for statistical analyses of health outcomes in the study entitled "Pesticide exposure, asthma and diabetes in Uganda (PEXADU)". Zenodo 2019. <https://doi.org/10.5281/zenodo.3552750>

## Analysis specification

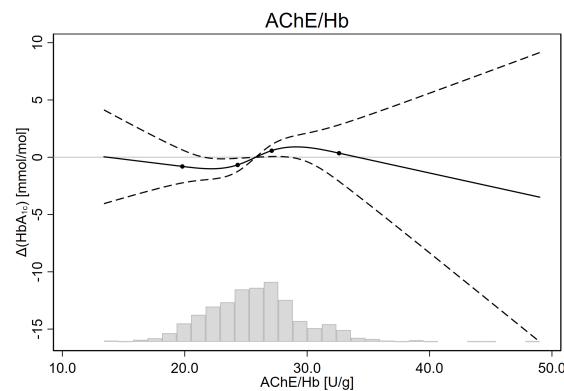
Model 01

Outcome: HbA<sub>1c</sub>

Unadjusted

Number of observations in model: 1,071

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.798 [-2.240 ; 0.643]
24.32	-0.667 [-1.242 ; -0.092]
25.80	0 [ref.]
27.10	0.578 [0.061 ; 1.095]
32.60	0.359 [-2.105 ; 2.824]

## Analysis specification

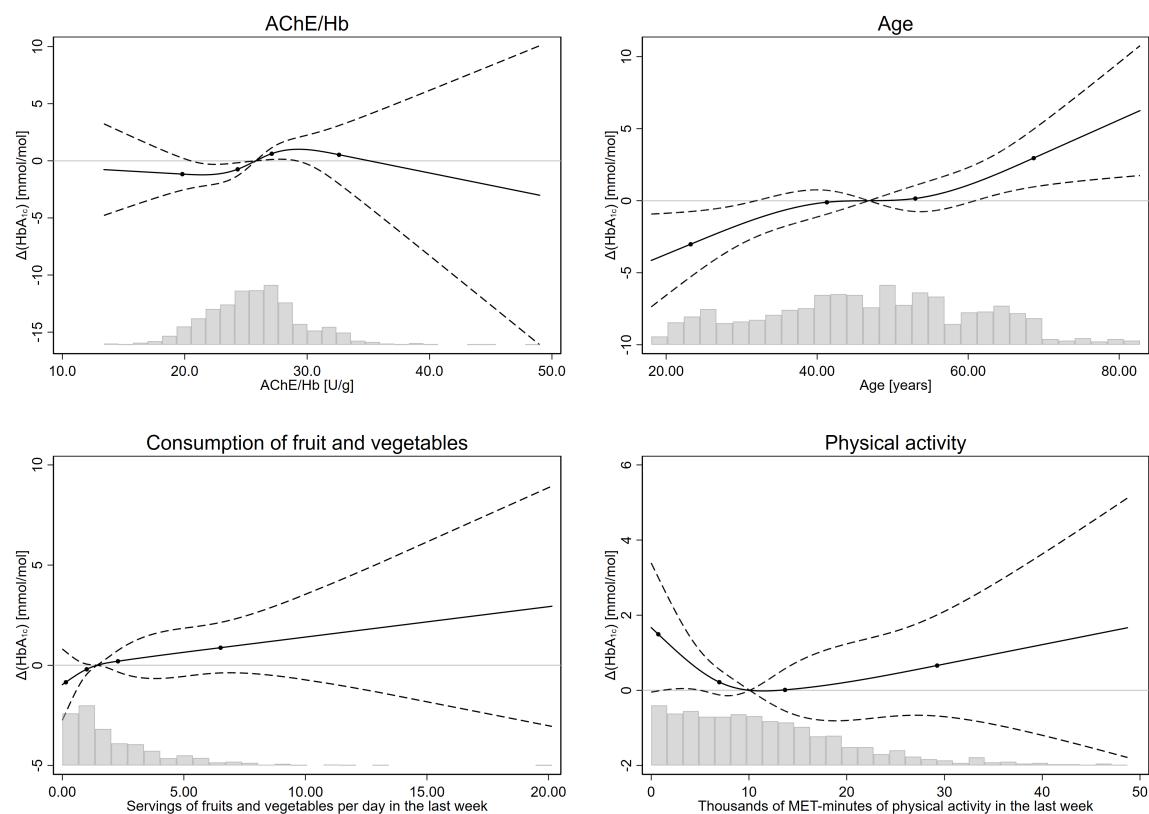
Model 01

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.159 [-2.569 ; 0.250]
24.32	-0.737 [-1.305 ; -0.168]
25.80	0 [ref.]
27.10	0.627 [0.117 ; 1.137]
32.60	0.536 [-2.017 ; 3.089]

Age

Value	Outcome estimate [CI]
23.23	-3.021 [-5.291 ; -0.752]
41.28	-0.106 [-0.934 ; 0.722]
46.84	0 [ref.]
52.99	0.157 [-0.751 ; 1.065]
68.67	2.960 [0.958 ; 4.962]

Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.845 [-2.364 ; 0.674]
1.00	-0.198 [-0.454 ; 0.059]
1.43	0 [ref.]
2.29	0.204 [-0.333 ; 0.741]
6.51	0.878 [-0.382 ; 2.138]

Physical activity

Value	Outcome estimate [CI]
0.72	1.494 [-0.016 ; 3.004]
6.96	0.219 [-0.122 ; 0.560]
10.08	0 [ref.]
13.68	0.013 [-0.547 ; 0.573]
29.24	0.661 [-0.685 ; 2.006]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.916 [-4.512 ; -1.319]
Grams of alcohol in the last week	0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.683 [-1.535 ; 0.169]

## Analysis specification

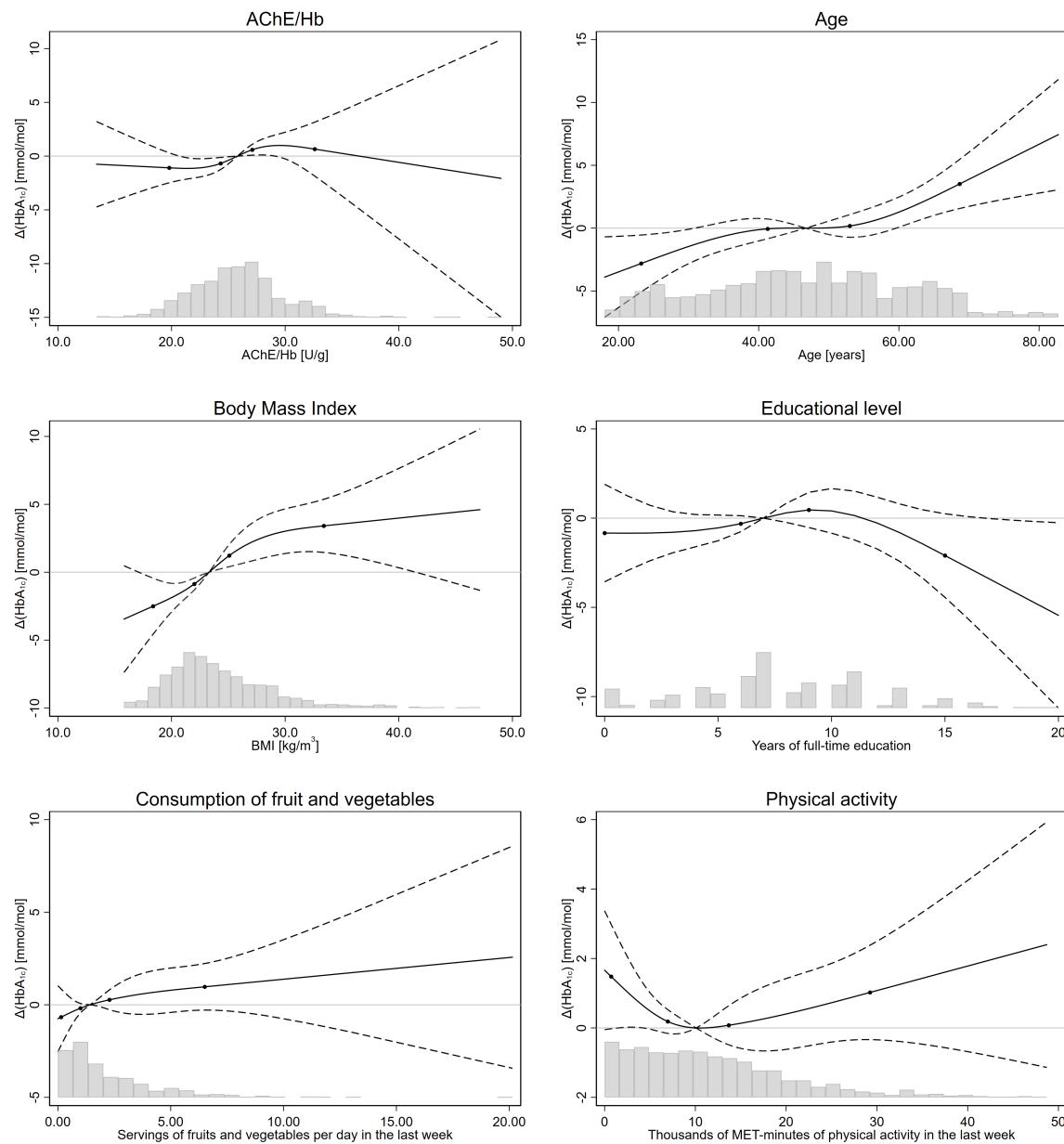
Model 01

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Extended

Number of observations in model: 1,037

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units)

## AChE/Hb

<b>Value</b>	<b>Outcome estimate [CI]</b>
19.80	-1.090 [-2.481 ; 0.302]
24.32	-0.684 [-1.245 ; -0.124]
25.80	0 [ref.]
27.10	0.589 [0.086 ; 1.091]
32.60	0.651 [-1.857 ; 3.158]

## Body Mass Index

<b>Value</b>	<b>Outcome estimate [CI]</b>
18.37	-2.505 [-4.574 ; -0.435]
22.01	-0.864 [-1.304 ; -0.425]
23.30	0 [ref.]
25.08	1.224 [0.407 ; 2.041]
33.40	3.415 [1.457 ; 5.373]

## Consumption of fruit and vegetables

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.14	-0.667 [-2.192 ; 0.857]
1.00	-0.185 [-0.443 ; 0.073]
1.43	0 [ref.]
2.29	0.269 [-0.266 ; 0.804]
6.51	0.971 [-0.286 ; 2.229]

## Physical activity

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.72	1.480 [-0.024 ; 2.985]
6.96	0.185 [-0.157 ; 0.528]
10.08	0 [ref.]
13.68	0.077 [-0.486 ; 0.641]
29.24	1.023 [-0.337 ; 2.382]

## Age

<b>Value</b>	<b>Outcome estimate [CI]</b>
23.23	-2.816 [-5.084 ; -0.548]
41.28	-0.059 [-0.842 ; 0.723]
46.71	0 [ref.]
52.99	0.174 [-0.726 ; 1.074]
68.67	3.516 [1.561 ; 5.470]

## Educational level

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.00	-0.837 [-3.570 ; 1.897]
6.00	-0.312 [-0.761 ; 0.137]
7.00	0 [ref.]
9.00	0.460 [-0.526 ; 1.447]
15.00	-2.097 [-4.438 ; 0.244]

Regression results for categorical and linear variables

<b>Parameter</b>	<b>Regression coef. [95% CI]</b>
Female sex	0 (ref.)
Male sex	-0.804 [-2.530 ; 0.922]
Grams of alcohol in the last week	0.001 [-0.003 ; 0.005]
Grams of tobacco per day in the last week	-0.792 [-1.629 ; 0.045]

## Analysis specification

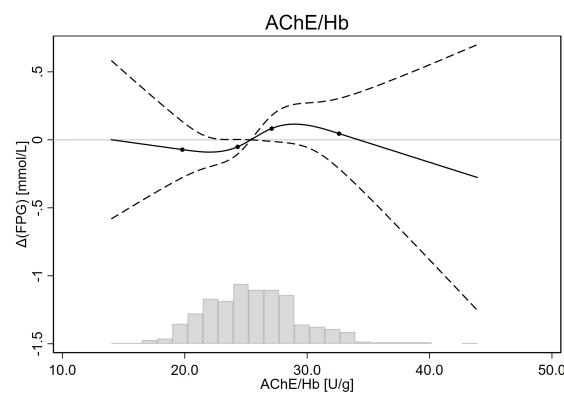
Model 02

Outcome: Fasting plasma glucose (FPG)

Unadjusted

Number of observations in model: 591

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.072 [-0.278 ; 0.135]
24.32	-0.051 [-0.105 ; 0.003]
25.40	0 [ref.]
27.10	0.083 [-0.012 ; 0.178]
32.60	0.046 [-0.212 ; 0.304]

## Analysis specification

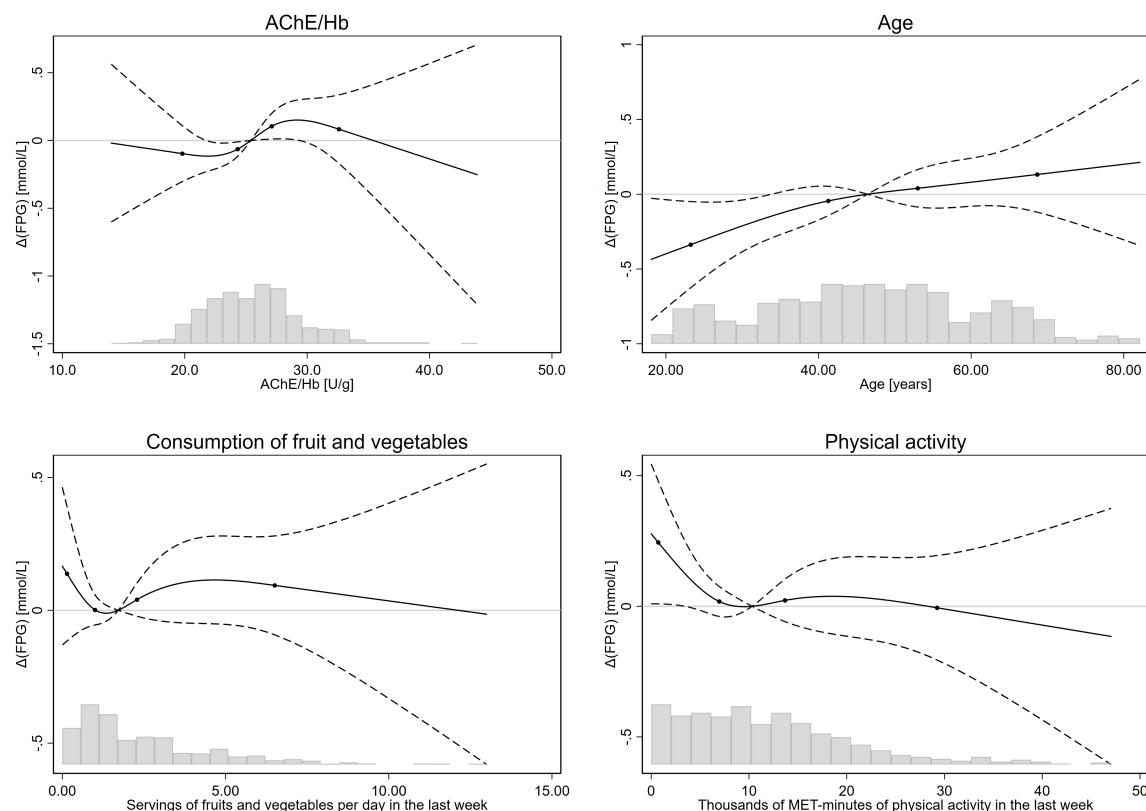
Model 02

Outcome: Fasting plasma glucose (FPG)

