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## Dietary acrylamide intake during pregnancy and postnatal growth and obesity: Results from the Norwegian Mother and Child Cohort Study (MoBa)

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1 **Title:** Dietary acrylamide intake during pregnancy and postnatal growth and obesity: results  
2 from the Norwegian Mother and Child Cohort Study (MoBa)

3

4 **Authors:**

5 Manik Kadawathagedara<sup>a,b</sup>, Jérémie Botton<sup>a,c</sup>, Blandine de Lauzon-Guillain<sup>a,b</sup>, Helle  
6 Margrete Meltzer<sup>d</sup>, Jan Alexander<sup>d</sup>, Anne Lise Brantsaeter<sup>e</sup>, Margaretha Haugen<sup>e</sup>, Eleni  
7 Papadopoulou<sup>e</sup>

8

9 **Affiliations:**

10 <sup>a</sup> INSERM, UMR1153 Epidemiology and Biostatistics Sorbonne Paris Cité Center (CRESS), Early  
11 determinants of the child's health and development Team (ORCHAD), Paris, F-75014 France.

12 <sup>b</sup> Paris Descartes University, Paris, France

13 <sup>c</sup> Univ. Paris-Sud, Université Paris-Saclay, F-92296, Châtenay-Malabry, France

14 <sup>d</sup> Norwegian Institute of Public Health, Oslo, Norway

15 <sup>e</sup> Department of Environmental Exposure and Epidemiology, Division of Infection Control and  
16 Environmental Health, Norwegian Institute of Public Health, Oslo, Norway

17

18 **Corresponding author:**

19 Manik Kadawathagedara

20 INSERM, CRESS, Team 6 ORCHAD

21 16 avenue Paul Vaillant Couturier, 94807 Villejuif Cedex, France

22 Phone number +33 145595101

23 Email: [manik.kadawathagedara@inserm.fr](mailto:manik.kadawathagedara@inserm.fr)

24

25       **Abstract**

26       **Background:** Prenatal acrylamide exposure has been negatively associated with fetal  
27 growth but the association with child growth is unknown.

28       **Objectives:** We studied the association between prenatal acrylamide exposure and child  
29 postnatal growth up to 8 years in the Norwegian Mother and Child Cohort Study (MoBa).

30       **Methods:** In 51,952 mother-child pairs from MoBa, acrylamide intake during pregnancy  
31 was estimated by combining maternal food intake with food concentrations of acrylamide.  
32 Mothers reported their child's weight and length/height up to 11 times between 6 weeks  
33 and 8 years. Weight and height growth trajectories were modelled using Jenss-Bayley's  
34 growth model. Logistic regression models were used to study the association with  
35 overweight/obese status at 3, 5 and 8 years, as identified using the International Obesity  
36 Task Force cut-offs. Linear mixed-effect models were used to explore associations with  
37 overall growth.

38       **Results:** At 3 years, the adjusted odds ratios (95% Confidence Intervals (CI)) of being  
39 overweight/obese were 1.10 (1.02, 1.20), 1.12 (1.04, 1.22) and 1.21 (1.11, 1.31) by  
40 increasing prenatal acrylamide exposure quartile. Similar dose-response associations were  
41 found at 5 and 8 years. Acrylamide intake during pregnancy was associated with higher  
42 weight growth velocity in childhood. Children exposed at the highest level had 22g (95%CI: 8,  
43 37), 57g (95%CI: 32, 81), and 194g (95%CI: 110, 278) higher weight at 0.5, 2, and 8 years,  
44 respectively, compared to their low exposed peers.

45       **Conclusions:** Children prenatally exposed to acrylamide in the highest quartile  
46 experienced a moderate increase in weight growth velocity during early childhood that  
47 resulted in a moderately increased prevalence of overweight/obesity compared to peers in

48 the lowest quartile. Our study is the first to link prenatal acrylamide exposure and postnatal  
49 growth.

50 **Keywords:** Acrylamide, pregnancy, postnatal growth, obesity, MoBa

51        **1. Introduction**

52        Childhood obesity is a large public health challenge worldwide (de Onis et al. 2010). The  
53        major risk factors for obesity are poor nutrition and lack of physical activity. New evidence  
54        suggests that exposure to obesogenic chemicals, i.e. chemicals that alter adipogenesis or  
55        metabolism, could play a role in obesity development (Heindel et al. 2015; Tang-Peronard et  
56        al. 2011). The fetuses and infants may be especially sensitive to exposure to obesogens, even  
57        in low concentrations, due to their immature detoxification pathways and developmental  
58        plasticity (Janesick and Blumberg 2012).

59        Acrylamide is a colourless, odourless, low molecular weight, highly water-soluble organic  
60        compound. Acrylamide does not occur naturally and has been industrially produced since  
61        the 1950s for various uses, including water and wastewater treatment, as gels in  
62        laboratories or in grout for tiling. More recently, it was found that acrylamide can form as a  
63        byproduct during the heating of starch-rich foods at high temperatures (>200 °C), by the  
64        Maillard reaction between asparagine and a sugar molecule (Dybing and Sanner 2003;  
65        Tareke et al. 2002). In occupationally exposed populations, the main routes of acrylamide  
66        exposure are inhalation and dermal absorption, while, in non-occupationally exposed  
67        populations, diet is the main source of exposure for non-smokers (Vikstrom et al. 2012).  
68        Acrylamide is also found in cigarette smoke, and smoking can contribute extensively to  
69        acrylamide exposure (Mojska et al. 2016). According to the Scientific Opinion by the  
70        European Food Safety Authority (EFSA), based on data from 24 European countries and  
71        approximately 43,000 acrylamide concentrations in foods, the main sources of exposure to  
72        adults are fried potatoes, bread, breakfast cereals, biscuits, crackers, crispbread and coffee,  
73        and the average exposure was 0.4-1.9 µg/kg body weight/day (EFSA 2015). After ingestion,  
74        acrylamide is extensively absorbed from the gastrointestinal tract, and after reaching the

75 systemic circulation, it is rapidly distributed into the tissues (Zodl et al. 2007). Acrylamide is a  
76 known neurotoxicant (Ferguson et al. 2010; IARC 1994) and can exert reproductive and  
77 developmental toxicity effects (Yilmaz et al. 2016). It is classified as “probably carcinogenic”  
78 in humans (group 2A) by the International Agency for Research on Cancer (IARC 1994). In the  
79 body, a significant fraction of ingested acrylamide is converted metabolically to the  
80 chemically reactive and genotoxic epoxide, glycidamide (Sweeney et al. 2010). Glycidamide  
81 is likely to play an important role in the carcinogenicity of acrylamide (Hogervorst et al.  
82 2010).

83 During pregnancy, 10-50% of dietary acrylamide is transferred via blood through the  
84 placenta to the fetus (Annola et al. 2008; Sorgel et al. 2002). Three epidemiological studies  
85 have shown a negative association between prenatal acrylamide exposure and birth weight  
86 or height or increased risk of having a small for gestational age (SGA) newborn (Duarte-Salles  
87 et al. 2013; Kadawathagedara et al. 2016; Pedersen et al. 2012). In Duarte-Salles et al., the  
88 adjusted OR for SGA was 1.11 (95% CI: 1.02, 1.21) and the birth weight change was -25.7 g  
89 (95% CI: -35.9, -15.4), for the highest vs. the lowest quartile of maternal acrylamide intake  
90 (Duarte-Salles et al. 2013). In Pedersen et al., the change on birth weight was -132 g (95% CI:  
91 -207, -56), for infants in the highest vs. the lowest quartile of acrylamide hemoglobin adduct  
92 (Pedersen et al. 2012). In Kadawathagedara et al., the adjusted OR for SGA was 1.11 (95% CI:  
93 1.03, 1.21) and the change in birth weight was -9.8 g (95%CI: -21.3, 1.7) per 10 µg/day  
94 increase in maternal acrylamide intake (Kadawathagedara et al. 2016). Taking into  
95 consideration the scarce epidemiological evidence, the CONTAM panel (Contaminant in the  
96 Food Chain) of EFSA recommended that further epidemiological studies should be  
97 conducted to confirm or refute the inverse relationship between dietary acrylamide intake  
98 and impaired fetal growth (EFSA 2015).

99 Several epidemiological studies have indicated that small size at birth is a risk factor for a  
100 range of metabolic disorders, including higher body mass index (BMI) in adulthood, insulin  
101 resistance, increased visceral adiposity and impaired glucose tolerance (Barker 1998; Calkins  
102 and Devaskar 2011; Gluckman et al. 2008; Stout et al. 2015). However, there is currently no  
103 epidemiological study that have examined the potential association between prenatal  
104 acrylamide exposure and postnatal growth.

105 Therefore, the aim of the present study was to investigate the association between  
106 maternal dietary acrylamide intake during pregnancy and postnatal growth in children up to  
107 age 8 years in a large population-based cohort study in Norway, the Norwegian Mother and  
108 Child Cohort Study (MoBa).

109

## 110 **2. Material and methods**

### 111 **2.1 Study population**

112 Our study was conducted within MoBa, which is a prospective population-based  
113 pregnancy cohort study conducted by the Norwegian Institute of Public Health (Magnus et  
114 al. 2016). In brief, participants from all over Norway were recruited by postal invitation prior  
115 to their 1<sup>st</sup> ultrasound visit (17-18<sup>th</sup> gestational week) during the years 1999 to 2008. The  
116 women consented to participation in 40.6% of the pregnancies. MoBa now encompasses  
117 114,500 children, 95,200 mothers and 75,200 fathers. Data used in this study are based on  
118 version 9 of the quality-assured data files, released for research in November 2015. All MoBa  
119 participants provided written informed consent before enrolment into the study.

120 The eligible study population included 80,453 women with singleton, live born babies  
121 without malformations and chromosomal anomalies and available acrylamide intake

122 estimates. After excluding mother-child pairs with missing information on parity (no  
123 missing), maternal age (no missing), maternal education (3% missing), pre-pregnancy BMI  
124 (3% missing), gestational weight gain (18% missing), maternal active (1% missing) and  
125 passive (1% missing) smoking during pregnancy, maternal alcohol consumption during  
126 pregnancy (14% missing), implausible energy intake (i.e. <4.5 MJ and >20 MJ, 2% excluded),  
127 paternal weight (5% missing), gestational age (0.4% missing), child gender (no missing), birth  
128 weight (0.1% missing) and length (3% missing), the population with non-missing information  
129 was 52,308 mother-child pairs. Additional mother-child pairs were excluded when no  
130 postnatal growth measurement was available, resulting in a final study population of 51,952  
131 mother-child pairs (65% of the source population).

132 The MoBa study was approved by the Regional Committee for Ethics in Medical Research  
133 (S-95113 and S-97045) and the Norwegian Data Inspectorate. The current study was  
134 approved by the Regional Committee of Medical Research Ethics for South-Eastern Norway  
135 (2016/377).

## 136 **2.2 Maternal dietary acrylamide intake**

137 The MoBa food frequency questionnaire (FFQ) was used to estimate the daily intake of  
138 acrylamide (in  $\mu\text{g}/\text{day}$ ) as previously described in detail by Duarte-Salles et al. (Duarte-Salles  
139 et al. 2013) and Brantsaeter et al. (Brantsæter et al. 2008b). In brief, food consumption data  
140 assessed by the FFQ, and food contamination data, comprising concentrations of acrylamide  
141 in various food items (data from Norwegian, Swedish and European food safety authorities)  
142 were combined (Institute for Reference Materials and Measurements 2005;  
143 Livsmedelsverket 2002; Norwegian Food Safety Authority 2002; Norwegian Food Safety  
144 Authority 2006; Scientific Committee of the Norwegian Food Control Authority 2002).  
145 Energy-adjusted acrylamide intake (in  $\mu\text{g}/\text{kcal}/\text{day}$ ) was calculated by dividing acrylamide



146 intake (in  $\mu\text{g}/\text{day}$ ) by total daily energy intake (kcal). The MoBa FFQ has been validated in  
147 119 pregnant women using a 4-day weighed food record and biological markers as reference  
148 methods (Brantsæter et al. 2008a). The validation study demonstrated that it provides valid  
149 estimates of dietary intakes and is a valid tool for ranking pregnant women along the  
150 distribution of energy, nutrients and foods. The validation study also reported fair  
151 agreement between acrylamide metabolite concentrations in 24-hour urine and estimated  
152 acrylamide intake (Brantsæter et al. 2008b).

153 The FFQ contains 225 food items that were aggregated into 100 detailed food groups.  
154 Twenty-seven out of 100 food groups contributed to acrylamide intake. In order to identify  
155 the main contributors to acrylamide intake during pregnancy, these 27 were further grouped  
156 into 12 main food groups. The 12 food groups were: cereals (porridge, cornflakes), bread  
157 (white bread, dark bread, rolls), crispbread (crispbread and crackers), pancakes and sweet  
158 bakery items (waffle and pancakes, buns, cakes, sweet biscuits), cooked potatoes, fried  
159 potatoes, coffee (coffee, decaffeinated coffee, fig coffee, milk based coffee), chocolate,  
160 sweets, salty snacks (potato crisps, potato snacks, peanuts and popcorn, pretzels), milk  
161 desserts (yoghurt with cereals, chocolate milk and chocolate pudding), and other (poultry,  
162 pizza and tacos, breaded fish, olives, dried fruits, chocolate/hazelnut spread).

### 163 **2.3 Children's diet**

164 We further assessed the exposure to acrylamide via the children's diet, by defining  
165 acrylamide food-scores that included possible contributors to the children's acrylamide  
166 intake, using previously applied methodology (Pedersen et al. 2012). The dietary information  
167 was collected via short food frequency questionnaires answered by the mother at child's age  
168 3 and 7 years. At 3 years, the possible contributors of acrylamide intake included: biscuits,  
169 buns, chips and bread. We further defined an acrylamide-food score by giving 0 points if the

170 child did not consume and 1 point if the child did consume the item (non-consumers:  
171 biscuits: 64%, buns: 60%, chips: 67%), while for bread, we assigned 0 points for consumption  
172 once per day or less (76%) and 1 point for more frequent consumption. The sub-scores for  
173 the different food items were summarizing and the acrylamide-food score grouped into 3-  
174 categories: low exposed children (n=5511, 25%), average exposed (n=7659, 34%) and high  
175 exposed (n=9181, 41%).

176 At 7 years, the possible contributors of acrylamide intake included: soft bread, crispbread,  
177 breakfast cereals, pancakes, buns and chips. To define the acrylamide food-score, 0 points  
178 were assigned when the child's intakes were: soft bread  $\leq$  median (4 slices/day, 67%),  
179 crispbread  $\leq$  median (1 slice/day, 69%), breakfast cereals  $\leq$  3 times/month (74%), pancakes  $\leq$  3  
180 times/month (88%), buns  $\leq$  3 times/month (78%), chips  $\leq$  3 times/month (61%), and 1 point  
181 was assigned for higher intake frequencies. The sub-scores for the different food items were  
182 summarizing and the acrylamide-food score grouped into 3-categories score: low exposed  
183 children (n=4169, 19%), average exposed children (n=7998, 36%) and high exposed children  
184 (n=10184, 46%).

## 185 **2.4 Children's postnatal growth**

186 Anthropometric measurements of the children were reported by the mothers at eleven  
187 time-points and in six different questionnaires: around the age of 6 weeks, 3 months and 6  
188 months (questionnaire administered at 6 months), around the age of 8 months, 1 year and  
189 18 months (questionnaire administered at 18 months), around the age of 2 years and 3 years  
190 (questionnaire administered at 3 years), around the age of 5 years (questionnaire  
191 administered at 5 years), the age of 7 years (questionnaire administered at 7 years) and 8  
192 years (questionnaire administered at 8 years). From 6 weeks to 18 months, mothers were  
193 asked to refer to their child's health card, while no specification was provided for

194 measurements from 2 to 8 years. From birth to 5 years, weight and height of Norwegian  
195 children are screened in scheduled free voluntarily appointments at the public health  
196 centers. On average, seven repeated measurements of weight and height (10<sup>th</sup> and 90<sup>th</sup>  
197 percentiles for weight as for height were 3 and 10 measurements) and a total of 373,261  
198 weight measurements and 365,578 height measurements were reported for the children  
199 included in our study. Of these, 2,101 children had all 11 reported values for both weight  
200 and height. The response rate of anthropometric measurements went down as the children  
201 grew older (**Supplementary Figure 1**).

202 We obtained growth trajectories by modelling the individual growth from 1 month to 8  
203 years, using the Jenss-Bayley growth curve model. This is a structural growth model,  
204 meaning that it implies a basic functional form of the growth and it is suitable for describing  
205 growth of weight or length up to 8 years, before growth starts to accelerate due to the start  
206 of puberty (Jenss and Bayley 1937). By this non-linear mixed effects model (with random  
207 effect on each parameter) and by applying the Stochastic Approximation of Expectation-  
208 Maximisation (SAEM) algorithm (Berkey 1982; Comets et al. 2014), individual weight and  
209 height were calculated using the Jenss-Bayley equation and individual weight and height  
210 growth velocities were calculated using the first derivative of the model, at several time  
211 points (1, 2, 3, 6, 9, 12, 18 months, 2, 3, 4, 5, 6, 7, 8 years). The predicted anthropometric  
212 values as well as their correlation with the measured values are presented in Supplemental  
213 material (**Supplementary table 1**). Implausible anthropometrics were identified and  
214 excluded by separately implementing two different methods: i) by identifying measured  
215 values with a  $>|3SD|$  difference from the predicted value as derived from the Jenss-Bayley  
216 growth curve model, and ii) by the conditional growth percentiles method (Yang and  
217 Hutcheon 2016). In total, 2% of weight and 2% of length/height measurements were

218 excluded as implausible. In order to define growth trajectories independent of birth size and  
219 to be able to further assess the effect of acrylamide on early growth independent of the  
220 effect on birth size (Duarte-Salles et al. 2012), birth weight and length were not included in  
221 the growth models.

222 Body mass index (BMI) was calculated as weight (in kg) divided by squared height (in m)  
223 using the predicted growth values (Botton et al. 2014). Further, we defined childhood  
224 overweight and obesity at 3, 5 and 8 years using the extended International Obesity Task  
225 Force (IOTF) cut offs for boys and girls (Cole and Lobstein 2012).

## 226 **2.5 Covariates**

227 Variables considered as potential confounders in this study were maternal and  
228 pregnancy-related characteristics previously identified as adjustment factors for the  
229 association between dietary acrylamide intake in pregnancy and fetal growth (Duarte-Salles  
230 et al. 2013; Kadawathagedara et al. 2016; Pedersen et al. 2012). The variables included  
231 parity (nulliparous vs multiparous), maternal age (years), maternal education ( $\leq 9$  years, 13-  
232 16 years,  $\geq 17$  years), maternal pre-pregnancy BMI ( $<18.5$ , 18.5-24.9, 25.0-29.9,  $\geq 30.0$   
233  $\text{kg/m}^2$ ), gestational weight gain (kg), smoking during pregnancy (no, occasional, daily) and  
234 gestational age (weeks). In addition, maternal alcohol consumption during pregnancy (yes  
235 vs. no), exposure to passive smoking during pregnancy (yes vs. no), total energy intake (kcal,  
236 assessed concomitantly with acrylamide), and paternal BMI ( $\text{kg/m}^2$ ) and height (m) were  
237 tested as potential confounders. We also tested for interaction between acrylamide intake  
238 and gender or birth weight. Variables were included in the model if the association with both  
239 the exposure variable and the outcome variable (overweight/obesity at 3 years) had a  $p$ -  
240 value less than 0.05. In addition, confounding by postnatal acrylamide exposure was

241 explored by further adjustment for children's acrylamide food-scores at 3 years and 7 years  
242 described above.

## 243 **2.6 Statistical analysis**

244 We described the specific sources of acrylamide by quartiles of intake and identified the  
245 main contributors for different levels of exposure.

246 Logistic regression models were used to investigate the association between maternal  
247 acrylamide intake (in quartiles) and the risk of overweight including obesity or the risk of  
248 obesity only, at 3, 5 and 8 years separately. Further, we used restricted cubic splines with  
249 four knots at percentiles 5, 35, 65 and 95, to assess the linearity of the association, visually  
250 and statistically, using the exposure variable in a continuous scale. The logistic regression  
251 models were adjusted for random effects of sibling clusters since some mothers participated  
252 with more than one pregnancy.

253 Linear mixed effect models were used to investigate the association between maternal  
254 acrylamide intake during pregnancy (in quartiles) and children's postnatal growth from 1  
255 month to 8 years. The effect estimates for each outcome were presented in line plots by  
256 quartiles of acrylamide intake.

257 The association between maternal acrylamide intake in pregnancy and postnatal growth  
258 was tested by using crude acrylamide intake (in  $\mu\text{g}/\text{day}$ ) and energy intake adjusted  
259 acrylamide intake (in  $\mu\text{g}/\text{kcal}/\text{day}$ ). The energy-adjusted analysis is presented as the main  
260 analysis and the non-adjusted in Supplemental material. We performed the following  
261 sensitivity analyses i) with and without adjustment for birth weight, ii) using only measured  
262 anthropometric data (not predicted values), iii) including only the children with a high  
263 number of anthropometric measurements ( $>7$ , the median) and limiting the age range to  $<5$   
264 years, iv) using acrylamide crude intake in  $\mu\text{g}/\text{day}$  with energy intake as a covariate in the

265 model, v) examining acrylamide intake as three independent variables reflecting the  
266 amounts from the principal contributors (crispbread, sweet bakery items and bread) and vi)  
267 we have further explored the association between maternal acrylamide intake and risk for  
268 overweight at 3, 5 and 8 years after conditioning for children's acrylamide food-score. First,  
269 the association was explored with no adjustment for the children's acrylamide food-score  
270 but in the same number of mother-child pairs with available information on the food score.  
271 Second the acrylamide food-score was added in the model and third stratified analysis for  
272 low and high exposed children was performed.