Covariate adjustment: Basic

Number of observations in model: 574

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.097 [-0.304 ; 0.110]
24.32	-0.064 [-0.118 ; -0.011]
25.40	0 [ref.]
27.10	0.105 [0.011 ; 0.199]
32.60	0.083 [-0.170 ; 0.337]

Age

Value	Outcome estimate [CI]
23.23	-0.337 [-0.626 ; -0.049]
41.28	-0.045 [-0.143 ; 0.053]
46.43	0 [ref.]
52.99	0.040 [-0.085 ; 0.165]
68.67	0.132 [-0.120 ; 0.384]

Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	0.138 [-0.116 ; 0.391]
1.00	0.001 [-0.055 ; 0.058]
1.71	0 [ref.]
2.29	0.040 [-0.022 ; 0.102]
6.51	0.094 [-0.093 ; 0.280]

Physical activity

Value	Outcome estimate [CI]
0.72	0.244 [0.009 ; 0.480]
6.96	0.019 [-0.039 ; 0.076]
10.32	0 [ref.]
13.68	0.023 [-0.059 ; 0.104]
29.24	-0.006 [-0.206 ; 0.194]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-0.032 [-0.235 ; 0.170]
Grams of alcohol in the last week	-0.000 [-0.002 ; 0.001]
Grams of tobacco per day in the last week	0.037 [-0.071 ; 0.146]

## Analysis specification

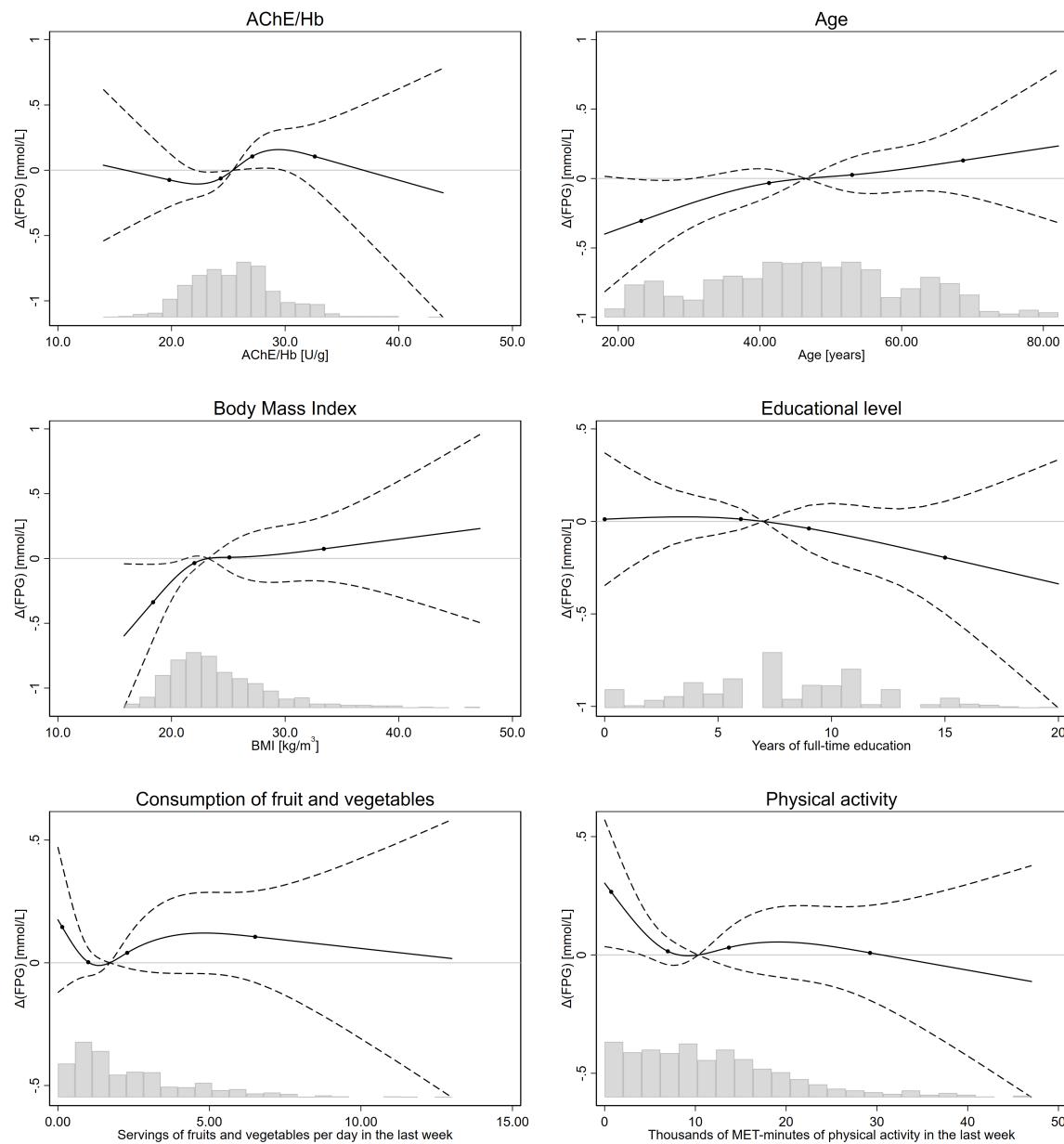
Model 02

Outcome: Fasting plasma glucose (FPG)

Covariate adjustment: Extended

Number of observations in model: 574

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units)

## AChE/Hb

<b>Value</b>	<b>Outcome estimate [CI]</b>
19.80	-0.074 [-0.280 ; 0.132]
24.32	-0.063 [-0.116 ; -0.009]
25.40	0 [ref.]
27.10	0.106 [0.012 ; 0.200]
32.60	0.106 [-0.146 ; 0.357]

## Body Mass Index

<b>Value</b>	<b>Outcome estimate [CI]</b>
18.37	-0.337 [-0.630 ; -0.044]
22.01	-0.035 [-0.087 ; 0.018]
23.22	0 [ref.]
25.08	0.009 [-0.102 ; 0.120]
33.40	0.075 [-0.175 ; 0.325]

## Consumption of fruit and vegetables

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.14	0.146 [-0.108 ; 0.399]
1.00	0.003 [-0.054 ; 0.060]
1.71	0 [ref.]
2.29	0.041 [-0.021 ; 0.103]
6.51	0.106 [-0.081 ; 0.293]

## Physical activity

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.72	0.267 [0.031 ; 0.502]
6.96	0.016 [-0.041 ; 0.073]
10.32	0 [ref.]
13.68	0.031 [-0.050 ; 0.112]
29.24	0.009 [-0.192 ; 0.210]

## Age

<b>Value</b>	<b>Outcome estimate [CI]</b>
23.23	-0.305 [-0.602 ; -0.008]
41.28	-0.032 [-0.131 ; 0.067]
46.43	0 [ref.]
52.99	0.026 [-0.099 ; 0.152]
68.67	0.130 [-0.122 ; 0.382]

## Educational level

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.00	0.012 [-0.347 ; 0.371]
6.00	0.013 [-0.044 ; 0.070]
7.00	0 [ref.]
9.00	-0.038 [-0.163 ; 0.087]
15.00	-0.195 [-0.498 ; 0.108]

Regression results for categorical and linear variables

<b>Parameter</b>	<b>Regression coef. [95% CI]</b>
Female sex	0 (ref.)
Male sex	0.054 [-0.169 ; 0.277]
Grams of alcohol in the last week	-0.000 [-0.002 ; 0.001]
Grams of tobacco per day in the last week	0.030 [-0.079 ; 0.138]

## Analysis specification

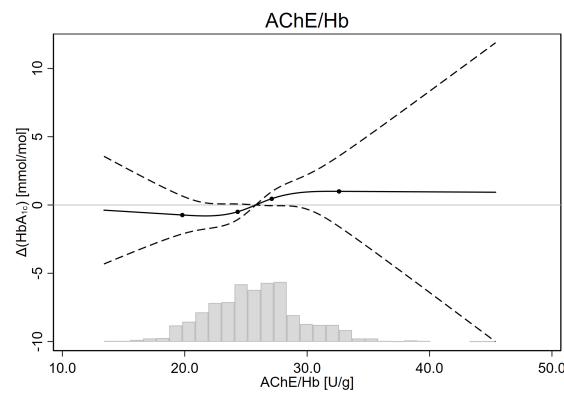
Model 03

Outcome: HbA<sub>1c</sub>

Unadjusted

Number of observations in model: 1,036

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.731 [-2.121 ; 0.658]
24.32	-0.498 [-1.071 ; 0.075]
25.80	0 [ref.]
27.10	0.459 [-0.052 ; 0.969]
32.60	1.000 [-1.583 ; 3.582]

## Analysis specification

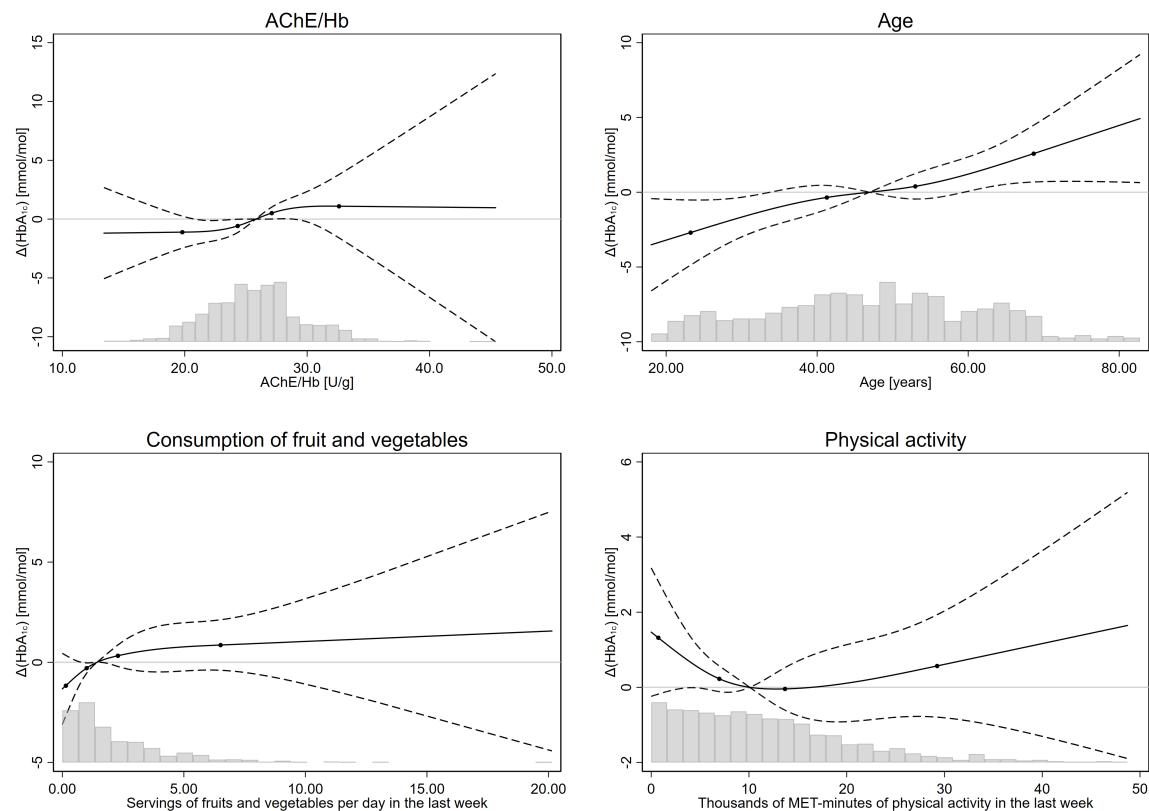
Model 03

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,010

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

#### AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.107 [-2.469 ; 0.254]
24.32	-0.579 [-1.144 ; -0.013]
25.80	0 [ref.]
27.10	0.513 [0.010 ; 1.015]
32.60	1.097 [-1.594 ; 3.788]

#### Age

Value	Outcome estimate [CI]
23.23	-2.697 [-4.875 ; -0.519]
41.28	-0.348 [-1.150 ; 0.455]
46.94	0 [ref.]
52.99	0.394 [-0.453 ; 1.242]
68.67	2.582 [0.685 ; 4.480]

#### Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-1.166 [-2.680 ; 0.347]
1.00	-0.289 [-0.544 ; -0.033]
1.43	0 [ref.]
2.29	0.327 [-0.209 ; 0.864]
6.51	0.861 [-0.399 ; 2.122]

#### Physical activity

Value	Outcome estimate [CI]
0.72	1.321 [-0.180 ; 2.822]
6.96	0.227 [-0.115 ; 0.570]
10.08	0 [ref.]
13.68	-0.042 [-0.607 ; 0.524]
29.24	0.569 [-0.794 ; 1.932]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-1.995 [-3.528 ; -0.461]
Grams of alcohol in the last week	0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.765 [-1.589 ; 0.059]