273 The analyses were performed using Stata 14 statistical software (Stata Corporation,  
274 College Station, Texas) except growth modelling that was conducted in R version 3.2.2 (R  
275 development Core Team 2016).

### 276 3. Results

277 The mean maternal age at delivery was 30.3 years. Forty-six percent of the women were  
278 primiparous and 65% of the women had a normal BMI. The average weight gain during  
279 pregnancy was 14.8 kg. A large majority (93%) of the women in our study were non-smokers.  
280 Their babies had an average birth weight of 3620 kg and were born at 40 weeks of  
281 amenorrhea (**Table 1**). The median and interquartile range (IQR) of dietary acrylamide intake  
282 was 24.7 µg/day (IQR 18.4, 33.2), corresponding to 0.011 µg/kcal/day (IQR 0.008, 0.014) in  
283 the 51,952 pregnant women. The main contributors to acrylamide intake were pancakes or  
284 sweet bakery items, bread and crispbread, and the contribution of each food differed from  
285 low to high exposure (**Figure 1**). Namely, in the 1<sup>st</sup> quartile of exposure, the main  
286 contributors were pancakes and sweet bakery items (22%) and bread (29%), while in the 4<sup>th</sup>  
287 (upper) quartile, the contribution from crispbread increased to 25% (9% in the 1st quartile)

288 and the contribution from bread decreased to 14%. In children, the prevalence of  
289 overweight was 10.6%, 14.8% and 7.8% and, of obesity only 0.8%, 1.6% and 0.4% at 3, 5 and  
290 8 years, respectively (**Supplementary table 2**).

291 Increasing maternal acrylamide intake during pregnancy was associated with higher odds  
292 of children being overweight/obese at 3, 5 and 8 years of age, after adjustment for  
293 confounders (**Table 2**). Children born to mothers with acrylamide intake at 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup>  
294 quartile had 10%, 12% and 21% higher odds of being overweight/obese at 3 years, compared  
295 to their low exposed peers. The associations were weaker at 5 and 8 years but similar  
296 positive trends were observed. Maternal acrylamide intake increased the ORs for obesity at  
297 3 and 5 years and similar dose-response trends were observed, while only the association for  
298 the highest acrylamide (Q4) intake and obesity at 3 years was statistically significant. At 8  
299 years, non-significant reduced odds were observed for Q2 and Q3 and increased odds for  
300 Q4. Assessing the exposure on a continuous scale, we found that the prevalence of  
301 overweight at 3 and 5 years (but not at 8 years) increased from no intake to an intake of 0.01  
302  $\mu\text{g}/\text{kcal}/\text{day}$  (~95<sup>th</sup> percentile of acrylamide intake) and then reached a plateau (**Figure 2**).  
303 There was no interaction between birth weight and acrylamide exposure on postnatal  
304 growth and no substantial difference when removing birth weight from the covariates  
305 (**Supplementary Table 3**). There was no effect-measure modification between gender and  
306 acrylamide exposure on postnatal growth (data not shown). When using the reported  
307 anthropometric data to define the outcome, the estimates were similar compared to  
308 predicted anthropometric values, but with greater variances (**Supplementary table 4**).

309 When assessing weight up to 8 years, we found that energy-adjusted acrylamide intake in  
310 the 3<sup>rd</sup> and 4<sup>th</sup> quartile was associated with higher weight from the first months onwards  
311 (**Figure 3a**). Regarding weight growth velocity, maternal acrylamide intake in the 4<sup>th</sup> quartile

312 was associated with higher weight gain velocity from 1<sup>st</sup> month to 5 years (**Figure 3b**).  
313 Finally, maternal energy-adjusted acrylamide intake higher than the 1<sup>st</sup> quartile was  
314 associated with higher BMI throughout the whole childhood (**Figure 3c**).

315 More specifically and focusing on the highest exposure level, 1 year old children  
316 prenatally exposed to high acrylamide levels weighed 34 g more, gained 2.5 g more per  
317 month and had 0.06 kg/m<sup>2</sup> higher BMI than their low exposed peers (**Table 3**). At eight  
318 years, children highly exposed during the prenatal period weighed between 110 g to 278 g  
319 more than their low exposed peers, while the effect estimates were of small magnitude  
320 (~0.4-1% higher than the average weight at 8 years). Further adjustment for children's  
321 height did not change the results (data not shown). In combination with the observed  
322 association with BMI trajectories, this indicates that the association between acrylamide and  
323 weight trajectory is independent of height. Restricting the analysis to children with seven or  
324 more measurements and assessing growth up to 5 years, we observed similar associations  
325 (**Supplementary Table 5**).

326 When using the crude acrylamide intake as the exposure variable (in µg/day) the  
327 associations with overweight and obesity were similar, while for obese children only, the  
328 associations were stronger for the 3<sup>rd</sup> quartile at 3 and 5 years and for the 4<sup>th</sup> quartile at 8  
329 years (**Supplementary table 6**). When investigating the associations of the main acrylamide  
330 dietary contributors with the outcomes, consistent associations were observed  
331 (**Supplementary table 7**).

332 When exploring the association between maternal acrylamide intake and risk of  
333 overweight after conditioning (adjustment and stratification) for children's acrylamide food-  
334 scores, the results were similar (**Supplementary Figures 2, 3 and 4**). At 3 years, further  
335 adjustment for the acrylamide food-score did not modify the estimates (**Supplementary**



336 **Figure 2).** After restricting to low or high exposed children, maternal acrylamide intake was  
337 still associated with child overweight, indicating no effect of postnatal diet. At 5 years, in line  
338 with the results at 3 years, adjustment for children's acrylamide food-score did not modify  
339 the association between prenatal acrylamide exposure and child overweight  
340 **(Supplementary Figure 3).** In addition, children with low exposure to acrylamide from their  
341 own diet, still were at higher risk for overweight due to high maternal acrylamide intake  
342 during pregnancy. After adjustment for acrylamide food-score at 8 years, the association  
343 between maternal acrylamide intake and overweight risk was attenuated, as also seen at the  
344 main analysis included in our manuscript **(Supplementary Figure 4).**

345

346 **4. Discussion**

347 We found that prenatal acrylamide exposure was associated with a moderate increase in  
348 the prevalence of children being overweight or obese and moderately increased weight  
349 growth velocity very early during childhood. To our knowledge, this is the first study on the  
350 relationship between prenatal acrylamide exposure and postnatal growth.

351 There are three previous epidemiological studies on the association between prenatal  
352 acrylamide exposure and fetal growth, while no previous animal or epidemiological studies  
353 have examined postnatal growth. The first study reporting an association with fetal growth  
354 was in a consortium of five European mother-child cohort studies, including a subsample  
355 from MoBa, using biomarkers of acrylamide exposure during gestation (Pedersen et al.  
356 2012), and the other two assessed acrylamide exposure through diet (Duarte-Salles et al.  
357 2013; Kadawathagedara et al. 2016). All three studies showed that high prenatal exposure to  
358 acrylamide was associated with impaired fetal growth. These results are consistent with  
359 animal studies showing a decrease in offspring body weight following maternal acrylamide  
360 exposure during gestation (El-Sayyad et al. 2011; Manson et al. 2005; Tyl and Friedman  
361 2003).

362 Our findings of increased prevalence of overweight associated with high prenatal  
363 acrylamide exposure are in line with the Fetal Programming (Barker 1998) and the  
364 Developmental Origins of Health and Disease hypotheses (Gluckman et al. 2008).  
365 Considering the absence of interaction between birth weight and prenatal exposure to  
366 acrylamide and that adjustment for birth weight did not change the association, the  
367 association between acrylamide exposure and postnatal growth is likely independent from  
368 the one with fetal growth.

369 There are only few studies showing that early life chemical exposure may be obesogenic  
370 (Botton et al. 2017), and they mainly focused on persistent organic pollutants that can act as  
371 endocrine disrupting chemicals (EDCs). EDCs are environmental compounds that can mimic  
372 or interfere with the effects of endogenous hormones such as estrogens, androgens,  
373 progestins, and thyroid, hypothalamic, and pituitary hormones (Newbold et al. 2007).  
374 Acrylamide is not known to be an EDC and the CONTAM panel of EFSA concluded that the  
375 epidemiological evidence from the available studies in the literature on hormonal and  
376 endocrine effects of acrylamide is equivocal (EFSA 2015). In a cross-sectional study from Lin  
377 et al., urinary acrylamide metabolites were negatively associated with free thyroxine (T4)  
378 (Lin et al. 2015). Although this result is coming from a cross-sectional study so we cannot  
379 exclude reverse causation, it provides an interesting new insight for a possible mechanism  
380 involved. Indeed, thyroid hormones are essential for an optimal growth but the literature is  
381 divergent regarding their effect on hypothyroidism and prenatal growth (Hou et al. 2016;  
382 Nazarpour et al. 2015).

383 Another possible biological mechanism between acrylamide exposure and growth is  
384 through oxidative stress and inflammation. Recently, acrylamide exposure was found to be  
385 inversely associated with several body composition measures in a sample of adults from the  
386 NHANES, and high oxidative stress was suggested as the mechanism involved (Chu et al.  
387 2017). During pregnancy, high acrylamide exposure can result in increased oxidative stress  
388 through increased expression of CYP2E1, resulting further in a heightened perinatal  
389 inflammatory status (Nguyen et al. 2015; Wang et al. 2003). Indeed, elevated maternal  
390 plasma C-reactive protein has been associated with a higher risk of childhood overall  
391 adiposity and central adiposity in the American Project Viva cohort, providing evidence that  
392 maternal inflammatory status might also contribute to explain our findings (Gaillard et al.

393 2016). Oxidative stress and inflammation are also mechanisms that are suspected to  
394 influence the relation between air pollution or exposure to tobacco smoke during pregnancy  
395 and low birth weight (Aycicek and Ipek 2008; Westergaard et al. 2017). The negative  
396 association of both types of prenatal exposure on birth weight has been well described  
397 (Pedersen et al. 2013; Valero De Bernabe et al. 2004), and the mechanisms involved might  
398 be similar for acrylamide. Unfortunately, information on inflammation status was not  
399 available in our study.