## Analysis specification

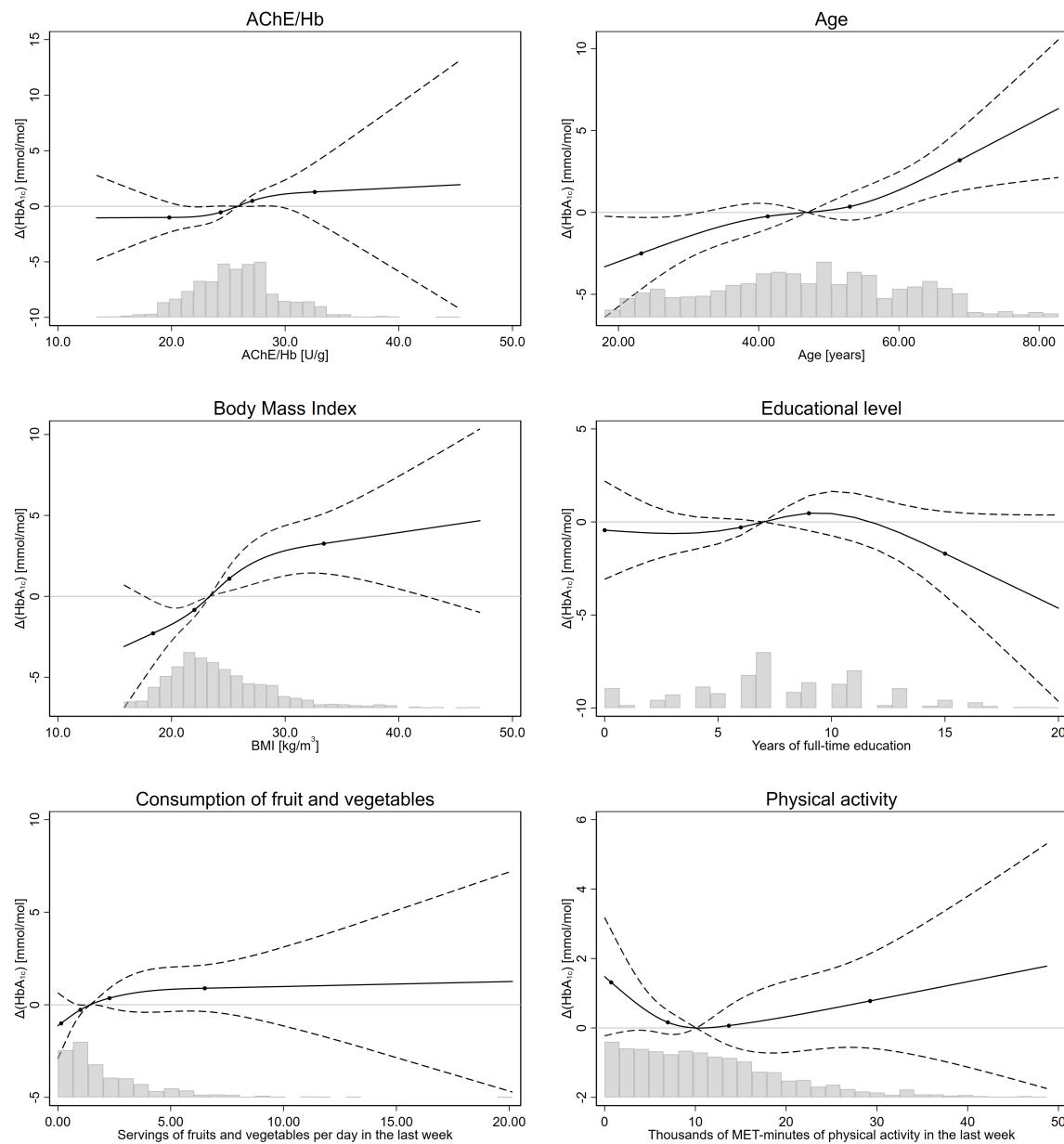
Model 03

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Extended

Number of observations in model: 1,006

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units)

## AChE/Hb

<b>Value</b>	<b>Outcome estimate [CI]</b>
19.80	-1.004 [-2.347 ; 0.339]
24.32	-0.537 [-1.095 ; 0.021]
25.80	0 [ref.]
27.10	0.491 [-0.005 ; 0.987]
32.60	1.291 [-1.346 ; 3.928]

## Body Mass Index

<b>Value</b>	<b>Outcome estimate [CI]</b>
18.37	-2.281 [-4.283 ; -0.279]
22.01	-0.833 [-1.279 ; -0.386]
23.36	0 [ref.]
25.08	1.093 [0.337 ; 1.850]
33.40	3.261 [1.408 ; 5.115]

## Consumption of fruit and vegetables

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.14	-1.002 [-2.523 ; 0.518]
1.00	-0.269 [-0.526 ; -0.012]
1.43	0 [ref.]
2.29	0.359 [-0.175 ; 0.894]
6.51	0.894 [-0.364 ; 2.152]

## Physical activity

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.72	1.315 [-0.183 ; 2.812]
6.96	0.162 [-0.179 ; 0.504]
10.08	0 [ref.]
13.68	0.066 [-0.500 ; 0.633]
29.24	0.778 [-0.585 ; 2.141]

## Age

<b>Value</b>	<b>Outcome estimate [CI]</b>
23.23	-2.499 [-4.690 ; -0.308]
41.28	-0.241 [-1.019 ; 0.538]
46.91	0 [ref.]
52.99	0.356 [-0.470 ; 1.183]
68.67	3.188 [1.319 ; 5.057]

## Educational level

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.00	-0.441 [-3.080 ; 2.197]
6.00	-0.291 [-0.720 ; 0.138]
7.00	0 [ref.]
9.00	0.472 [-0.468 ; 1.412]
15.00	-1.701 [-3.958 ; 0.556]

Regression results for categorical and linear variables

<b>Parameter</b>	<b>Regression coef. [95% CI]</b>
Female sex	0 (ref.)
Male sex	-0.250 [-1.898 ; 1.399]
Grams of alcohol in the last week	0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.847 [-1.658 ; -0.036]

## Analysis specification

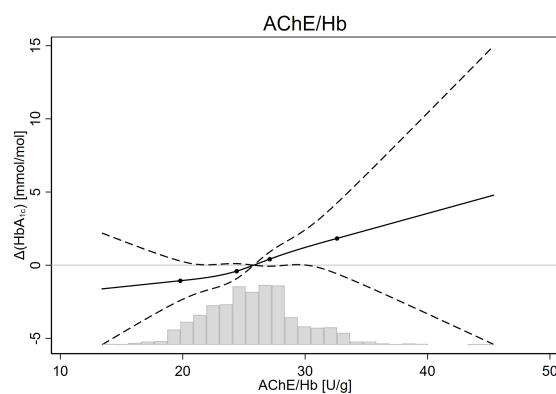
Model 04

Outcome: HbA<sub>1c</sub>

Unadjusted

Number of observations in model: 1,071

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.061 [-2.409 ; 0.287]
24.40	-0.406 [-0.921 ; 0.108]
25.80	0 [ref.]
27.10	0.414 [-0.074 ; 0.902]
32.60	1.829 [-0.587 ; 4.245]

## Analysis specification

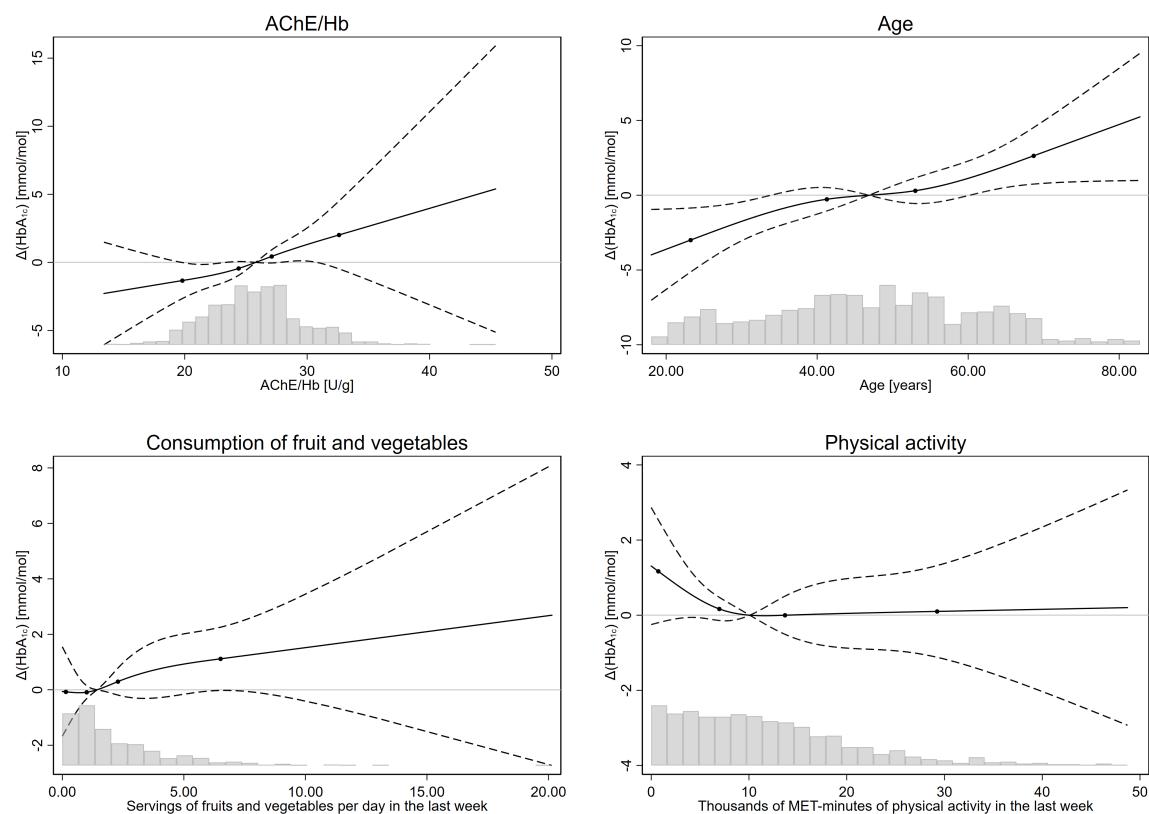
Model 04

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.333 [-2.657 ; -0.009]
24.40	-0.442 [-0.951 ; 0.067]
25.80	0 [ref.]
27.10	0.440 [-0.042 ; 0.922]
32.60	2.015 [-0.475 ; 4.505]

Age

Value	Outcome estimate [CI]
23.23	-2.997 [-5.139 ; -0.855]
41.28	-0.269 [-1.051 ; 0.512]
46.84	0 [ref.]
52.99	0.303 [-0.554 ; 1.160]
68.67	2.636 [0.746 ; 4.527]

Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.073 [-1.449 ; 1.303]
1.00	-0.089 [-0.322 ; 0.144]
1.43	0 [ref.]
2.29	0.296 [-0.190 ; 0.782]
6.51	1.117 [-0.023 ; 2.257]

Physical activity

Value	Outcome estimate [CI]
0.72	1.169 [-0.200 ; 2.539]
6.96	0.167 [-0.142 ; 0.476]
10.08	0 [ref.]
13.68	-0.001 [-0.508 ; 0.506]
29.24	0.100 [-1.121 ; 1.322]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.473 [-3.970 ; -0.975]
Grams of alcohol in the last week	-0.001 [-0.004 ; 0.003]
Grams of tobacco per day in the last week	-0.423 [-1.209 ; 0.363]

## Analysis specification

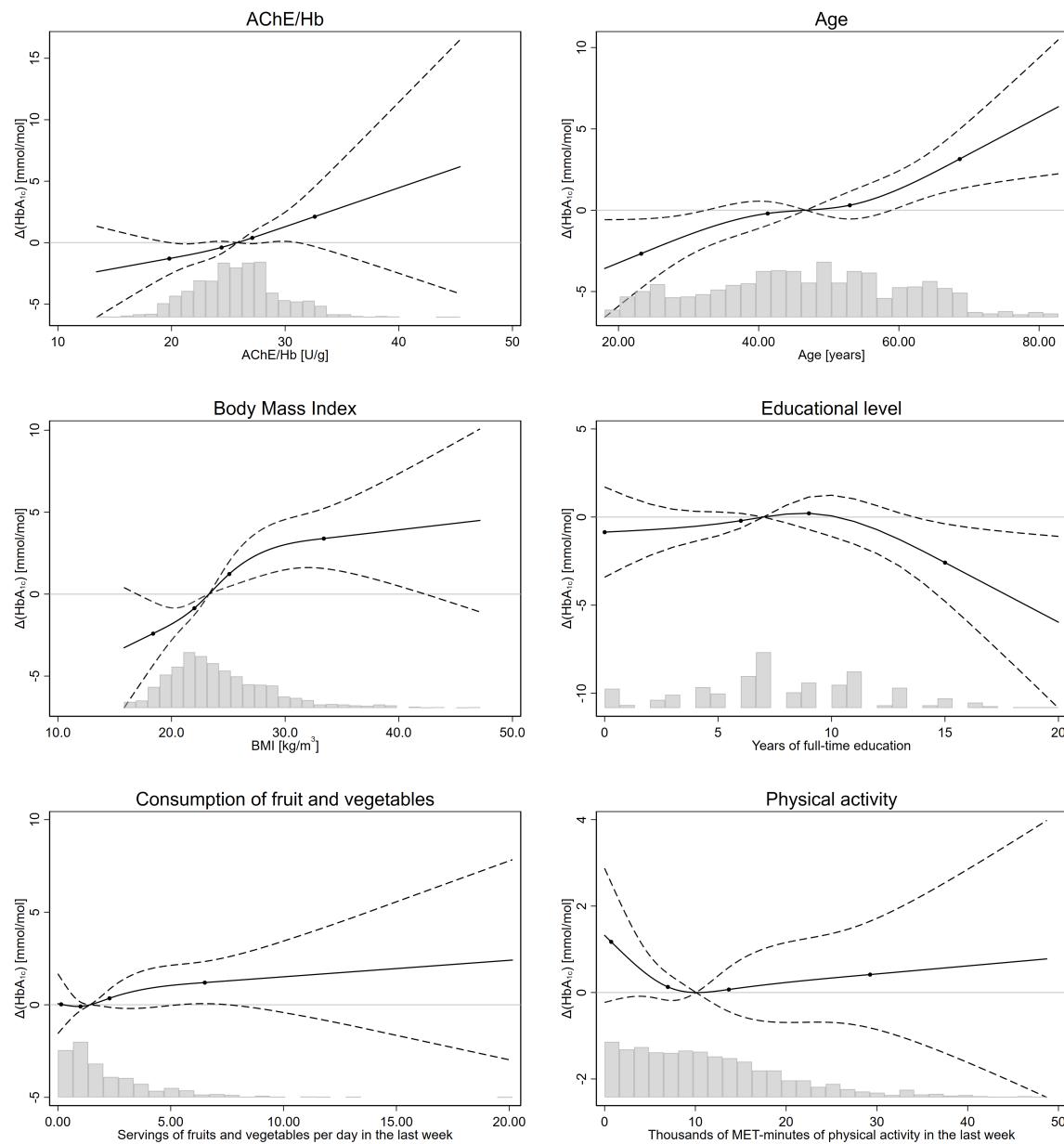
Model 04

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Extended

Number of observations in model: 1,037

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units)

## AChE/Hb

<b>Value</b>	<b>Outcome estimate [CI]</b>
19.80	-1.291 [-2.590 ; 0.007]
24.40	-0.386 [-0.887 ; 0.115]
25.80	0 [ref.]
27.10	0.393 [-0.080 ; 0.867]
32.60	2.120 [-0.317 ; 4.558]

## Body Mass Index

<b>Value</b>	<b>Outcome estimate [CI]</b>
18.37	-2.406 [-4.343 ; -0.470]
22.01	-0.858 [-1.270 ; -0.446]
23.30	0 [ref.]
25.08	1.230 [0.467 ; 1.992]
33.40	3.392 [1.561 ; 5.224]

## Consumption of fruit and vegetables

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.14	0.026 [-1.354 ; 1.406]
1.00	-0.087 [-0.320 ; 0.147]
1.43	0 [ref.]
2.29	0.352 [-0.132 ; 0.836]
6.51	1.201 [0.063 ; 2.339]

## Physical activity

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.72	1.174 [-0.190 ; 2.537]
6.96	0.130 [-0.180 ; 0.441]
10.08	0 [ref.]
13.68	0.070 [-0.440 ; 0.580]
29.24	0.416 [-0.818 ; 1.649]

## Age

<b>Value</b>	<b>Outcome estimate [CI]</b>
23.23	-2.668 [-4.795 ; -0.540]
41.28	-0.198 [-0.932 ; 0.536]
46.71	0 [ref.]
52.99	0.306 [-0.537 ; 1.150]
68.67	3.148 [1.312 ; 4.985]