400 We acknowledge that the maternal dietary pattern related to high acrylamide exposure,  
401 rather than the acrylamide exposure itself, might confound the observed association. In  
402 other populations, acrylamide intake has been related with high intake of fast-foods, like  
403 chips (Pedersen et al. 2015), while in the present population of Norwegian women high  
404 acrylamide exposure was driven by crispbread intake. Crispbread has a high content of  
405 dietary fiber and is not associated with an unhealthy dietary pattern. Hence, in this  
406 population, it is less likely that an unhealthy dietary pattern during pregnancy would explain  
407 our findings. Another major source of acrylamide in our study population was dark bread,  
408 which is also high in fiber. Intakes of both whole-grain foods and fiber are recommended as  
409 components of a healthy diet and are included in the Norwegian food guidelines and Nordic  
410 Nutrition Recommendations (von Ruesten et al. 2014). In addition, fiber-rich bread,  
411 including dark bread and crispbread, has been identified as a component of a “prudent diet”  
412 in the same population (Englund-Ogge et al. 2014).

### 413 ***Strengths and limitations***

414 This study is the first to assess the relationship between prenatal acrylamide intake and  
415 postnatal growth in a large population based study (N=51,952). It is a follow-up of a previous  
416 study describing the link between prenatal exposure to acrylamide and fetal growth (Duarte-

417 Salles et al. 2013). These two studies assessed acrylamide exposure *via* diet, as estimated  
418 using a FFQ and a food-chemical concentration database in the same population. Duarte-  
419 Salles et al. reported a positive correlation between estimated acrylamide intake and Hb  
420 adducts in maternal blood (Spearman correlation: 0.24, 95% CI: 0.00, 0.44). This level of  
421 correlation is in agreement with previous reports (Kutting et al. 2008; Tran et al. 2010;  
422 Wilson et al. 2009a; Wilson et al. 2009b; Wirfalt et al. 2008). The use of dietary intake  
423 estimations to assess acrylamide exposure can be seen as a strength of our study, as an  
424 alternative method (i.e biomarkers) would be more burdensome and expensive to be  
425 applied in such a large population. In addition, dietary assessment is highly relevant as food  
426 is the primary source of acrylamide exposure in non-smokers and non-occupationally  
427 exposed populations (Dybing et al. 2005) and less than 8 % of women smoked during  
428 pregnancy in our study. Nevertheless, the chance of a misclassification (bias of the  
429 exposure), related to the dietary recall through the self-administered FFQ or the  
430 representativeness of the food contamination database, cannot be excluded. However, the  
431 classification bias is unlikely to be differential and, although the loss of power is  
432 compensated by the large sample size in our study, the size of the associations is likely  
433 underestimated (Pearce et al. 2007).

434 An additional strength is the use of growth modelling that takes attrition bias into  
435 account and handles the missing body size measurements. The correlations between the  
436 measured and the predicted body size measurements were strong at all ages ( $r > 0.93$  except  
437 one coefficient at 0.85, see Supplementary table 1). In sensitivity analyses restricted to the  
438 measured data, similar associations were found as with the predicted body size data  
439 (Supplementary table 4). This provides some reassurance on the validity of the predicted  
440 anthropometrics. However, we still acknowledge the potential for outcome misclassification

441 bias as only 26% of the study population had anthropometric data at 8 years (Supplementary  
442 Table 1), though in part because all our population (17%) had still not reached the age of 8  
443 years. The mixed-effect growth modelling will predict the values also for the children lost to  
444 follow-up balancing between their previous observed values and the average population  
445 trajectory. The shrinkage due to this approach is likely to predict values closer to the mean  
446 compared to the actual child's growth, leading again to a loss of power and attenuation in  
447 the associations with acrylamide exposure (McCulloch et al. 2008). When conducting the  
448 longitudinal analysis in a subsample of children with many measurements ( $\geq 7$ ) and up to 5  
449 years only, similar conclusions were drawn. We also acknowledge that the effect estimates  
450 in the longitudinal growth analysis are of small magnitude, pointing into cautionary  
451 interpretation of our findings. Nevertheless, the magnitude of the effect estimates does not  
452 reduce the importance of our findings. We found consistent associations between high  
453 maternal acrylamide intake during pregnancy and increases in all the studied weight status-  
454 and growth parameters (continuous and categorical) and we consider this as a strength of  
455 our observational study. In addition, attenuation of the observed association with  
456 overweight after 5 years might be explained by possible misclassification of the outcome  
457 through another source. The development of all Norwegian children is assessed, from birth  
458 to 5 years, in voluntarily scheduled appointments with a public health nurse. Hence, parental  
459 misreporting of the child's weight and height after 5 years might induce misclassification of  
460 the outcome.

461

462 Finally, we decided to consider potential confounders when the variable was associated  
463 with both the exposure and the outcomes. Although this practice has been criticized, given  
464 the large sample size, it is unlikely that we missed important confounders (Rothman et al.

465 2008). Controlling for confounding by postnatal exposure to acrylamide can be considered a  
466 strength of our study. We used an acrylamide food-score to account for children's  
467 acrylamide intake at 3 and 7 years. Conditioning on child acrylamide intake did not modify  
468 the observed associations between maternal acrylamide intake during pregnancy and weight  
469 status in childhood. In addition, the acrylamide food-score could also be interpreted as a  
470 proxy of an unhealthy diet, as it reflects consumption of sweet bakery products and chips. In  
471 this case, through the above mentioned analysis, we can still argue that an unhealthy diet  
472 during childhood cannot entirely explain our observed associations between prenatal  
473 acrylamide exposure and postnatal growth. Overall, it is less likely that the associations  
474 between high maternal acrylamide intake during pregnancy and the increased risk for  
475 overweight in childhood, as well as a modified growth trajectory, can be explained by  
476 maternal or child adherence to an unhealthy diet.

477 The association between acrylamide exposure during pregnancy with child adiposity and  
478 other metabolic markers can provide more insight into the negative developmental  
479 programming effects of acrylamide and should be investigated by future studies.

## 480 **5. Conclusion**

481 In summary, this large population-based study provides the first epidemiological  
482 indication of a significant association between prenatal dietary exposure to acrylamide and a  
483 moderate increase of the prevalence of being overweight or obese and moderately  
484 increased risk of being in higher growth trajectories during early childhood and pre-school  
485 age. These findings need to be confirmed in other studies.

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691

692

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703 **Table 1.** Characteristics of study population overall and by quartile of acrylamide intake  
704

	Energy adjusted acrylamide intake during pregnancy (quartiles-in µg/kcal/day)									
	All		Q1 (≤18.3)		Q2 (18.4 – 24.6)		Q3 (26.7 – 33.1)		Q4 (≥33.2)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<b>Maternal age (years)</b>	30.3	4.4	30.0	4.5	30.2	4.3	30.4	4.4	30.5	4.5
<b>Gestational weight gain (kg)</b>	14.8	5.8	14.8	6.0	14.7	5.7	14.8	5.7	14.7	5.9
<b>Birth weight (g)</b>	3620	520	3626	521	3623	521	3618	521	3620	520
<b>Gestational age (weeks)</b>	40.0	1.6	40.0	1.6	40.0	1.6	40.0	1.6	40.1	1.5
	N	%	N	%	N	%	N	%	N	%
<b>Maternal education</b>										
Low (≤12 years)	14,405	28	3,634	29	3,392	26	3,470	26	3,909	30
Medium (13-16 years)	22,993	44	5,356	42	5,904	45	6,009	46	5,724	44
High (≥ 17 years)	14,554	28	3,636	29	3,853	29	3,699	28	3,366	26
<b>Pre-pregnancy BMI</b>										
<18.5	1,287	3	357	3	326	3	304	2	300	2
18.5-25	33,929	65	8,234	65	8,722	66	8,626	66	8,347	64
25-30	11,947	23	2,829	22	2,905	22	3,057	23	3,156	25
>30	4,789	9	1,206	10	1,196	9	1,191	9	1,196	9
<b>Parity</b>										
Nulliparous	24,060	46	6,252	50	6,129	47	5,959	45	5,720	44
Multiparous	27,892	54	6,374	50	7,020	53	7,219	55	7,279	56
<b>Smoking during pregnancy</b>										
No	48,439	93	11,861	94	12,420	95	12,320	94	11,838	91
Occasionally	1,227	2	246	2	270	2	317	2	394	3
Daily	2,286	5	519	4	459	3	541	4	767	6
<b>Exposure to 2<sup>nd</sup> hand smoking</b>										
No	47,107	91	11,368	90	12,013	91	12,304	91	11,692	90
Yes	4,845	9	1,258	10	1,136	9	1,144	9	1,307	10
<b>Alcohol consumption during pregnancy</b>										
No	45,803	88	11,398	90	11,682	89	11,520	87	11,203	86
Yes	6,149	12	1,228	10	1,467	11	1,658	13	1,796	14
<b>Children's diet</b>										
<b>Acrylamide food-score at 3 years<sup>a</sup></b>										
Low	5,511	25	1,541	29	1,428	25	1,367	24	1,175	21
Average	7,659	34	1,889	35	2,083	26	1,907	33	1,780	32
High	9,181	41	1,894	36	2,260	39	2,492	43	2,535	46
<b>Acrylamide food-score at 7 years<sup>a</sup></b>										
Low	4,169	19	1,124	21	1,171	20	1,008	17	866	16
Average	7,998	36	2,042	38	2,073	36	2,005	35	1,878	34
High	10,184	45	2,158	41	2,527	44	2,753	48	2,746	50

<sup>a</sup> N=22,351 mother-child pairs

705

706 **Table 2. Maternal acrylamide intake in pregnancy and children's overweight/obesity and obesity only at age 3, 5 and 8 years (n=51,952).**

Maternal energy-adjusted acrylamide intake ( $\mu\text{g}/\text{kcal}/\text{day}$ )	N cases/ N total	Risk for overweight and/or obesity <sup>a</sup>								
		At 3 years			At 5 years			At 8 years		
		OR	95% CI	N cases/ N total	OR	95% CI	N cases/ N total	OR	95% CI	
Quartiles of intake										
Q1 ( $\leq 18.3$ )	1,259/12,801	1.00		1,954/12,801	1.00		577/12,801	1.00		
Q2 (18.4 – 24.6)	1,354/13,012	1.10	1.02,1.20	2,088/13,012	1.08	1.01,1.16	583/13,012	1.02	0.91,1.15	
Q3 (26.7 – 33.1)	1,456/13,063	1.12	1.04,1.22	2,223/13,063	1.11	1.04,1.19	662/13,063	1.12	0.99,1.25	
Q4 ( $\geq 33.2$ )	1,461/13,076	1.21	1.11,1.31	2,240/13,076	1.17	1.10,1.26	681/13,076	1.12	1.00,1.26	
<i>p for trend</i>		<i>&lt;0.001</i>			<i>&lt;0.001</i>			<i>0.023</i>		
<i>Acrylamide intake, 1-IQR increase</i>		1.07 (1.04, 1.11)			1.06 (1.03, 1.09)			1.04 (1.00, 1.09)		
Risk for obesity only <sup>a</sup>										
Q1 ( $\leq 18.3$ )	109/12,801	1.00		308/12,801	1.00		29/12,801	1.00		
Q2 (18.4 – 24.6)	116/13,012	1.09	0.84,1.41	306/13,012	1.07	0.92,1.26	27/13,012	0.76	0.46,1.25	
Q3 (26.7 – 33.1)	152/13,063	1.11	0.86,1.44	381/13,063	1.13	0.96,1.32	46/13,063	0.96	0.60,1.53	
Q4 ( $\geq 33.2$ )	141/13,076	1.35	1.06,1.73	356/13,076	1.16	0.99,1.36	52/13,076	1.46	0.96,2.23	
<i>p for trend</i>		<i>0.018</i>			<i>0.048</i>			<i>0.045</i>		
<i>Acrylamide intake, 1-IQR increase</i>		1.12 (1.03,1.22)			1.06 (1.00,1.13)			1.25 (1.09,1.42)		

All models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight.