## Educational level

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.00	-0.854 [-3.413 ; 1.705]
6.00	-0.209 [-0.630 ; 0.213]
7.00	0 [ref.]
9.00	0.214 [-0.710 ; 1.138]
15.00	-2.584 [-4.780 ; -0.388]

Regression results for categorical and linear variables

<b>Parameter</b>	<b>Regression coef. [95% CI]</b>
Female sex	0 (ref.)
Male sex	-0.357 [-1.961 ; 1.247]
Grams of alcohol in the last week	-0.000 [-0.004 ; 0.003]
Grams of tobacco per day in the last week	-0.546 [-1.317 ; 0.224]

## Analysis specification

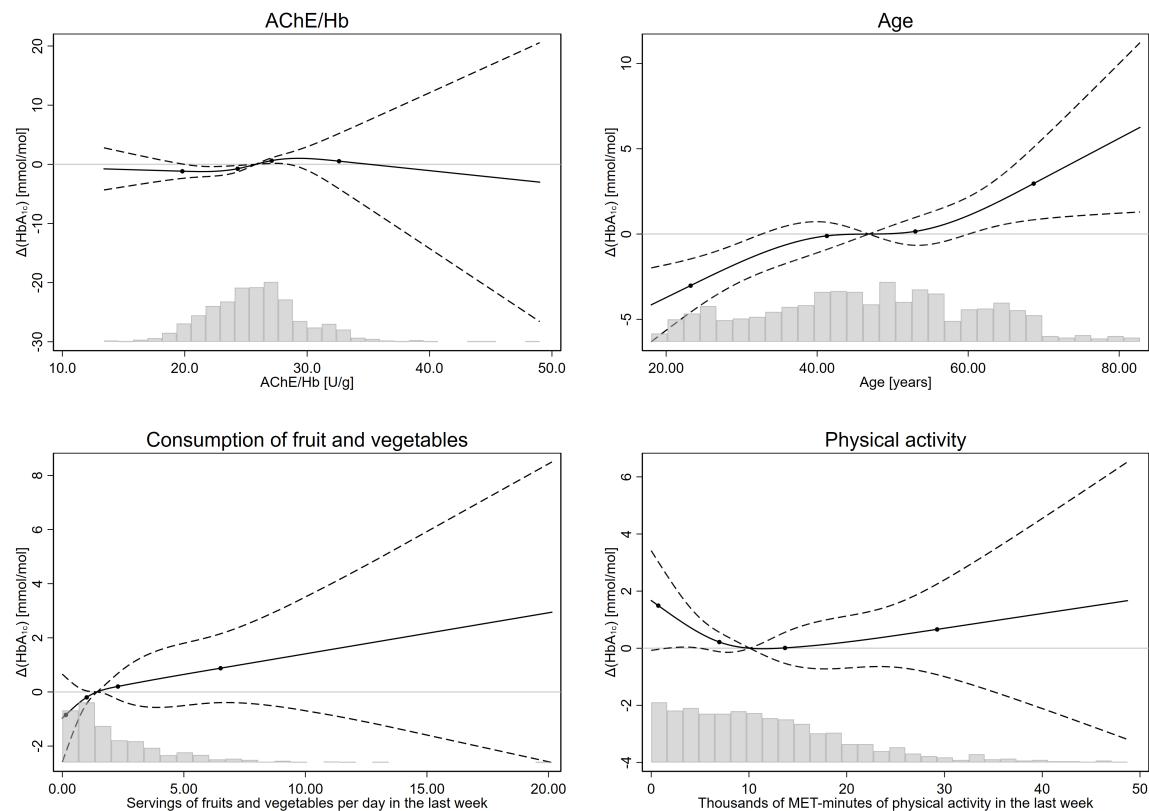
Model 05

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

#### AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.159 [-2.379 ; 0.061]
24.32	-0.737 [-1.279 ; -0.195]
25.80	0 [ref.]
27.10	0.627 [0.157 ; 1.097]
32.60	0.536 [-4.133 ; 5.205]

#### Age

Value	Outcome estimate [CI]
23.23	-3.021 [-4.584 ; -1.459]
41.28	-0.106 [-0.903 ; 0.691]
46.84	0 [ref.]
52.99	0.157 [-0.659 ; 0.973]
68.67	2.960 [0.835 ; 5.085]

#### Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.845 [-2.231 ; 0.541]
1.00	-0.198 [-0.435 ; 0.039]
1.43	0 [ref.]
2.29	0.204 [-0.276 ; 0.685]
6.51	0.878 [-0.394 ; 2.150]

#### Physical activity

Value	Outcome estimate [CI]
0.72	1.494 [-0.039 ; 3.027]
6.96	0.219 [-0.122 ; 0.560]
10.08	0 [ref.]
13.68	0.013 [-0.531 ; 0.557]
29.24	0.661 [-0.926 ; 2.248]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.916 [-4.379 ; -1.452]
Grams of alcohol in the last week	0.000 [-0.005 ; 0.005]
Grams of tobacco per day in the last week	-0.683 [-2.060 ; 0.694]

## Analysis specification

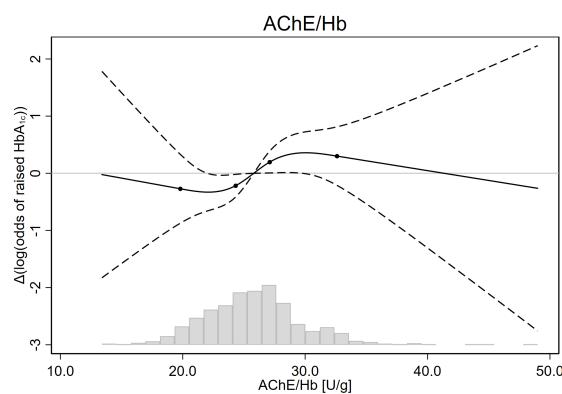
Model 06

Outcome: Odds of raised HbA<sub>1c</sub> ( $\geq 39$  mmol/mol)

Unadjusted

Number of observations in model: 1,071

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.271 [-0.873 ; 0.332]
24.32	-0.217 [-0.415 ; -0.018]
25.80	0 [ref.]
27.10	0.196 [0.006 ; 0.386]
32.60	0.301 [-0.211 ; 0.812]

## Analysis specification

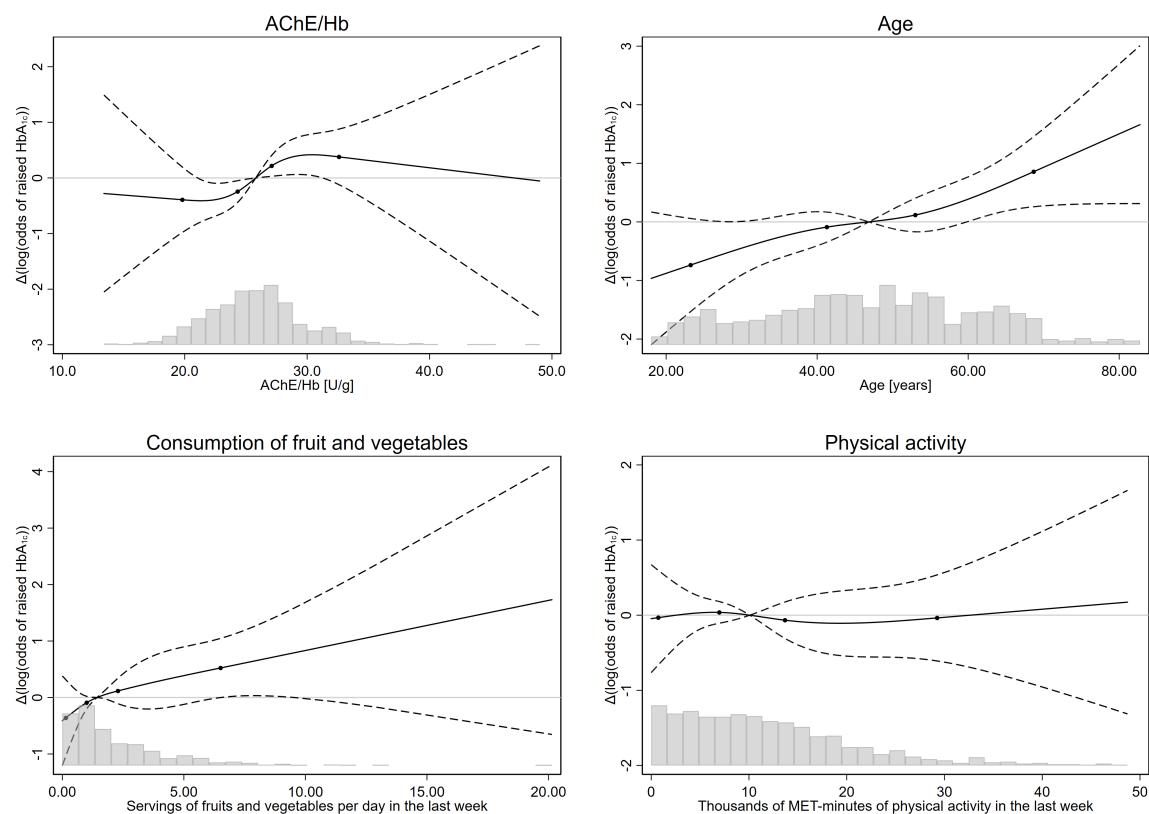
Model 06

Outcome: Odds of raised HbA<sub>1c</sub> ( $\geq 39$  mmol/mol)

Covariate adjustment: Basic

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

#### AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.392 [-0.981 ; 0.197]
24.32	-0.245 [-0.440 ; -0.049]
25.80	0 [ref.]
27.10	0.218 [0.030 ; 0.405]
32.60	0.379 [-0.121 ; 0.878]

#### Age

Value	Outcome estimate [CI]
23.23	-0.736 [-1.532 ; 0.059]
41.28	-0.089 [-0.345 ; 0.168]
46.84	0 [ref.]
52.99	0.118 [-0.169 ; 0.404]
68.67	0.857 [0.259 ; 1.454]

#### Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.361 [-1.038 ; 0.315]
1.00	-0.092 [-0.204 ; 0.021]
1.43	0 [ref.]
2.29	0.116 [-0.109 ; 0.341]
6.51	0.523 [-0.001 ; 1.047]

#### Physical activity

Value	Outcome estimate [CI]
0.72	-0.033 [-0.663 ; 0.597]
6.96	0.037 [-0.107 ; 0.182]
10.08	0 [ref.]
13.68	-0.067 [-0.309 ; 0.176]
29.24	-0.036 [-0.609 ; 0.536]

### Regression results for categorical and linear variables

Parameter	Odds ratio [95% CI]
Female sex	0 (ref.)
Male sex	0.356 [0.206 ; 0.614]
Grams of alcohol in the last week	1.000 [0.997 ; 1.002]
Grams of tobacco per day in the last week	0.681 [0.338 ; 1.370]

## Analysis specification

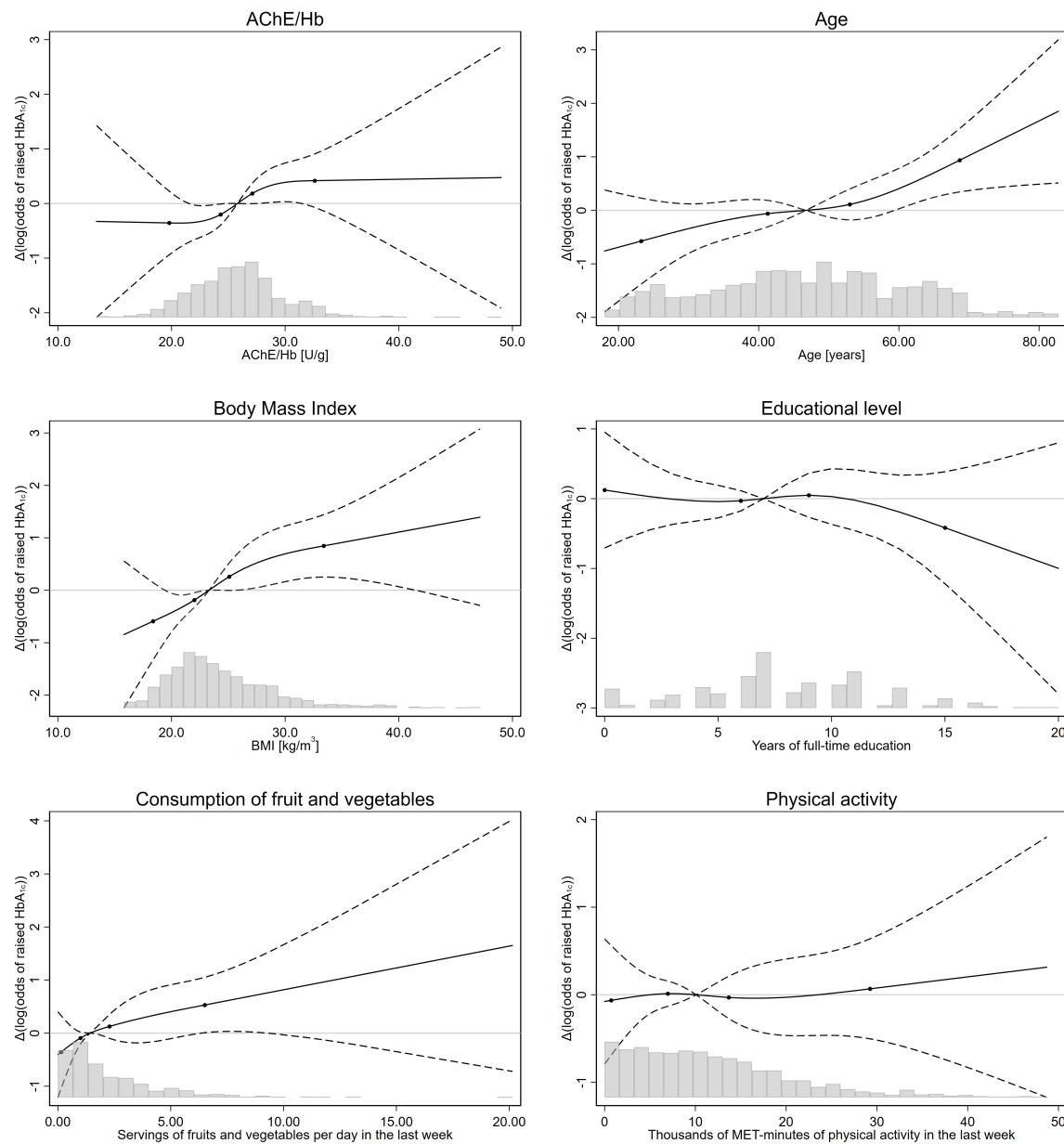
Model 06

Outcome: Odds of raised HbA<sub>1c</sub> ( $\geq 39$  mmol/mol)

Covariate adjustment: Extended

Number of observations in model: 1,037

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units)

## AChE/Hb

<b>Value</b>	<b>Outcome estimate [CI]</b>
19.80	-0.356 [-0.939 ; 0.227]
24.32	-0.202 [-0.395 ; -0.009]
25.80	0 [ref.]
27.10	0.183 [-0.003 ; 0.368]
32.60	0.419 [-0.071 ; 0.908]