<sup>a</sup>Overweight and/or obese children were defined according to IOTF definition, using the predicted anthropometric measurements.

707

708 **Table 3. Association between maternal acrylamide intake in pregnancy and children's**  
709 **weight, weight gain velocity and BMI from 1<sup>st</sup> month to 8 years. The 1<sup>st</sup> quartile of**  
710 **maternal acrylamide intake is used as the reference.**

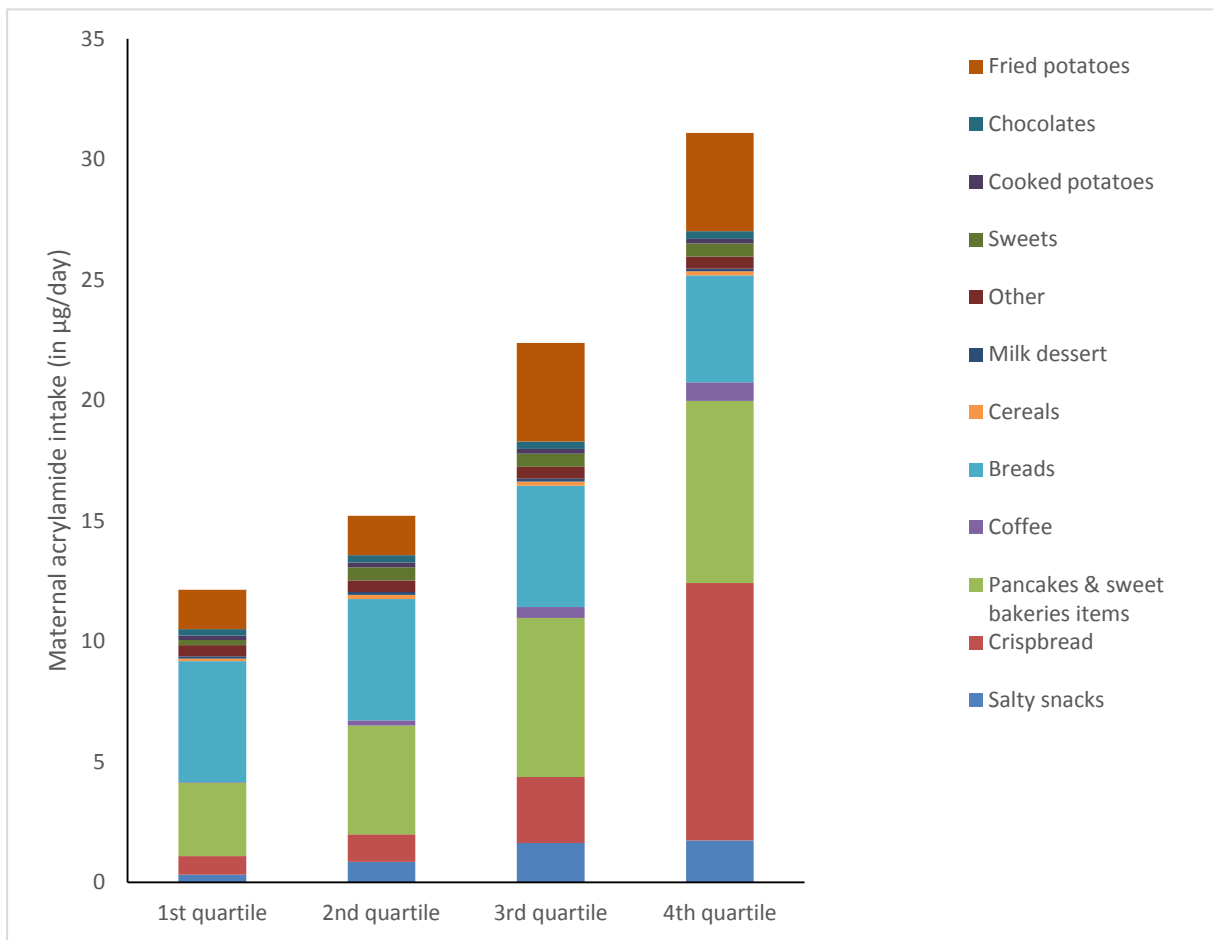
	Energy-adjusted maternal dietary acrylamide exposure ( $\mu\text{g}/\text{kcal}/\text{day}$ ) in quartile			
	1 <sup>st</sup> quartile Mean (SD)	2 <sup>nd</sup> quartile $\beta$ (95% CI)	3 <sup>rd</sup> quartile $\beta$ (95% CI)	4 <sup>th</sup> quartile $\beta$ (95% CI)
<b>Weight (in g)<sup>a</sup></b>				
3months	6,328 (613)	-0.1 (-14 , 14)	11 (-2.7 , 25)	17 (2.5 , 31)
6months	7,976 (794)	2.6 (-12 , 17)	14 (-0.2 , 29)	22 (7.7 , 37)
12months	9,904 (989)	8.2 (-8.7 , 25)	21 (3.6 , 37)	34 (17 , 51)
2years	12,558 (1,265)	19 (-5.0 , 44)	33 (8.4 , 57)	57 (32 , 81)
5years	19,799 (2470)	53 (-0.4 , 106)	70 (17 , 123)	125 (73 , 179)
8years	27,000 (3,942)	86 (2.5 , 169)	107 (23 , 190)	194 (110 , 278)
<b>Weight gain velocity (in g/month)<sup>a</sup></b>				
3months	711 (98)	0.8 (-1.4 , 3.1)	1.5 (-0.7 , 3.7)	2.6 (0.4 , 4.8)
6months	429 (70)	0.9 (-1.2 , 3.0)	1.5 (-0.6 , 3.6)	2.6 (0.4 , 4.7)
12months	256 (43)	0.9 (-1.0 , 2.8)	1.5 (-0.5 , 3.4)	2.5 (0.6 , 4.5)
2years	206 (41)	1.0 (-0.7 , 2.7)	1.4 (-0.2 , 3.1)	2.4 (0.8 , 4.1)
5years	200 (44)	1.2 (-0.8 , 3.3)	1.3 (-0.8 , 3.3)	2.2 (0.1 , 4.3)
8years	200 (44)	1.5 (-2.0 , 5.0)	1.1 (-2.4 , 4.6)	1.9 (-1.6 , 5.5)
<b>BMI (in <math>\text{kg}/\text{m}^2</math>)<sup>a</sup></b>				
3months	16.8 (1.1)	0.03 (0.00 , 0.05)	0.03 (0.01 , 0.06)	0.05 (0.02 , 0.07)
6months	17.4 (1.2)	0.03 (0.00 , 0.05)	0.03 (0.01 , 0.06)	0.05 (0.03 , 0.07)
12months	16.8 (1.2)	0.03 (0.01 , 0.05)	0.04 (0.01 , 0.06)	0.06 (0.03 , 0.08)
2years	16.3 (1.2)	0.04 (0.01 , 0.06)	0.04 (0.02 , 0.07)	0.07 (0.04 , 0.09)
5years	16.1 (1.4)	0.06 (0.03 , 0.09)	0.06 (0.03 , 0.09)	0.10 (0.07 , 0.13)
8years	15.3 (1.7)	0.08 (0.04 , 0.12)	0.08 (0.03 , 0.12)	0.13 (0.09 , 0.17)

All linear mixed models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight.

<sup>a</sup> Predicted anthropometric measurements were used to define outcomes.

711

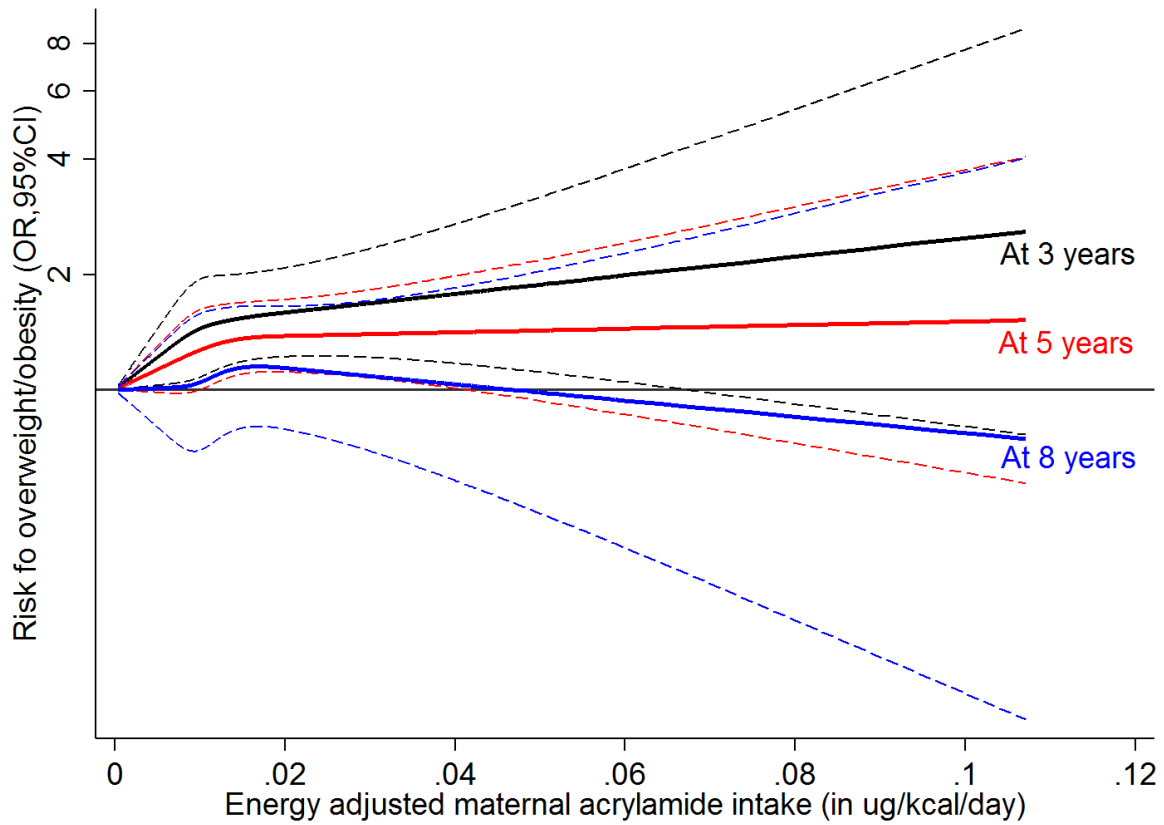
712 **Figure 1.** Sources of maternal acrylamide intake according to quartiles of total acrylamide  
713 intake (n=51,952) women in MoBa.