## Body Mass Index

<b>Value</b>	<b>Outcome estimate [CI]</b>
18.37	-0.591 [-1.330 ; 0.147]
22.01	-0.187 [-0.326 ; -0.047]
23.30	0 [ref.]
25.08	0.259 [-0.003 ; 0.521]
33.40	0.847 [0.252 ; 1.442]

## Consumption of fruit and vegetables

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.14	-0.357 [-1.045 ; 0.331]
1.00	-0.094 [-0.208 ; 0.020]
1.43	0 [ref.]
2.29	0.126 [-0.098 ; 0.349]
6.51	0.530 [0.007 ; 1.052]

## Physical activity

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.72	-0.064 [-0.691 ; 0.563]
6.96	0.012 [-0.132 ; 0.157]
10.08	0 [ref.]
13.68	-0.031 [-0.272 ; 0.211]
29.24	0.068 [-0.504 ; 0.639]

## Age

<b>Value</b>	<b>Outcome estimate [CI]</b>
23.23	-0.575 [-1.379 ; 0.229]
41.28	-0.061 [-0.308 ; 0.186]
46.71	0 [ref.]
52.99	0.111 [-0.177 ; 0.398]
68.67	0.937 [0.344 ; 1.529]

## Educational level

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.00	0.124 [-0.706 ; 0.954]
6.00	-0.031 [-0.177 ; 0.115]
7.00	0 [ref.]
9.00	0.050 [-0.267 ; 0.366]
15.00	-0.416 [-1.219 ; 0.386]

Regression results for categorical and linear variables

<b>Parameter</b>	<b>Odds ratio [95% CI]</b>
Female sex	0 (ref.)
Male sex	0.594 [0.330 ; 1.067]
Grams of alcohol in the last week	1.000 [0.997 ; 1.002]
Grams of tobacco per day in the last week	0.724 [0.397 ; 1.320]

## Analysis specification

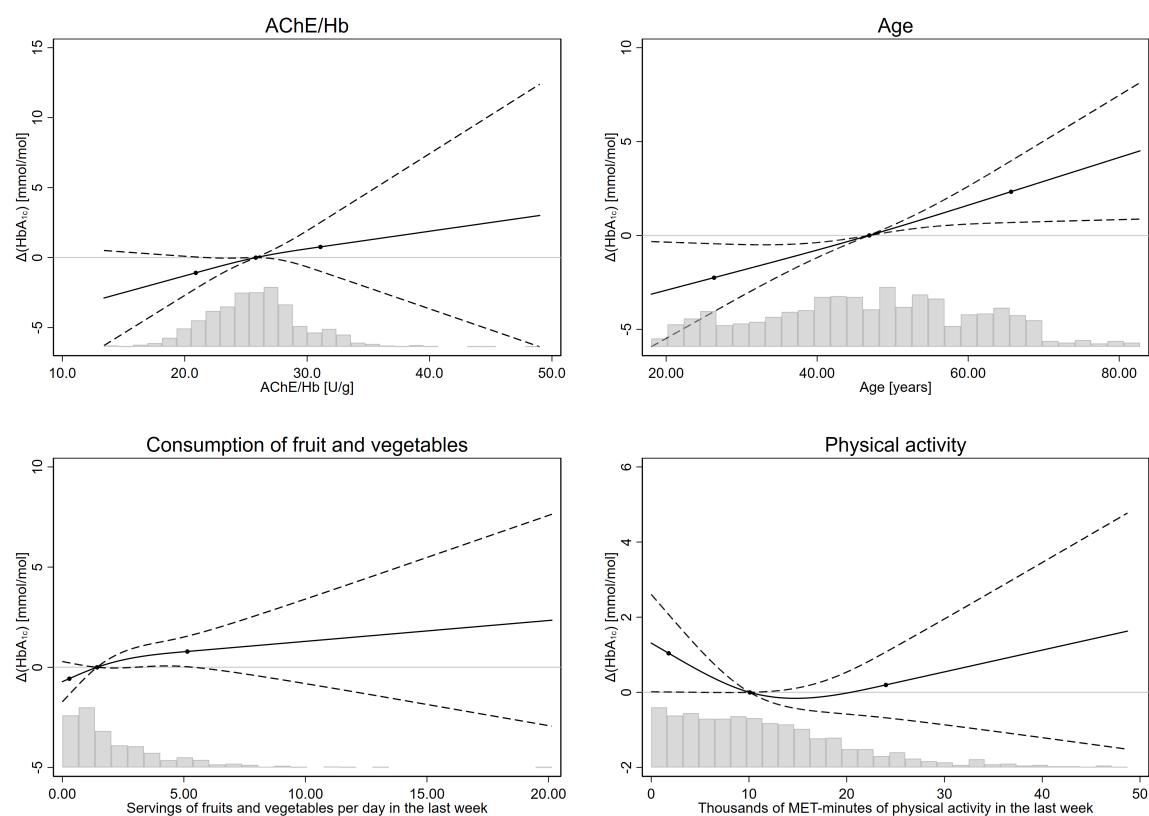
Model 07

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
20.90	-1.087 [-2.219 ; 0.046]
25.80	0.000 [0.000 ; 0.000]
25.80	0 [ref.]
31.08	0.766 [-0.980 ; 2.512]

Age

Value	Outcome estimate [CI]
26.34	-2.246 [-4.052 ; -0.441]
46.84	0 [ref.]
46.90	0.006 [0.004 ; 0.009]
65.67	2.331 [0.689 ; 3.973]

Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.29	-0.567 [-1.355 ; 0.222]
1.43	0 [ref.]
1.43	0.000 [0.000 ; 0.000]
5.14	0.789 [0.027 ; 1.551]

Physical activity

Value	Outcome estimate [CI]
1.78	1.041 [0.010 ; 2.073]
10.08	0.000 [0.000 ; 0.000]
10.08	0 [ref.]
24.00	0.197 [-0.679 ; 1.073]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.739 [-4.300 ; -1.177]
Grams of alcohol in the last week	-0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.673 [-1.522 ; 0.175]

## Analysis specification

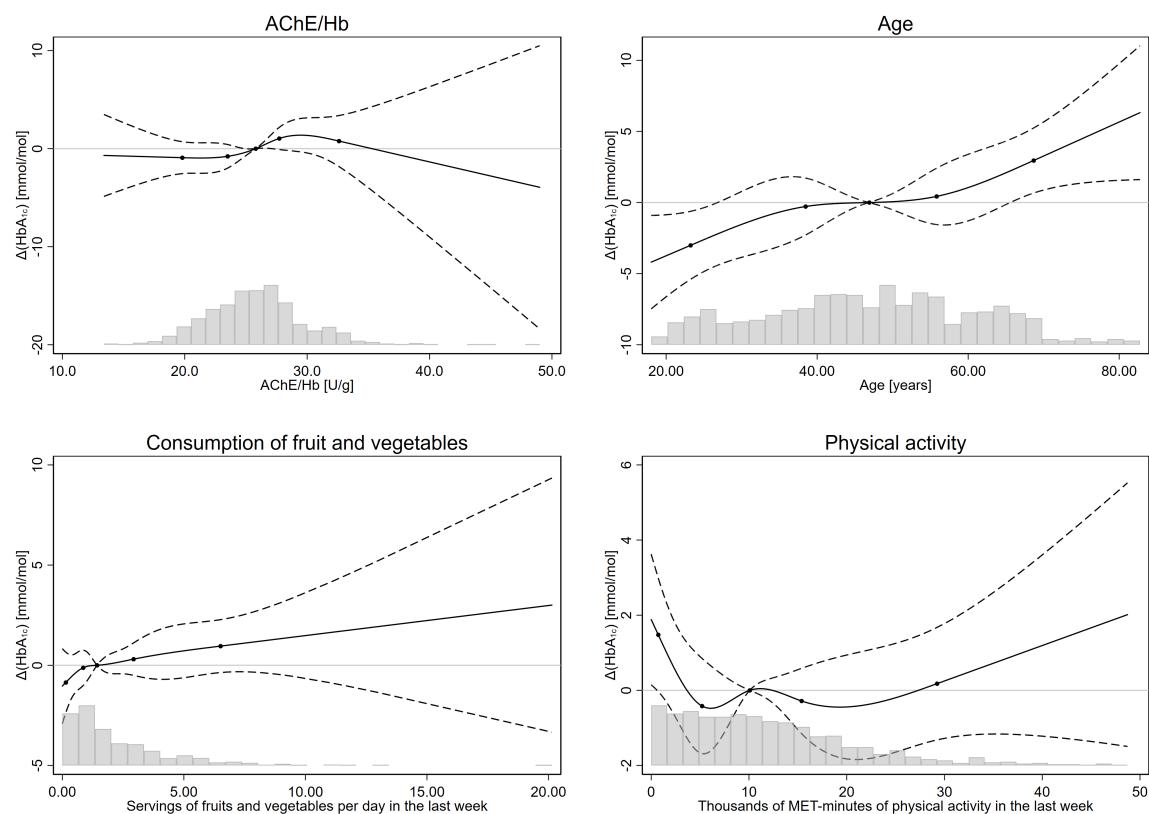
Model 08

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

#### AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.922 [-2.551 ; 0.707]
23.50	-0.784 [-1.988 ; 0.420]
25.80	0.000 [0.000 ; 0.000]
25.80	0 [ref.]
27.72	1.037 [-0.092 ; 2.166]
32.60	0.773 [-1.830 ; 3.376]

#### Age

Value	Outcome estimate [CI]
23.23	-3.008 [-5.400 ; -0.617]
38.47	-0.280 [-2.282 ; 1.723]
46.84	0 [ref.]
46.90	0.001 [-0.008 ; 0.009]
55.82	0.433 [-1.547 ; 2.413]
68.67	2.954 [0.666 ; 5.242]

#### Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.858 [-2.371 ; 0.656]
0.86	-0.122 [-1.014 ; 0.769]
1.43	0 [ref.]
1.43	0.000 [0.000 ; 0.000]
2.93	0.306 [-0.504 ; 1.116]
6.51	0.957 [-0.363 ; 2.277]

#### Physical activity

Value	Outcome estimate [CI]
0.72	1.480 [-0.032 ; 2.991]
5.20	-0.418 [-1.685 ; 0.849]
10.08	0.000 [0.000 ; 0.000]
10.08	0 [ref.]
15.38	-0.283 [-1.151 ; 0.585]
29.24	0.178 [-1.321 ; 1.676]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.940 [-4.546 ; -1.333]
Grams of alcohol in the last week	0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.683 [-1.537 ; 0.170]

## Analysis specification

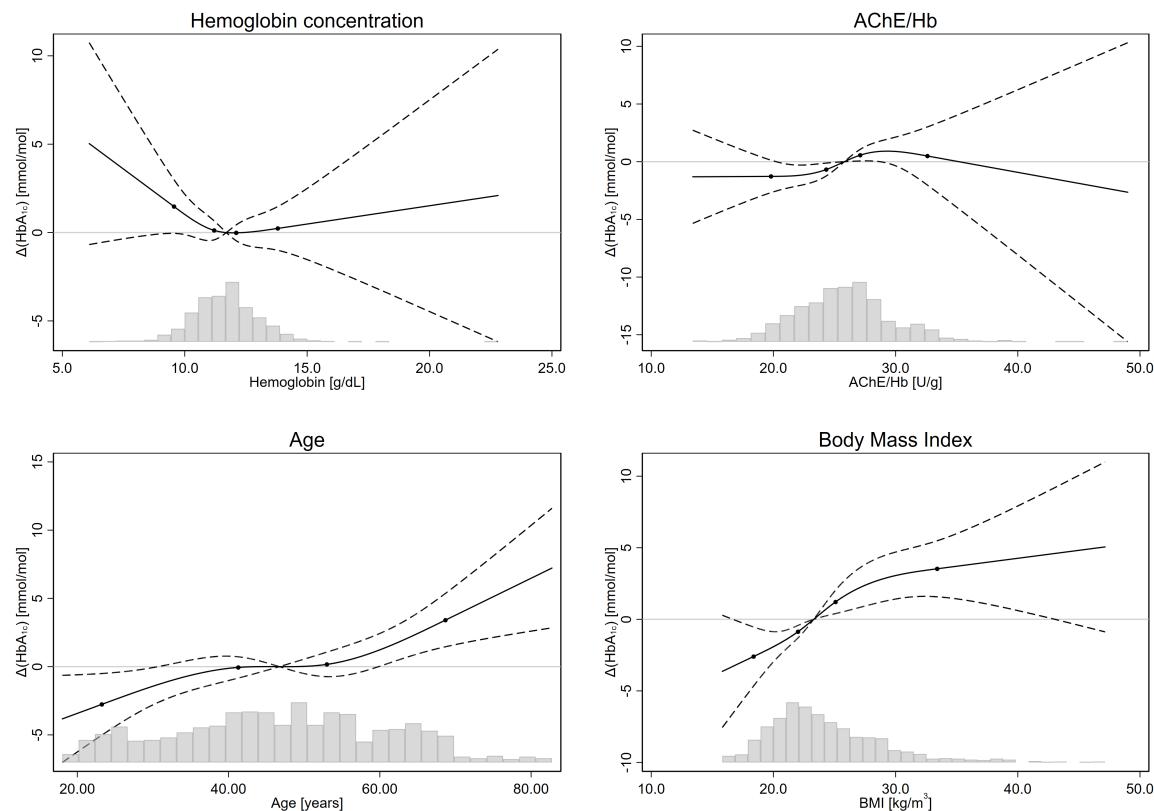
Model 10

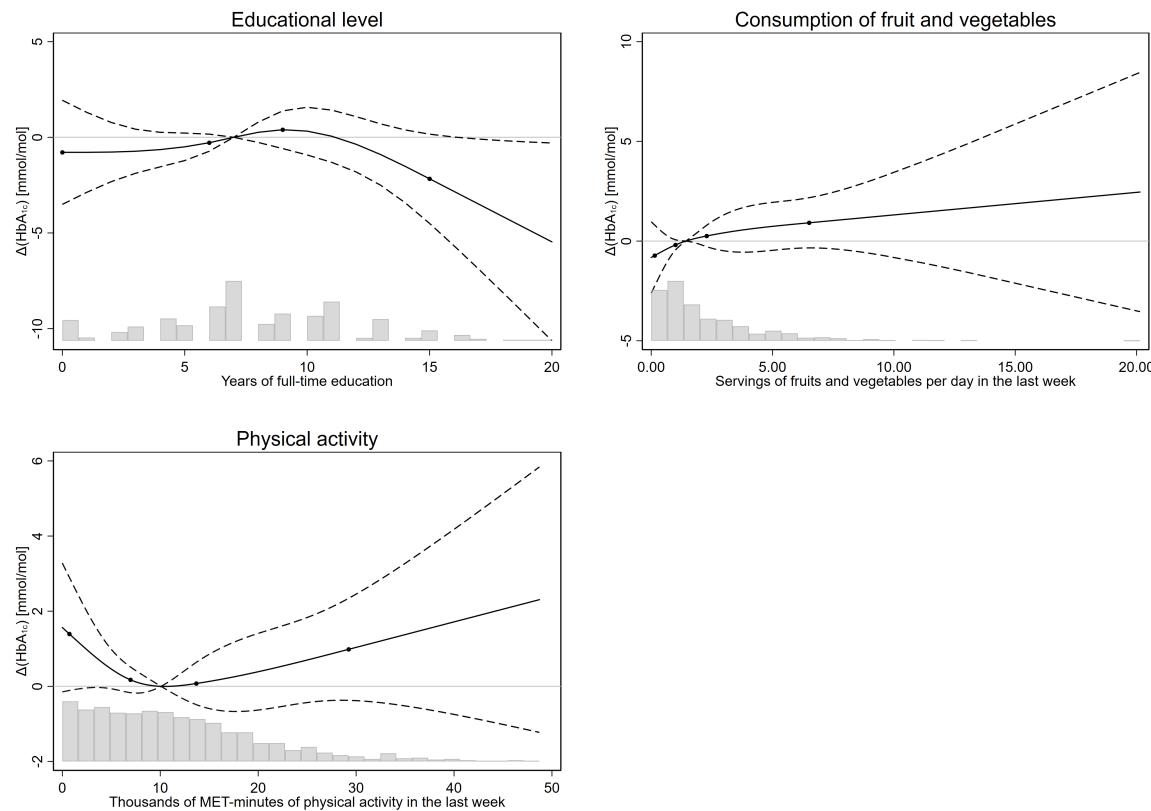
Outcome: HbA<sub>1c</sub>

Covariate adjustment: Extended + hemoglobin

Number of observations in model: 1,037

### Regression results for variables modeled using splines





#### Numerical results for variables modeled using splines (see graphs for units)

##### Hemoglobin concentration

Value	Outcome estimate [CI]
9.56	1.474 [-0.047 ; 2.995]
11.20	0.124 [-0.414 ; 0.663]
11.70	0 [ref.]
12.10	-0.014 [-0.460 ; 0.432]
13.80	0.234 [-1.003 ; 1.471]

##### AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.273 [-2.682 ; 0.135]
24.32	-0.679 [-1.239 ; -0.120]
25.80	0 [ref.]
27.10	0.565 [0.062 ; 1.067]
32.60	0.494 [-2.026 ; 3.013]

##### Age

Value	Outcome estimate [CI]
23.23	-2.764 [-5.025 ; -0.504]
41.28	-0.058 [-0.838 ; 0.723]
46.71	0 [ref.]
52.99	0.166 [-0.732 ; 1.064]
68.67	3.409 [1.456 ; 5.362]

##### Body Mass Index

Value	Outcome estimate [CI]
18.37	-2.600 [-4.665 ; -0.535]
22.01	-0.866 [-1.304 ; -0.427]
23.30	0 [ref.]
25.08	1.214 [0.399 ; 2.029]
33.40	3.530 [1.574 ; 5.486]

##### Educational level

Value	Outcome estimate [CI]
0.00	-0.785 [-3.506 ; 1.936]
6.00	-0.282 [-0.730 ; 0.166]
7.00	0 [ref.]
9.00	0.397 [-0.587 ; 1.381]
15.00	-2.168 [-4.501 ; 0.165]

##### Physical activity

Value	Outcome estimate [CI]
0.72	1.395 [-0.111 ; 2.900]
6.96	0.173 [-0.169 ; 0.516]
10.08	0 [ref.]
13.68	0.076 [-0.487 ; 0.638]
29.24	0.985 [-0.374 ; 2.344]

##### Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.725 [-2.254 ; 0.803]
1.00	-0.192 [-0.449 ; 0.066]
1.43	0 [ref.]
2.29	0.256 [-0.280 ; 0.793]
6.51	0.917 [-0.342 ; 2.176]

#### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-0.493 [-2.407 ; 1.421]
Grams of alcohol in the last week	0.001 [-0.003 ; 0.005]
Grams of tobacco per day in the last week	-0.806 [-1.641 ; 0.030]

## Analysis specification

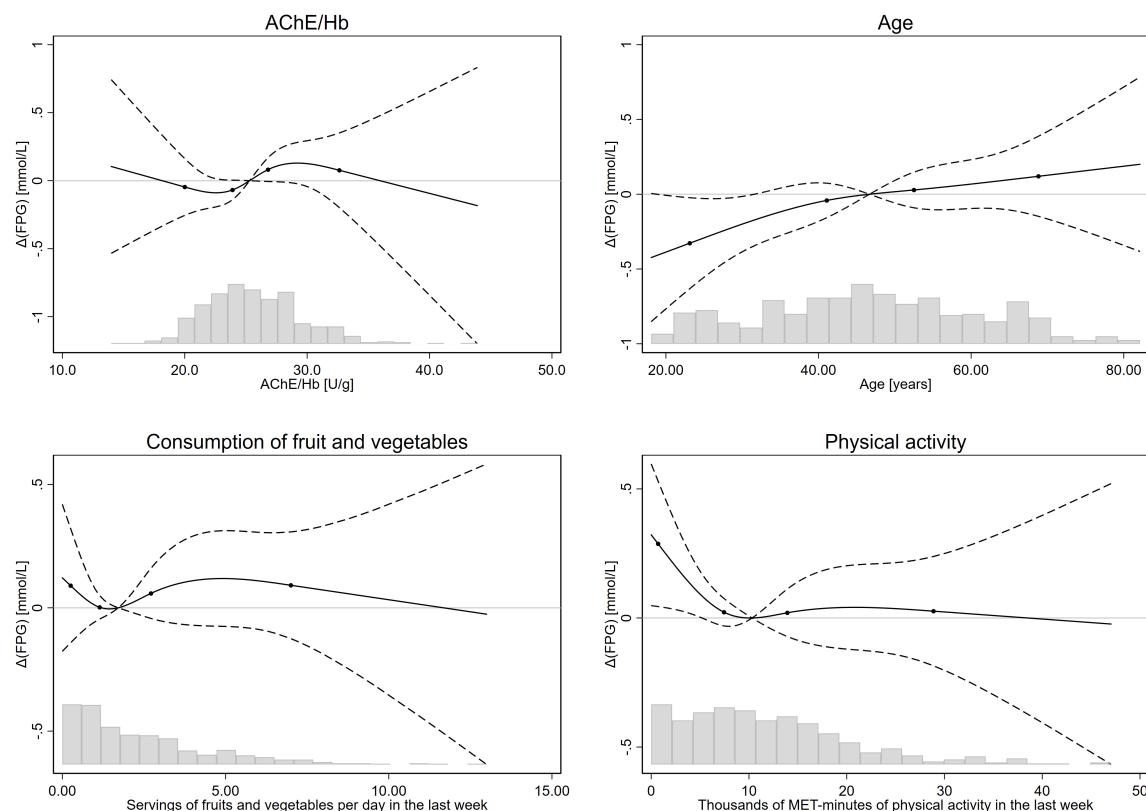
### Model 11

Outcome: Fasting plasma glucose (FPG)

Covariate adjustment: Basic

Number of observations in model: 518

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb	
Value	Outcome estimate [CI]
20.00	-0.046 [-0.255 ; 0.163]
23.90	-0.068 [-0.140 ; 0.004]
25.30	0 [ref.]
26.80	0.081 [-0.006 ; 0.168]
32.63	0.077 [-0.198 ; 0.351]

Age	
Value	Outcome estimate [CI]
23.12	-0.328 [-0.632 ; -0.023]
41.08	-0.042 [-0.157 ; 0.074]
46.68	0 [ref.]
52.50	0.028 [-0.090 ; 0.147]
68.82	0.120 [-0.148 ; 0.388]

Consumption of fruit and vegetables	
Value	Outcome estimate [CI]
0.25	0.090 [-0.142 ; 0.322]
1.14	0.002 [-0.046 ; 0.050]
1.71	0 [ref.]
2.71	0.058 [-0.043 ; 0.160]
7.00	0.091 [-0.125 ; 0.308]

Physical activity	
Value	Outcome estimate [CI]
0.70	0.288 [0.044 ; 0.531]
7.44	0.023 [-0.031 ; 0.076]
10.32	0 [ref.]
13.92	0.020 [-0.072 ; 0.112]
28.87	0.026 [-0.185 ; 0.238]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-0.018 [-0.232 ; 0.196]
Grams of alcohol in the last week	-0.000 [-0.002 ; 0.001]
Grams of tobacco per day in the last week	-0.050 [-0.205 ; 0.105]

## Analysis specification

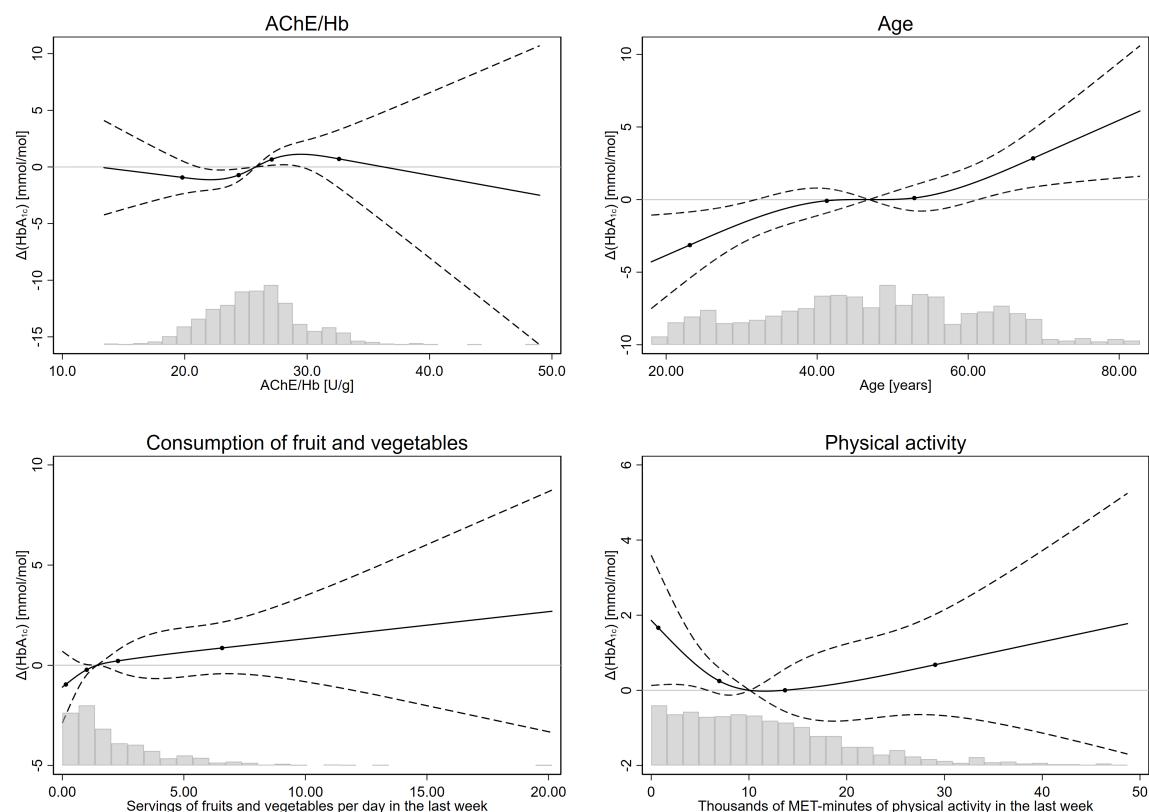
Model 12

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic

Number of observations in model: 1,032

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-0.921 [-2.374 ; 0.531]
24.40	-0.714 [-1.259 ; -0.169]
25.80	0 [ref.]
27.10	0.668 [0.148 ; 1.187]
32.60	0.713 [-1.853 ; 3.280]

Age

Value	Outcome estimate [CI]
23.13	-3.132 [-5.415 ; -0.848]
41.27	-0.081 [-0.919 ; 0.758]
46.87	0 [ref.]
52.86	0.112 [-0.777 ; 1.000]
68.59	2.846 [0.855 ; 4.837]

Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.955 [-2.482 ; 0.572]
1.00	-0.221 [-0.479 ; 0.037]
1.43	0 [ref.]
2.29	0.220 [-0.322 ; 0.762]
6.57	0.865 [-0.420 ; 2.149]

Physical activity

Value	Outcome estimate [CI]
0.72	1.667 [0.144 ; 3.189]
6.96	0.250 [-0.095 ; 0.595]
10.08	0 [ref.]
13.68	0.003 [-0.561 ; 0.568]
29.04	0.682 [-0.657 ; 2.020]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.872 [-4.470 ; -1.273]
Grams of alcohol in the last week	0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.688 [-1.540 ; 0.164]

## Analysis specification

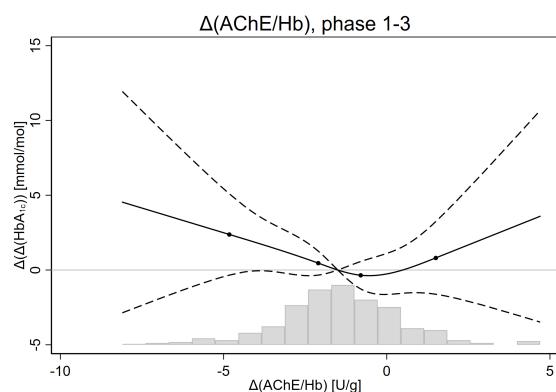
Model 13

Outcome:  $\Delta(\text{HbA}_{1c})$ , phase 1-3

Unadjusted

Number of observations in model: 354

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

$\Delta(\text{AChE}/\text{Hb})$ , phase 1-3

Value	Outcome estimate [CI]
-4.83	2.379 [-0.345 ; 5.102]
-2.10	0.462 [-0.341 ; 1.266]
-1.50	0 [ref.]
-0.80	-0.350 [-1.265 ; 0.565]
1.50	0.808 [-1.620 ; 3.237]