714



715 **Figure 2.** Maternal acrylamide intake ( $\mu\text{g}/\text{kcal}/\text{day}$ ) in pregnancy (in continuous scale) and  
716 child overweight/obesity at 3 (black lines), 5 (red lines) and 8 (blue lines) years ( $n=51,952$ ).  
717 Solid lines represent Odd Ratios (OR) and dotted lines represent 95% Confidence Intervals  
718 (CI).



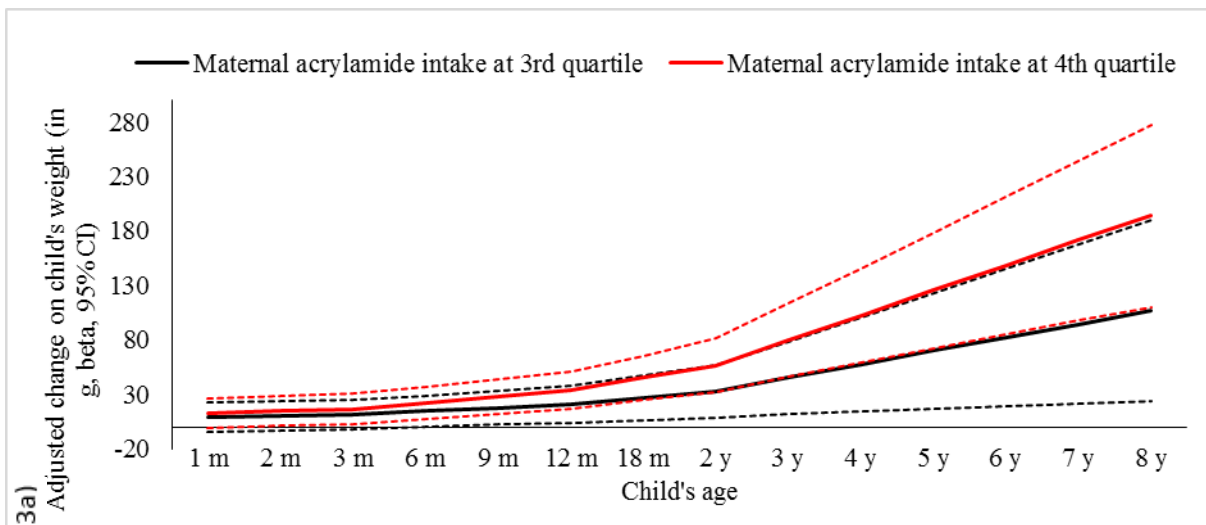
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720 **Figure 3.** Adjusted changes in children's A) weight, B) weight gain velocity and C) BMI from  
721 1st month to 8 years, associated with 3rd and 4th maternal acrylamide intake quartiles  
722 (energy-adjusted).

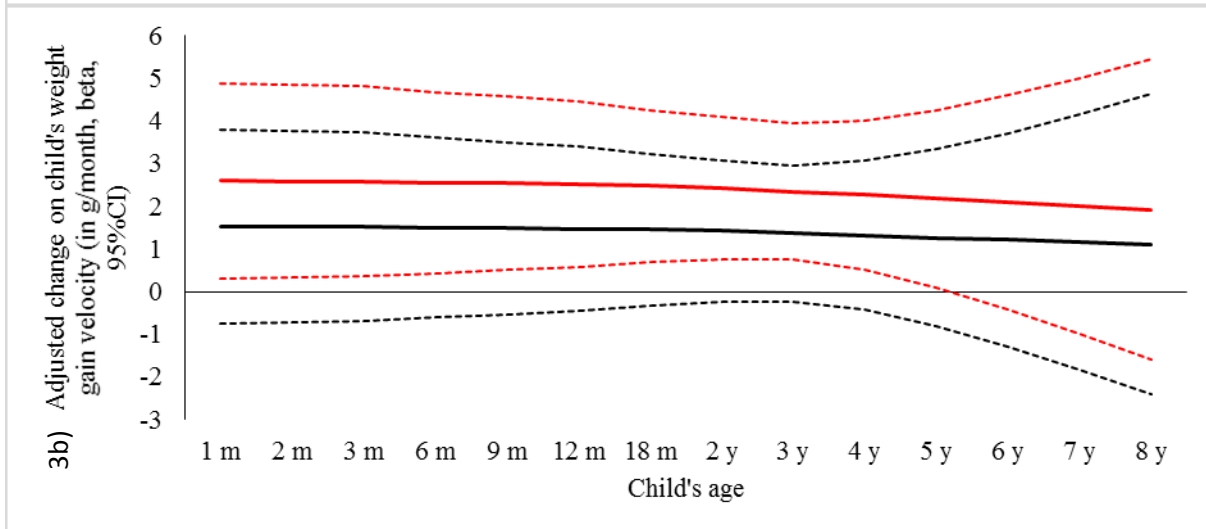
723 Footnote: All models are adjusted for maternal age, parity, maternal education, pre-  
724 pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational  
725 age, maternal alcohol consumption during pregnancy, second hand smoking and birth  
726 weight.

727

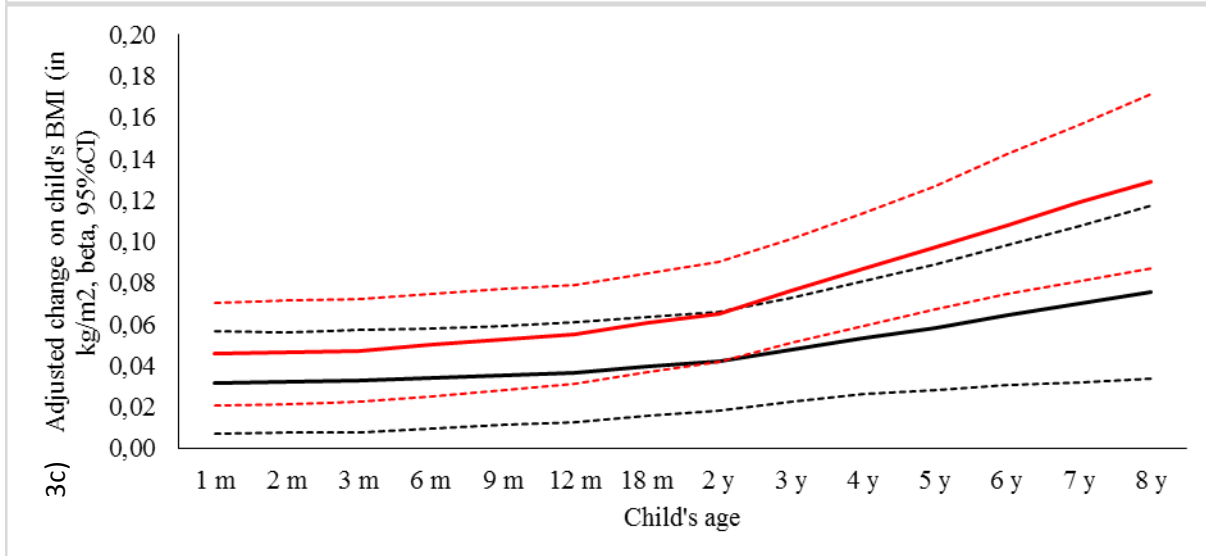
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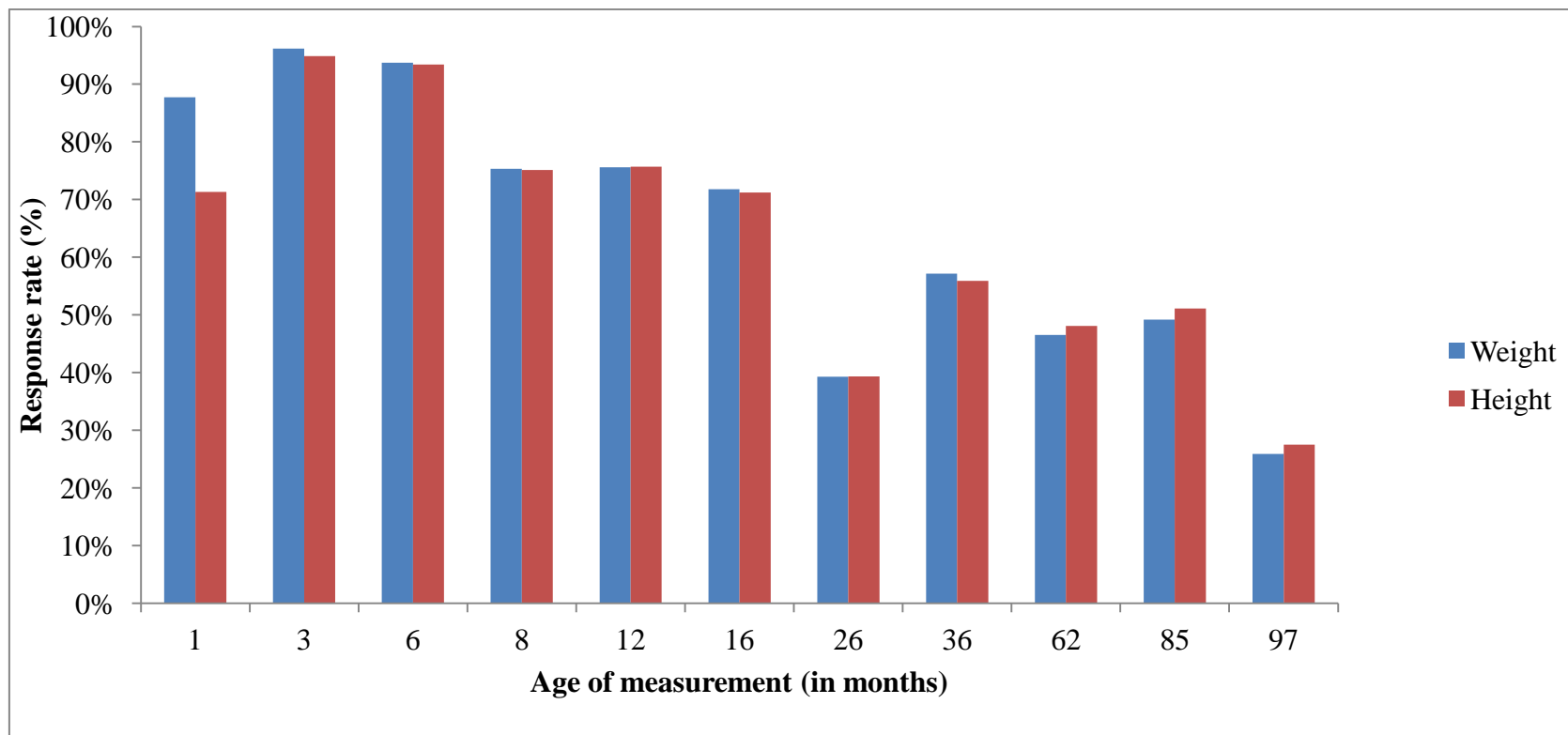