## Analysis specification

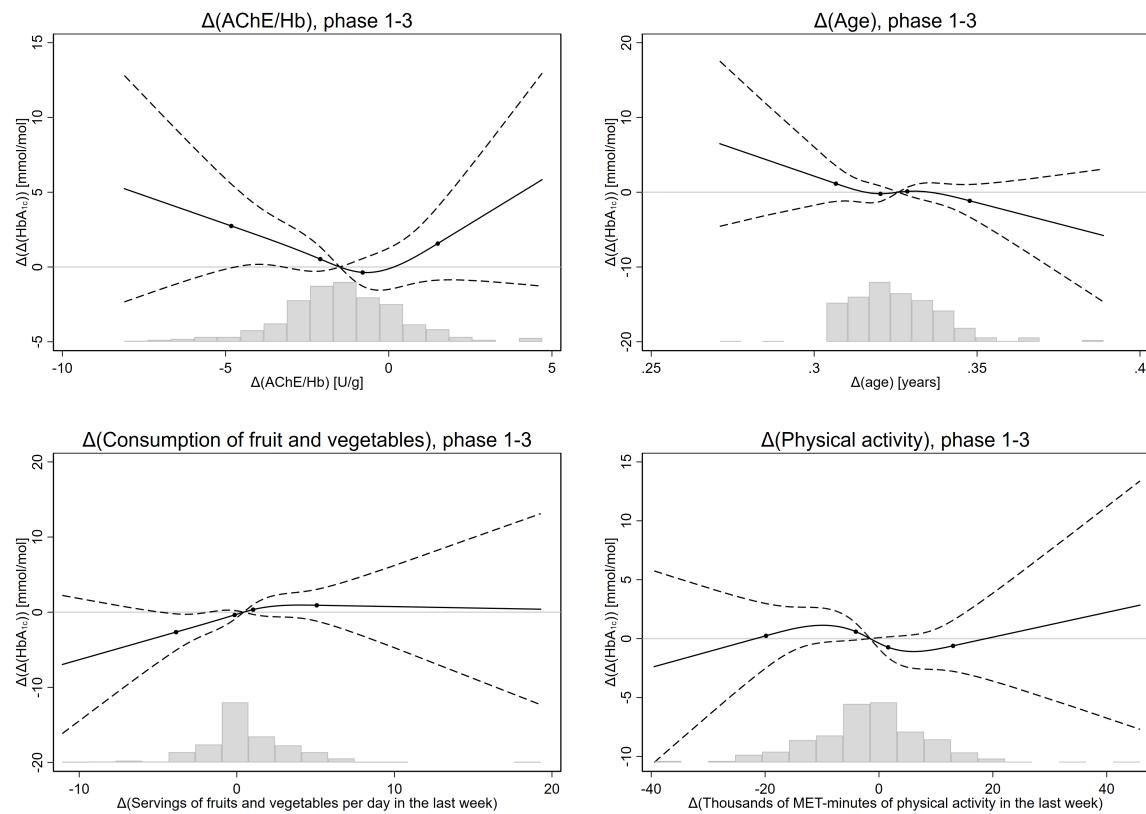
Model 13

Outcome:  $\Delta(\text{HbA}_{1c})$ , phase 1-3

Covariate adjustment: Basic

Number of observations in model: 337

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

$\Delta(\text{AChE/Hb})$ , phase 1-3

Value	Outcome estimate [CI]
-4.83	2.748 [-0.055 ; 5.550]
-2.10	0.532 [-0.277 ; 1.342]
-1.50	0 [ref.]
-0.80	-0.361 [-1.282 ; 0.559]
1.50	1.569 [-0.877 ; 4.016]

$\Delta(\text{Age})$ , phase 1-3

Value	Outcome estimate [CI]
0.31	1.160 [-1.228 ; 3.547]
0.32	-0.206 [-1.254 ; 0.842]
0.33	0 [ref.]
0.33	0.120 [-0.427 ; 0.667]
0.35	-1.139 [-3.313 ; 1.035]

$\Delta(\text{Consumption of fruit and vegetables})$ , phase 1-3

Value	Outcome estimate [CI]
-3.86	-2.647 [-5.067 ; -0.227]
-0.14	-0.366 [-0.959 ; 0.228]
0.43	0 [ref.]
1.04	0.346 [-0.300 ; 0.991]
5.07	0.924 [-1.189 ; 3.037]

$\Delta(\text{Physical activity})$ , phase 1-3

Value	Outcome estimate [CI]
-19.85	0.243 [-2.490 ; 2.976]
-4.07	0.595 [-0.120 ; 1.309]
-1.56	0 [ref.]
1.60	-0.729 [-1.607 ; 0.150]
13.00	-0.610 [-2.779 ; 1.558]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
$\Delta(\text{Alcohol consumption in the last week})$ [grams]	-0.001 [-0.006 ; 0.005]
$\Delta(\text{Grams of tobacco per day in the last week})$	-1.786 [-3.235 ; -0.337]

## Analysis specification

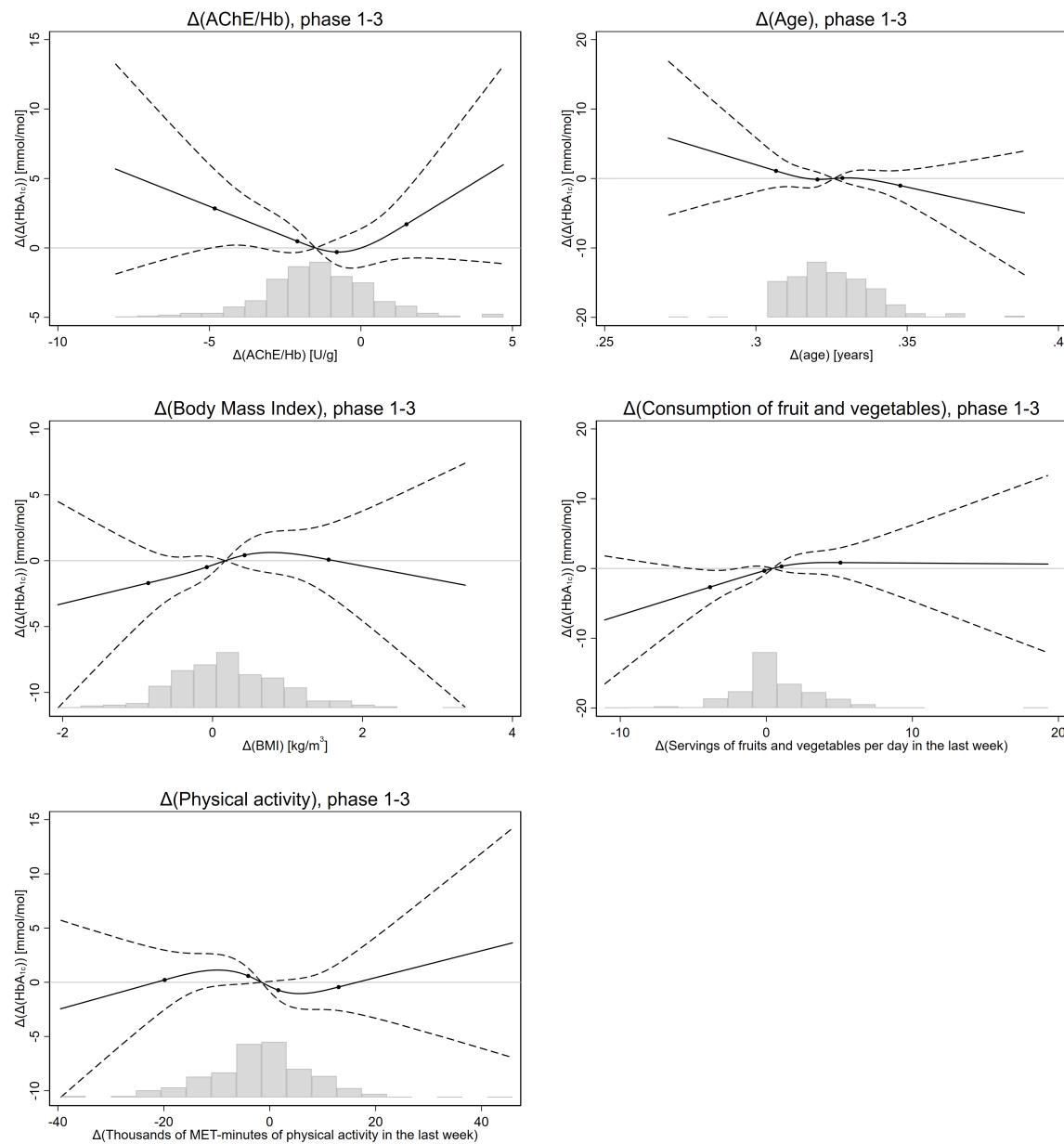
Model 13

Outcome:  $\Delta(\text{HbA}_{1c})$ , phase 1-3

Covariate adjustment: Extended

Number of observations in model: 336

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units) $\Delta(\text{AChE/Hb})$ , phase 1-3

Value	Outcome estimate [CI]
-4.83	2.846 [0.051 ; 5.642]
-2.10	0.485 [-0.325 ; 1.295]
-1.50	0 [ref.]
-0.80	-0.294 [-1.217 ; 0.628]
1.50	1.707 [-0.743 ; 4.156]

 $\Delta(\text{Age})$ , phase 1-3

Value	Outcome estimate [CI]
0.31	1.103 [-1.280 ; 3.486]
0.32	-0.136 [-1.200 ; 0.929]
0.33	0 [ref.]
0.33	0.085 [-0.471 ; 0.640]
0.35	-1.020 [-3.194 ; 1.155]

 $\Delta(\text{Body Mass Index})$ , phase 1-3

Value	Outcome estimate [CI]
-0.86	-1.695 [-4.229 ; 0.839]
-0.08	-0.485 [-1.312 ; 0.341]
0.17	0 [ref.]
0.43	0.419 [-0.526 ; 1.364]
1.55	0.081 [-2.623 ; 2.786]

 $\Delta(\text{Consumption of fruit and vegetables})$ , phase 1-3

Value	Outcome estimate [CI]
-3.86	-2.671 [-5.084 ; -0.258]
-0.14	-0.325 [-0.920 ; 0.269]
0.43	0 [ref.]
1.04	0.300 [-0.347 ; 0.946]
5.07	0.846 [-1.268 ; 2.960]

 $\Delta(\text{Physical activity})$ , phase 1-3

Value	Outcome estimate [CI]
-19.85	0.219 [-2.524 ; 2.962]
-4.07	0.594 [-0.119 ; 1.307]
-1.56	0 [ref.]
1.60	-0.719 [-1.596 ; 0.158]
13.00	-0.436 [-2.611 ; 1.739]

Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
$\Delta(\text{Alcohol consumption in the last week})$ [grams]	-0.001 [-0.006 ; 0.005]
$\Delta(\text{Grams of tobacco per day in the last week})$	-1.859 [-3.315 ; -0.403]

## Analysis specification

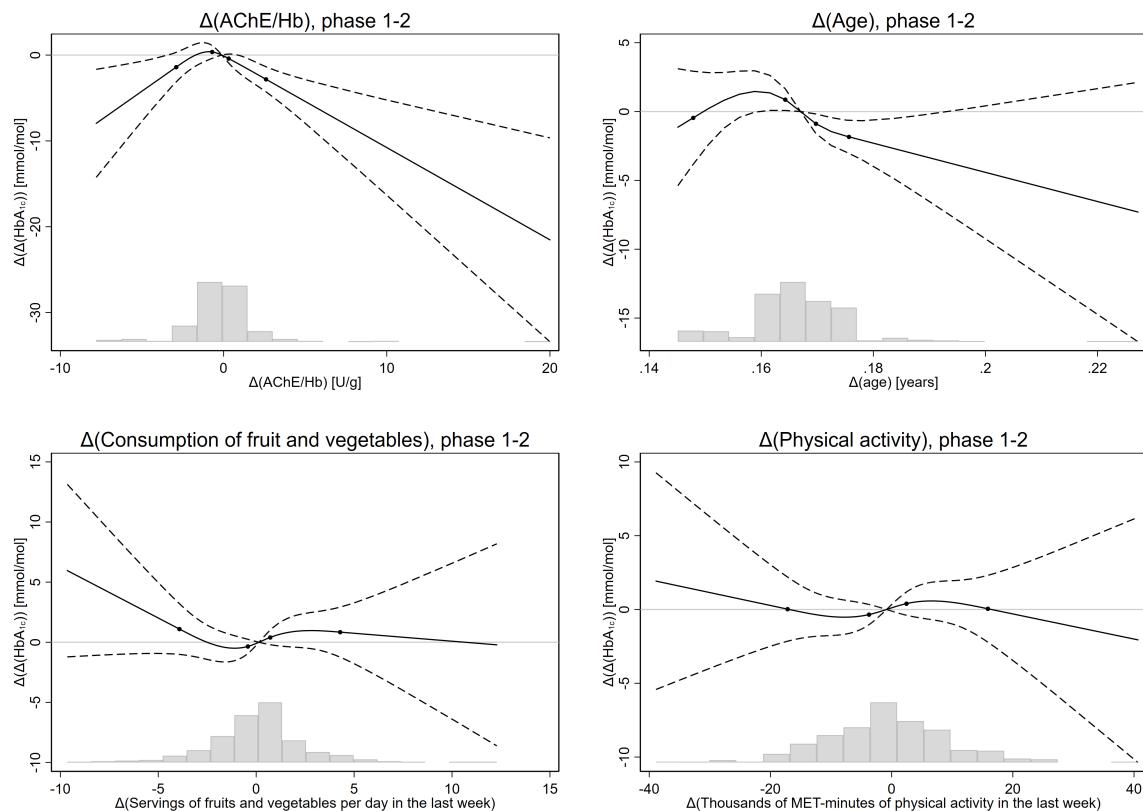
Model 14

Outcome:  $\Delta(\text{HbA}_{1c})$ , phase 1-2

Covariate adjustment: Basic

Number of observations in model: 334

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

$\Delta(\text{AChE/Hb})$ , phase 1-2

Value	Outcome estimate [CI]
-2.90	-1.401 [-3.126 ; 0.324]
-0.70	0.368 [-0.383 ; 1.119]
-0.10	0 [ref.]
0.31	-0.398 [-0.916 ; 0.120]
2.60	-2.817 [-4.279 ; -1.355]

$\Delta(\text{Age})$ , phase 1-2

Value	Outcome estimate [CI]
0.15	-0.456 [-3.836 ; 2.925]
0.16	0.867 [0.078 ; 1.656]
0.17	0 [ref.]
0.17	-0.885 [-1.593 ; -0.177]
0.18	-1.837 [-3.040 ; -0.635]

$\Delta(\text{Consumption of fruit and vegetables})$ , phase 1-2

Value	Outcome estimate [CI]
-3.92	1.101 [-1.011 ; 3.213]
-0.43	-0.349 [-0.944 ; 0.246]
0.14	0 [ref.]
0.71	0.401 [-0.204 ; 1.005]
4.29	0.841 [-1.241 ; 2.924]

$\Delta(\text{Physical activity})$ , phase 1-2

Value	Outcome estimate [CI]
-17.17	0.025 [-2.150 ; 2.200]
-3.73	-0.344 [-1.029 ; 0.340]
-0.84	0 [ref.]
2.44	0.397 [-0.389 ; 1.184]
15.87	0.052 [-2.212 ; 2.315]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
$\Delta(\text{Alcohol consumption in the last week})$ [grams]	0.001 [-0.004 ; 0.006]
$\Delta(\text{Grams of tobacco per day in the last week})$	0.133 [-1.365 ; 1.632]