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731

**Supplemental Figure 1. Response rate of anthropometric measurements for 51,952 mother-child pairs.**



**Supplementary Table 1. Measured and predicted growth measurements (weight and height) in children, based on maternal reports, at 11 time points in the Norwegian Mother and Child Cohort Study (MoBa).**

Time point	Measured growth					Predicted growth		Correlation between measured and predicted growth	
	Age (months)	Weight (in kg) N=373,261	Height (in cm) N=365,578	Weight (in kg) N=571,472	Height (in cm) N=571,472	Weight	Height	Pearson's r	Pearson's r
	Mean (SD)	Measurements distribution (%)	Mean (SD)	Measurements distribution (%)	Mean (SD)	Mean (SD)	Mean (SD)	Pearson's r	Pearson's r
1	1.4 (0.2)	12	5.0 (0.7)	10	56.9 (2.3)	5.0 (0.5)	57.3 (1.9)	0.85	0.95
2	3.1 (0.3)	13	6.4 (0.8)	13	62.1 (2.4)	6.4 (0.7)	61.7 (2.1)	0.94	0.95
3	5.8 (0.5)	13	7.9 (0.9)	13	67.9 (2.5)	7.9 (0.8)	67.5 (2.3)	0.95	0.96
4	8.1 (0.8)	11	8.8 (1.0)	11	71.3 (2.7)	8.8 (0.9)	71.3 (2.5)	0.96	0.96
5	12.2 (0.6)	11	9.9 (1.1)	11	76.5 (2.7)	10.0 (1.0)	76.8 (2.5)	0.96	0.96
6	16 (1.2)	10	10.9 (1.2)	10	80.6 (2.9)	10.9 (1.1)	80.9 (2.7)	0.96	0.96
7	25.5 (2)	5	12.9 (1.5)	6	88.7 (3.5)	12.9 (1.4)	88.9 (3.3)	0.94	0.95
8	36.2 (1.4)	8	15.0 (1.7)	8	96.6 (3.7)	15.1 (1.6)	96.4 (3.5)	0.93	0.96
9	62.4 (3.4)	6	19.9 (2.6)	7	113.1 (5.1)	20.2 (3.5)	112.6 (4.6)	0.96	0.97

10	85.2 (1.6)	7	24.9 (3.7)	7	125.8 (5.3)	25.0 (3.5)	125.8 (5.0)	0.98	0.98
11	96.9 (1)	4	28.0 (4.3)	4	131.9 (5.5)	27.7 (4.1)	132.4 (5.3)	0.99	0.98

---

**Supplementary Table 2. Prevalence of overweight/obesity and obesity only at age 2-8 years in our study population, defined by using measured or predicted anthropometric data.**

	Child's age						
	2 years	3 years	4 years <sup>a</sup>	5 years	6 years <sup>a</sup>	7 years	8years
<i>Using measured anthropometric data</i>							
N total	20,151	22,856	181	22,481	1,032	24,803	13,068
% cases of overweight/obesity	10.5	12.2	9.9	11.1	8.2	11.3	11.5
% cases of obesity only	1.2	1.5	2.2	1.3	0.6	1.1	0.7
<i>Using predicted anthropometric data</i>							
N total (with measured data available)	20,151	22,856	181	22,481	1,032	24,803	13,068
% cases of overweight/obesity	5.7	10.6	12.7	14.8	10.6	10.7	7.8
% cases of obesity only	0.2	0.8	2.2	1.6	0.8	0.8	0.4
N total	51,952	51,952	51,952	51,952	51,952	51,952	51,952
% cases of overweight/obesity	5.3	10.7	15.5	16.4	13.2	8.6	4.8
% cases of obesity only	0.3	1.0	2.3	2.6	1.7	0.9	0.3
% Overlap of cases of overweight/obesity <sup>b</sup>	82	69	61	63	69	86	96
% Overlap of cases of obesity only <sup>b</sup>	80	58	50	54	50	85	94

<sup>a</sup> The number of children at 4 and 6 years is low because the follow-up was conducted at 3, 5 and 7 years.

<sup>b</sup> % Overlap represents the percentage of the cases defined by the predicted anthropometric data who rank as cases also by using measured anthropometric data.

**Supplementary Table 3. Associations between maternal acrylamide intake in pregnancy and overweight/obesity and obesity only at 3, 5 and 8 years, without adjustment for birth weight.**

Maternal energy-adjusted acrylamide intake (µg/kcal/day)	Risk for overweight and/or obesity <sup>a</sup>					
	At 3 years		At 5 years		At 8 years	
	OR	95% CI	OR	95% CI	OR	95% CI
Quartiles of intake						
Q1	1.00		1.00		1.00	
Q2	1.09	1.01,1.19	1.07	1.00,1.15	1.02	0.90,1.14
Q3	1.11	1.02,1.20	1.10	1.03,1.18	1.11	0.99,1.24
Q4	1.18	1.09,1.28	1.15	1.08,1.24	1.11	0.98,1.24
<i>p for trend</i>		<0.001		<0.001		0.038
Risk for obesity only <sup>a</sup>						
Q1	1.00		1.00		1.00	
Q2	1.08	0.84,1.40	1.07	0.91,1.25	0.76	0.46,1.26
Q3	1.10	0.85,1.42	1.12	0.95,1.31	0.96	0.60,1.53
Q4	1.33	1.04,1.70	1.14	0.98,1.34	1.47	0.96,2.24
<i>p for trend</i>		0.026		0.075		0.043

All models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking.

<sup>a</sup> Overweight and/or obese children were defined according to IOTF definition, using the predicted anthropometric measurements.



**Supplementary Table 4. Maternal energy-adjusted acrylamide intake in pregnancy and overweight/obesity and obesity only at 3, 5 and 8 years, using measured anthropometric measurements.**

Energy adjusted maternal acrylamide intake (µg/day)	Risk for overweight and/or obesity <sup>a</sup>								
	Prevalence (%)	At 3 years O R	95% CI	Prevalence (%)	At 5 years O R	95% CI	Prevalence (%)	At 8 years OR	95% CI
Quartiles of intake									
Q1		1.0			1.0			1.0	
	11.12	0		10.57	0		10.94	0	
Q2		1.0	0.96,1.21		1.0	0.93,1.18		1.1	0.95,1.30
	11.83	7		10.89	5		11.84	1	
Q3		1.0	0.97,1.22		1.1	0.97,1.24		1.0	0.89,1.22
	12.01	9		11.42	0		11.34	4	
Q4		1.2	1.15,1.44		1.0	0.97,1.23		1.0	0.92,1.26
	13.92	8		11.55	9		11.85	7	
<i>p for trend</i>			<0.001			0.119			0.579
Obesity only <sup>a</sup>									
Q1		1.0			1.0			1.0	
	1.33	0		1.28	0		0.78	0	
Q2		0.9	0.68,1.30		1.0	0.73,1.43		0.7	0.44,1.43
	1.25	4		1.27	2		0.60	9	
Q3		1.3	0.98,1.79		1.1	0.85,1.62		0.7	0.42,1.39
	1.76	2		1.47	7		0.60	7	
Q4		1.3	1.00,1.84		1.0	0.75,1.46		1.2	0.71,2.06
	1.80	6		1.35	5		0.97	1	
<i>p for trend</i>			0.009			0.602			0.493

All models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight.

<sup>a</sup> Overweight and/or obese children were defined according to IOTF definition, using the measured anthropometric measurements.

**Supplementary Table 5. Association between maternal acrylamide intake in pregnancy and child's weight, weight gain velocity and BMI from 1<sup>st</sup> month to 5 years, for 31,358 children with more than 6 measurements. The 1<sup>st</sup> quartile of maternal acrylamide intake is used as the reference.**

	Energy-adjusted maternal acrylamide intake ( $\mu\text{g}/\text{kcal}/\text{day}$ ) in quartiles								
	Beta	2 <sup>nd</sup> quartile (95% CI)	Beta	3 <sup>rd</sup> quartile (95% CI)	Beta	4 <sup>th</sup> quartile (95% CI)			
<i>Weight (in g) <sup>a</sup></i>									
3months	-12	(-28 , 5)	8.6	(-8.0 , 25)	12	(-5.0 , 29)			
6months	-8.7	(-27 , 9.2)	12	(-6.0 , 30)	18	(0.1 , 36)			
12months	-2.7	(-25 , 19)	19	(-3.4 , 40)	31	(8.8 , 53)			
2years	9.3	(-24 , 42)	32	(-1.2 , 65)	56	(23 , 90)			
5years	45	(-27 , 118)	72	(-0.6 , 144)	133	(59 , 206)			
<i>Weight gain velocity (in g/month) <sup>a</sup></i>									
3months	0.3	(-2.8 , 3.5)	1.7	(-1.4 , 4.8)	2.5	(-0.6 , 5.7)			
6months	0.5	(-2.4 , 3.3)	1.7	(-1.0 , 4.4)	2.5	(-0.2 , 5.2)			
12months	0.7	(-1.9 , 3.2)	1.6	(-0.9 , 4.2)	2.5	(-0.1 , 5.0)			
2years	1.1	(-1.3 , 3.5)	1.5	(-0.9 , 3.9)	2.4	(0.0 , 4.8)			
5years	2.4	(-3.1 , 7.8)	1.2	(-4.2 , 6.6)	2.3	(-3.2 , 7.7)			
<i>BMI (in <math>\text{kg}/\text{m}^2</math>) <sup>a</sup></i>									
3months	0.002	(-0.03 , 0.03)	0.03	(-0.002 , 0.06)	0.03	(-0.004 , 0.06)			
6months	0.006	(-0.03 , 0.04)	0.03	(0.0002 , 0.06)	0.03	(0.0003 , 0.06)			
12months	0.01	(-0.02 , 0.04)	0.03	(0.004 , 0.07)	0.04	(0.009 , 0.07)			
2years	0.02	(-0.007 , 0.06)	0.04	(0.01 , 0.07)	0.06	(0.02 , 0.09)			
5years	0.06	(0.02 , 0.19)	0.06	(0.01 , 0.11)	0.11	(0.06 , 0.15)			

All linear mixed models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight.

<sup>a</sup> Predicted anthropometric measurements were used to define outcomes.

**Supplementary Table 6. Maternal acrylamide intake in pregnancy and overweight/obesity at 3, 5 and 8 years, using predicted anthropometric measurements (n=51,952).**

Maternal acrylamide intake (µg/day)	Risk for overweight and/or obesity <sup>a</sup>								
	At 3 years			At 5 years			At 8 years		
	Prevalence (%)	O R	95% CI	Prevalence (%)	O R	95% CI	Prevalence (%)	O R	95% CI
Quartiles of intake									
Q1	9.84	1.00		15.26	1.00		4.51	1.00	
Q2	10.41	1.06	0.98,1.15	16.05	1.06	0.99,1.13	4.48	0.99	0.88,1.12
Q3	11.21	1.16	1.07,1.25	17.02	1.14	1.06,1.22	5.07	1.13	1.01,1.27
Q4	11.17	1.14	1.05,1.24	17.13	1.14	1.06,1.22	5.21	1.15	1.02,1.29
<i>p for trend</i>			<0.001			<0.001			0.010
Risk for obesity only <sup>a</sup>									
Q1	0.85	1.00		2.41	1.00		0.23	1.00	
Q2	0.89	1.05	0.80,1.36	2.35	0.98	0.83,1.15	0.21	0.92	0.54,1.55
Q3	1.16	1.37	1.07,1.76	2.92	1.22	1.05,1.42	0.35	1.54	0.96,2.45
Q4	1.08	1.22	0.95,1.58	2.72	1.11	0.95,1.30	0.40	1.62	1.02,2.56
<i>p for trend</i>			0.033			0.032			0.008

All models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight.

<sup>a</sup> Overweight and obesity children were defined according to IOTF definition, using the predicted anthropometric measurements.



**Supplementary Table 7. Maternal acrylamide intake from crispbread, sweet bakery items and bread and overweight/obesity at 3, 5 and 8 years.**

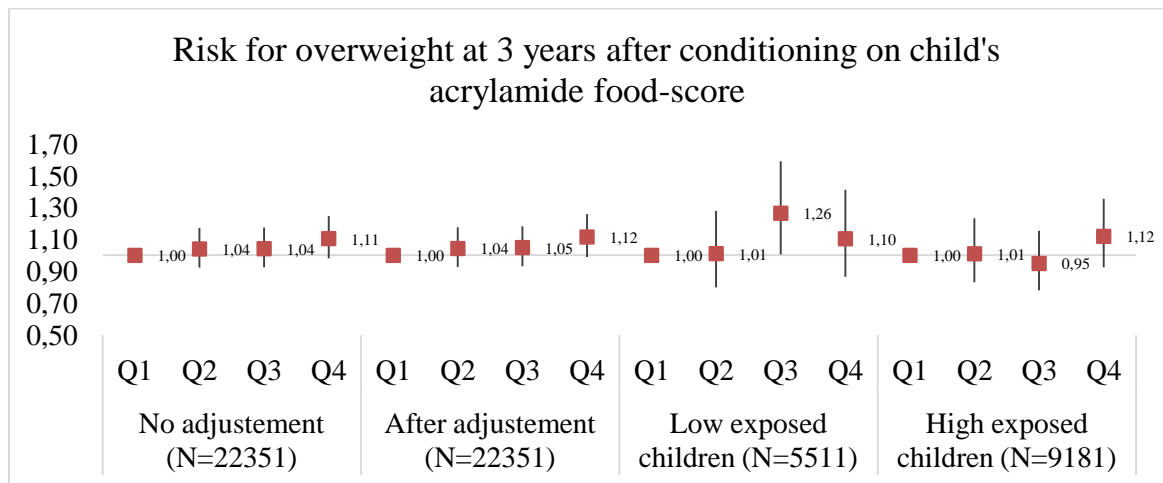
	Overweight/obesity <sup>a</sup>					
	3 years		5 years		8 years	
	O	95%CI	O	95%CI	O	95%CI
	R		R		R	
Energy acrylamide intake from crispbread adjusted from						
<75 <sup>th</sup> percentile	1.00		1.00		1.00	
>75 <sup>th</sup> percentile	1.08	1.01,1.15	1.04	0.99,1.10	1.09	0.99,1.20
Energy acrylamide intake from sweet bakery items adjusted from						
<75 <sup>th</sup> percentile	1.00		1.00		1.00	
>75 <sup>th</sup> percentile	1.09	1.02,1.16	1.11	1.05,1.17	1.06	0.96,1.16
Energy acrylamide intake from bread adjusted from						
<75 <sup>th</sup> percentile	1.00		1.00		1.00	
>75 <sup>th</sup> percentile	1.02	0.99,1.04	1.02	1.00,1.04	1.02	0.99,1.05
Acrylamide intake from crispbread						
<75 <sup>th</sup> percentile	1.00		1.00		1.00	
>75 <sup>th</sup> percentile	1.08	1.01,1.15	1.04	0.99,1.10	1.08	0.98,1.18
Acrylamide intake from sweet bakery						
<75 <sup>th</sup> percentile	1.00		1.00		1.00	
>75 <sup>th</sup> percentile	1.09	1.02,1.17	1.09	1.03,1.15	1.05	0.96,1.16
Acrylamide intake from bread						
<75 <sup>th</sup> percentile	1.00		1.00		1.00	
>75 <sup>th</sup> percentile	1.01	1.00,1.01	1.00	1.00,1.01	1.01	1.00,1.02

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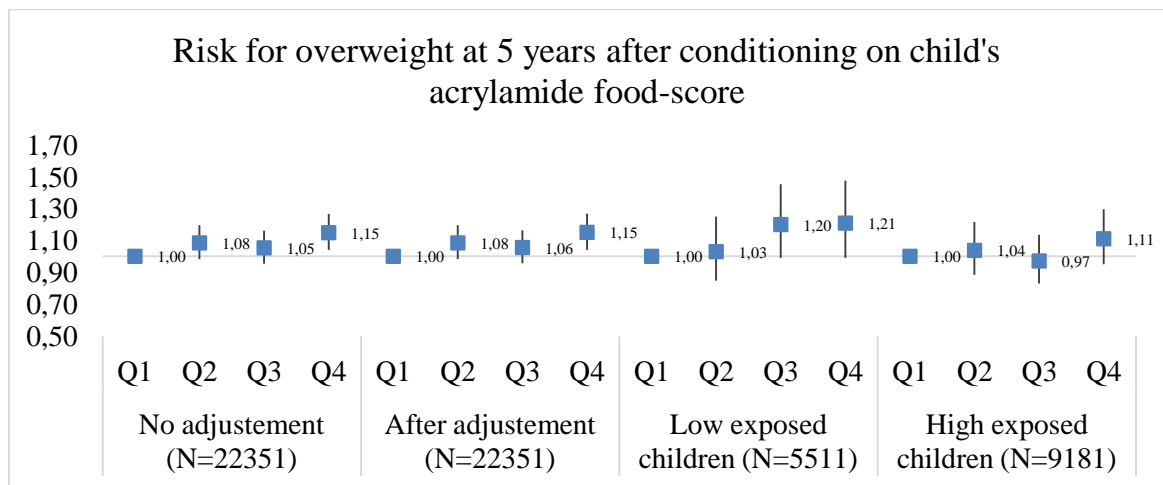
All models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight. Models are also mutually adjusted for the 3 food groups.

<sup>a</sup> Overweight/obesity were defined according to IOTF definition, using the predicted anthropometric measurements.

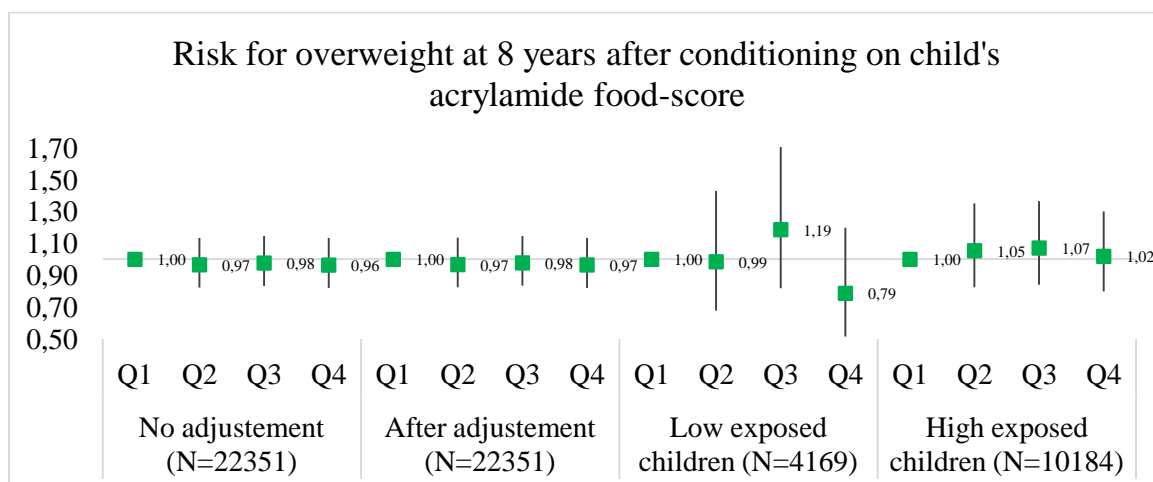
**Supplementary Figure 2.** Association between maternal acrylamide intake and child's risk for overweight at 3 years, after conditioning for child's acrylamide food-score at 3 years.



**Supplementary Figure 3.** Association between maternal acrylamide intake and child's risk for overweight at 5 years, after conditioning for child's acrylamide food-score at 3 years.



**Supplementary Figure 4.** Association between maternal acrylamide intake and child's risk for overweight at 8 years, after conditioning for child's acrylamide food-score at 7 years.



**Supplementary Table 8:** Association between maternal acrylamide intake in pregnancy and child's weight, weight gain velocity and BMI from 1<sup>st</sup> month to 8 years. The 1<sup>st</sup> quartile of maternal acrylamide intake is used as the reference.

	Energy-adjusted maternal dietary acrylamide exposure ( $\mu\text{g}/\text{kcal}/\text{day}$ ) in quartile			
	1 <sup>st</sup> quartile	2 <sup>nd</sup> quartile $\beta$ (95% CI)	3 <sup>rd</sup> quartile $\beta$ (95% CI)	4 <sup>th</sup> quartile $\beta$ (95% CI)
<b>Weight after adjustment for height (in g)<sup>a</sup></b>				
3months	Ref.	-6 (-22,10)	12 (-4, 28)	11 (-5, 28)
6months	Ref.	-2 (-18, 14)	15 (-1, 31)	<b>17 (1, 33)</b>
12months	Ref.	5 (-13, 23)	<b>21 (4, 39)</b>	<b>29 (11, 47)</b>
2years	Ref.	19 (-7, 45)	<b>34 (8, 60)</b>	<b>52 (25, 78)</b>
5years	Ref.	<b>62 (1, 123)</b>	<b>72 (12, 133)</b>	<b>121 (59, 182)</b>
8years	Ref.	<b>105 (7, 204)</b>	<b>111 (13, 209)</b>	<b>190 (90, 289)</b>

All linear mixed models are adjusted for maternal age, parity, maternal education, pre-pregnancy BMI, gestational weight gain, maternal smoking during pregnancy, gestational age, maternal alcohol consumption during pregnancy, second hand smoking and birth weight.

<sup>a</sup> Predicted anthropometric measurements were used to define outcomes.