## Analysis specification

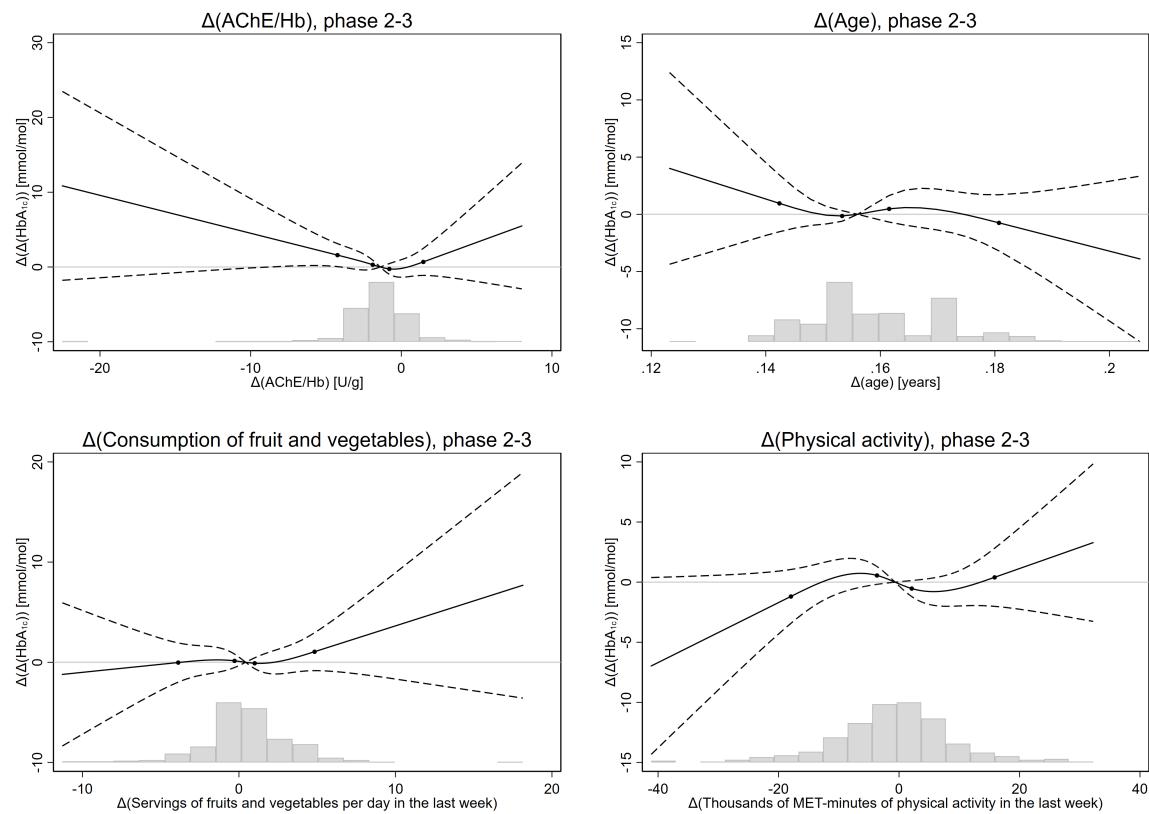
Model 15

Outcome:  $\Delta(\text{HbA}_{1c})$ , phase 2-3

Covariate adjustment: Basic

Number of observations in model: 332

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

$\Delta(\text{AChE/Hb})$ , phase 2-3

Value	Outcome estimate [CI]
-4.24	1.593 [0.053 ; 3.133]
-1.90	0.310 [-0.297 ; 0.917]
-1.40	0 [ref.]
-0.80	-0.255 [-0.963 ; 0.454]
1.46	0.685 [-1.126 ; 2.496]

$\Delta(\text{Age})$ , phase 2-3

Value	Outcome estimate [CI]
0.14	0.962 [-1.523 ; 3.447]
0.15	-0.142 [-0.606 ; 0.322]
0.16	0 [ref.]
0.16	0.483 [-0.677 ; 1.644]
0.18	-0.741 [-3.192 ; 1.709]

$\Delta(\text{Consumption of fruit and vegetables})$ , phase 2-3

Value	Outcome estimate [CI]
-3.89	-0.025 [-1.988 ; 1.937]
-0.29	0.149 [-0.525 ; 0.823]
0.43	0 [ref.]
1.00	-0.093 [-0.628 ; 0.443]
4.83	1.057 [-0.834 ; 2.948]

$\Delta(\text{Physical activity})$ , phase 2-3

Value	Outcome estimate [CI]
-17.96	-1.191 [-3.434 ; 1.053]
-3.66	0.558 [-0.184 ; 1.300]
-0.66	0 [ref.]
2.09	-0.530 [-1.195 ; 0.135]
15.86	0.402 [-2.014 ; 2.817]

### Regression results for categorical and linear variables

Parameter	Regression coef. [95% CI]
$\Delta(\text{Alcohol consumption in the last week})$ [grams]	0.002 [-0.016 ; 0.021]
$\Delta(\text{Grams of tobacco per day in the last week})$	-4.842 [-7.750 ; -1.935]

## Analysis specification

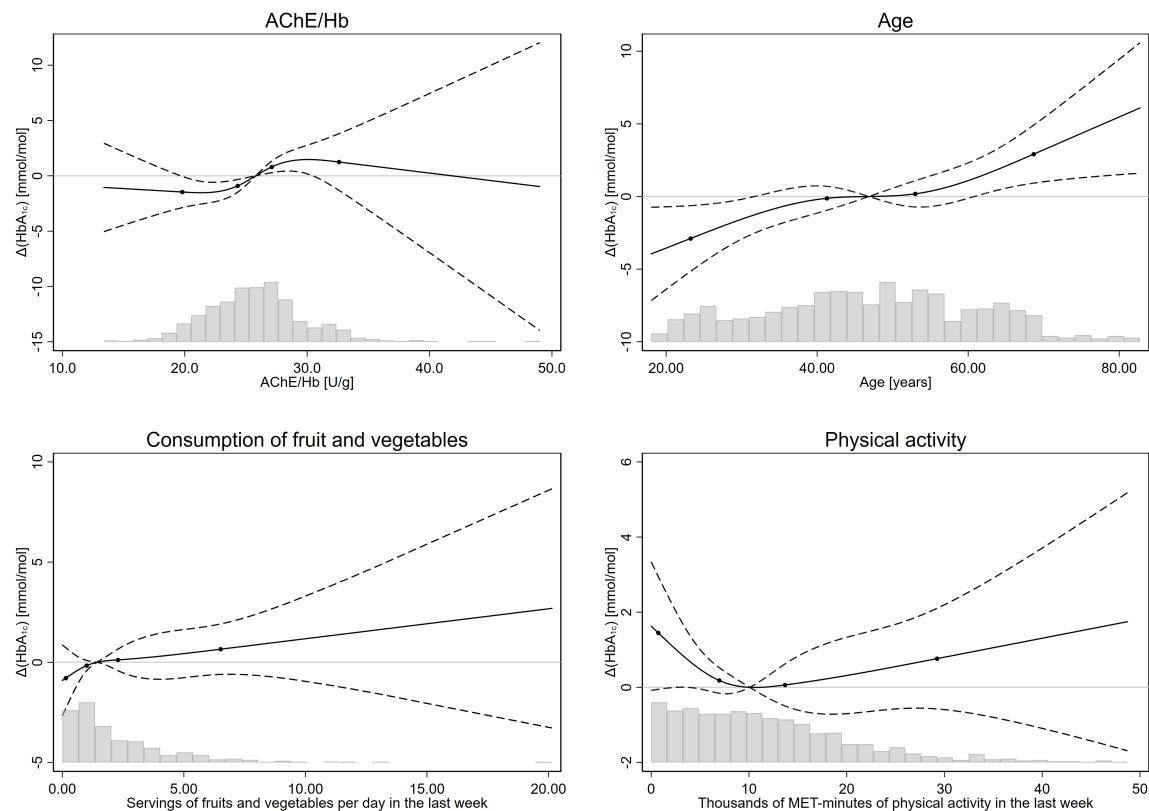
Model 16

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Basic + project phase

Number of observations in model: 1,044

### Regression results for variables modeled using splines



### Numerical results for variables modeled using splines (see graphs for units)

AChE/Hb

Value	Outcome estimate [CI]
19.80	-1.464 [-2.878 ; -0.049]
24.32	-0.911 [-1.486 ; -0.336]
25.80	0 [ref.]
27.10	0.802 [0.284 ; 1.320]
32.60	1.247 [-1.315 ; 3.808]

Age

Value	Outcome estimate [CI]
23.23	-2.892 [-5.155 ; -0.629]
41.28	-0.126 [-0.950 ; 0.699]
46.84	0 [ref.]
52.99	0.183 [-0.721 ; 1.088]
68.67	2.913 [0.919 ; 4.908]

Consumption of fruit and vegetables

Value	Outcome estimate [CI]
0.14	-0.789 [-2.305 ; 0.728]
1.00	-0.165 [-0.422 ; 0.091]
1.43	0 [ref.]
2.29	0.119 [-0.417 ; 0.655]
6.51	0.653 [-0.606 ; 1.912]

Physical activity

Value	Outcome estimate [CI]
0.72	1.450 [-0.053 ; 2.952]
6.96	0.183 [-0.157 ; 0.523]
10.08	0 [ref.]
13.68	0.063 [-0.495 ; 0.621]
29.24	0.764 [-0.577 ; 2.105]

**Regression results for categorical and linear variables**

Parameter	Regression coef. [95% CI]
Female sex	0 (ref.)
Male sex	-2.976 [-4.565 ; -1.387]
Grams of alcohol in the last week	0.000 [-0.004 ; 0.004]
Grams of tobacco per day in the last week	-0.686 [-1.534 ; 0.163]
Phase 1	0 (ref.)
Phase 2	-0.609 [-1.484 ; 0.267]
Phase 3	0.990 [0.074 ; 1.906]

## Analysis specification

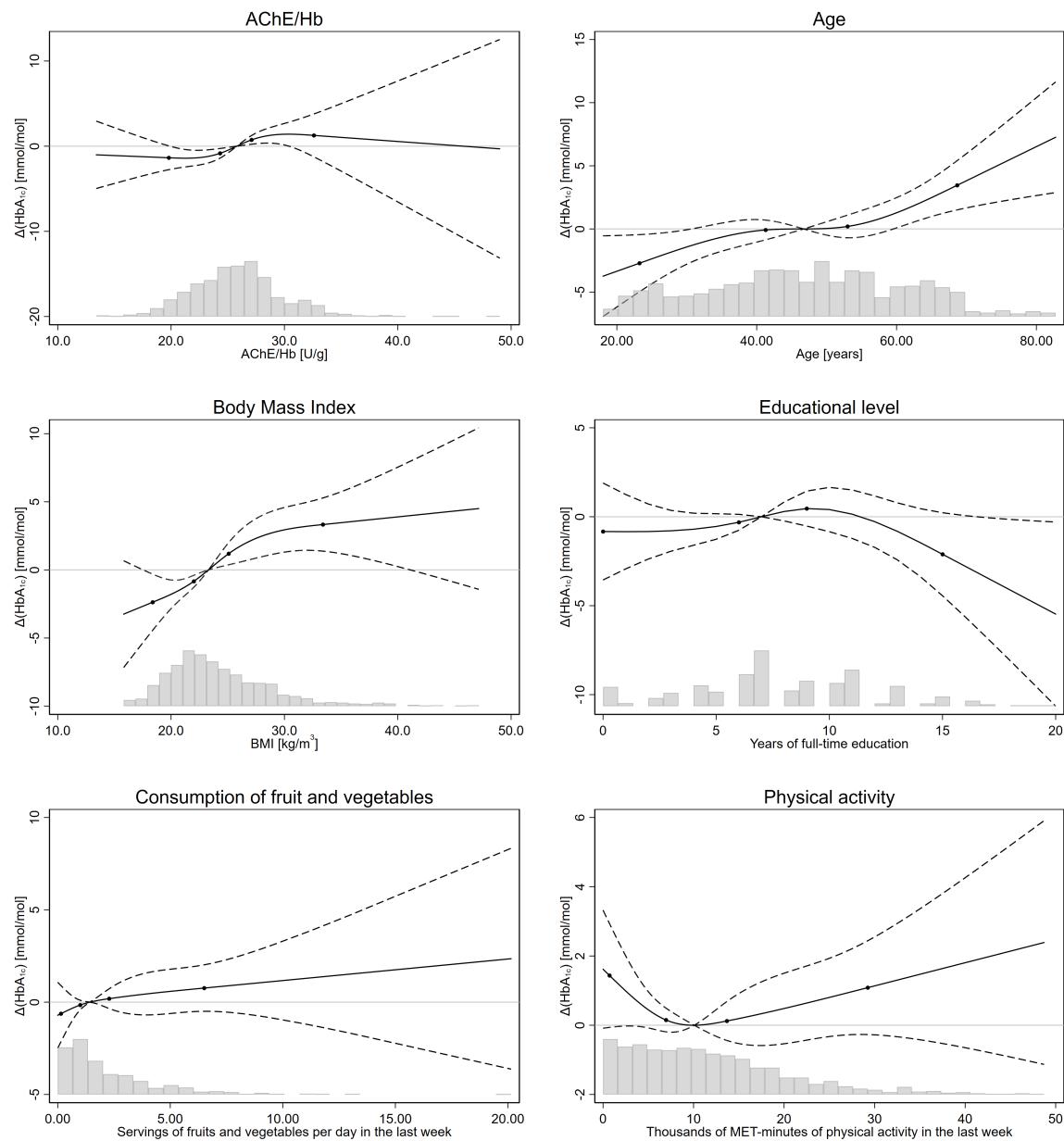
Model 16

Outcome: HbA<sub>1c</sub>

Covariate adjustment: Extended + project phase

Number of observations in model: 1,037

### Regression results for variables modeled using splines



Numerical results for variables modeled using splines (see graphs for units)

## AChE/Hb

<b>Value</b>	<b>Outcome estimate [CI]</b>
19.80	-1.360 [-2.757 ; 0.037]
24.32	-0.836 [-1.403 ; -0.270]
25.80	0 [ref.]
27.10	0.741 [0.231 ; 1.251]
32.60	1.266 [-1.251 ; 3.783]

## Body Mass Index

<b>Value</b>	<b>Outcome estimate [CI]</b>
18.37	-2.373 [-4.437 ; -0.309]
22.01	-0.834 [-1.273 ; -0.396]
23.30	0 [ref.]
25.08	1.191 [0.376 ; 2.006]
33.40	3.330 [1.378 ; 5.282]

## Consumption of fruit and vegetables

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.14	-0.623 [-2.147 ; 0.900]
1.00	-0.156 [-0.414 ; 0.102]
1.43	0 [ref.]
2.29	0.189 [-0.346 ; 0.724]
6.51	0.763 [-0.495 ; 2.022]

## Physical activity

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.72	1.436 [-0.062 ; 2.934]
6.96	0.151 [-0.191 ; 0.493]
10.08	0 [ref.]
13.68	0.123 [-0.439 ; 0.685]
29.24	1.085 [-0.270 ; 2.441]

## Age

<b>Value</b>	<b>Outcome estimate [CI]</b>
23.23	-2.713 [-4.976 ; -0.451]
41.28	-0.080 [-0.860 ; 0.701]
46.71	0 [ref.]
52.99	0.199 [-0.698 ; 1.096]
68.67	3.457 [1.508 ; 5.406]

## Educational level

<b>Value</b>	<b>Outcome estimate [CI]</b>
0.00	-0.831 [-3.555 ; 1.894]
6.00	-0.312 [-0.759 ; 0.136]
7.00	0 [ref.]
9.00	0.460 [-0.523 ; 1.443]
15.00	-2.108 [-4.442 ; 0.225]

Regression results for categorical and linear variables

<b>Parameter</b>	<b>Regression coef. [95% CI]</b>
Female sex	0 (ref.)
Male sex	-0.907 [-2.627 ; 0.814]
Grams of alcohol in the last week	0.001 [-0.003 ; 0.005]
Grams of tobacco per day in the last week	-0.789 [-1.623 ; 0.045]
Phase 1	0 (ref.)
Phase 2	-0.532 [-1.413 ; 0.349]
Phase 3	0.916 [-0.003 ; 1.834]