Physical fitness in young adults born preterm

Marjaana Tikanmäki, MD^{a,b}, Tuija Tammelin, MSc^c, Marika Sipola-Leppänen, MD^{a,b,d}, Nina Kaseva, MD, PhD^{a,e}, Hanna-Maria Matinolli, MHealthSci^{a,b}, Satu Miettola, MD^{a,b,f}, Johan G Eriksson, MD, DMSc^{g,h}, Marjo-Riitta Järvelin, MD, PhD^{i,j,k,l}, Marja Vääräsmäki, MD, PhD^{f,m} and Eero Kajantie, MD, PhD^{a,e,f}

Affiliations: ^aChronic Disease Prevention Unit, National Institute for Health and Welfare, Oulu and Helsinki, Finland; ^bInstitute of Health Sciences, University of Oulu, Oulu, Finland; ^cLIKES - Research Center for Sport and Health Sciences, Jyväskylä, Finland; ^dDepartment of Pediatrics and Adolescence, Oulu University Hospital, Oulu, Finland; ^eChildren's Hospital, Helsinki University Hospital, University of Helsinki, Helsinki, Finland; ^fDepartment of Obstetrics and Gynaecology, Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland; ^gDepartment of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; ^hFolkhälsan Research Centre, Helsinki, Finland; ⁱDepartment of Epidemiology and Biostatistics, MRC Health Protection Agency (HPA) Centre for Environment and Health, School of Public Health, Imperial College London, London, United Kingdom; ^jCenter for Life Course Epidemiology, Faculty of Medicine, University of Oulu; ^kBiocenter Oulu, Oulu, Finland; ^lUnit of Primary Care, Oulu University Hospital, Oulu, Finland; and ^mChildren, Adolescents and Families, National Institute for Health and Welfare, Oulu, Finland.

Address correspondence to: Marjaana Tikanmäki, Department of Health, Chronic Disease Prevention Unit, National Institute for Health and Welfare, P.O. Box 310, 90101 Oulu, Finland [marjaana.tikanmaki@thl.fi]

Short title: Physical fitness in young adults born preterm

Funding Source: The ESTER study was supported by grants from the Academy of Finland (SALVE program for 2009–2012 and grants 127437, 129306, 130326, 134791 and 263924 to EK), Doctoral Programme for Public Health, University of Tampere (to MSL), the Emil Aaltonen Foundation (to EK), European Commission (Framework 5 award QLG1-CT-2000-001643; to MRJ), the Finnish Foundation for Pediatric Research (to EK), the Finnish Government Special Subsidiary for Health Sciences (evo) (to JGE), Finnish Medical Societies: Duodecim (to EK) and Finska Läkaresällskapet (to JGE and NK), the Jalmari and Rauha Ahokas Foundation (to EK), the Juho Vainio Foundation (to EK and MSL), the National Graduate School of Clinical Investigation (to MT), the Novo Nordisk Foundation (to EK and MV), the Signe and Ane Gyllenberg Foundation (to EK and JGE), the Sigrid Jusélius Foundation (to EK), and the Yrjö Jahnsson Foundation (EK, MSL and MV).

Financial Disclosure: The authors report no financial relationships relevant to this article.

Potential Conflict of Interest: The authors report no potential conflicts of interest.

Abbreviations: CI – Confidence interval; EPT, early preterm (<34 gestational weeks); ESTER – ESTER Preterm Birth Study “Ennenaikainen syntymä ja aikuisiän terveys; Preterm birth and early life programming of adult health and disease”; FMBR – the Finnish Medical Birth Register; GDM – Gestational diabetes mellitus; LGA – Large for gestational age; LPT, late preterm (34–36 gestational weeks); METh – Metabolic equivalent hours; N – Newton; NFBC – Northern Finland Birth Cohort 1986; SGA – Small for gestational age; SD – Standard deviation

Key Words: premature birth, physical fitness, physical activity

What's Known on This Subject

Young adults born preterm have higher levels of cardiometabolic risk factors and lower physical activity than term-born peers. Earlier studies, limited to those born very preterm or at very low birth weight, also suggest lower physical fitness in this group.

45 **What This Study Adds**

46 Young adults born preterm have lower muscular fitness and rate themselves as being less fit than
47 those born at term. There was no difference in cardiorespiratory fitness in this sample across the
48 entire range of preterm birth versus the controls.
49

50 **Contributors' Statement:**

51 Dr. Tikanmäki designed and carried out the initial analyses, drafted the initial manuscript, participated in
52 data collection, and approved the final manuscript as submitted.

53 Drs. Tammelin, Sipola-Leppänen and Vääräsmäki participated in the study design and data collection and
54 reviewed, revised, and approved the final manuscript as submitted.

55 Ms. Matinolli and Dr. Miettola participated in the data collection and reviewed, revised and approved the
56 final manuscript as submitted.

57 Dr. Kaseva participated in the study design (focus on the analyses) and reviewed, revised and approved the
58 final manuscript as submitted.

59 Drs. Eriksson and Järvelin participated in the study design and data collection and reviewed, revised and
60 approved the final manuscript as submitted.

61 Dr. Kajantie conceptualized and designed the study, was responsible for the data collection, and reviewed,
62 revised and approved the final manuscript as submitted.

63

64

65 **Abstract**

66 **Background:** Young adults born preterm have higher levels of cardiometabolic risk factors than
67 their term-born peers. Muscular and cardiorespiratory fitness are strong predictors of
68 cardiometabolic health and have many other health benefits. We assessed muscular,
69 cardiorespiratory, and self-rated fitness in preterm-born young adults.

70 **Methods:** We studied unimpaired participants of the ESTER birth cohort study at age 23.3 (SD 1.2)
71 years: 139 born early preterm (<34 weeks; EPT), 247 born late preterm (34 to 36 weeks; LPT), and
72 352 born at term (control group). We measured muscular fitness with the number of modified push-
73 ups performed in 40 seconds and maximal hand grip strength (N) of the dominant hand,
74 cardiovascular fitness with heart rate at the end of a 4-minute step test, and self-rated fitness. and
75 Data was analyzed with linear regression.

76 **Results:** Both young adults born EPT (-0.8 [95% CI-1.5; -0.1; adjusted for sex, age and source
77 cohort]) and LPT (-0.8 [-1.4; -0.3]) performed fewer modified push-ups in 40 seconds than controls.
78 Hand grip strength was 23.8 N (0.9-46.8) lower in EPT. Cardiorespiratory fitness, measured by
79 submaximal step test, was similar. On a self-rated fitness scale (1-5), the EPT adults reported on
80 average 0.2 (0.0; 0.4) lower scores than controls. After adjustment for early life confounders, the
81 results remained. They attenuated after further adjustment for mediating factors.

82 **Conclusions:** Young adults born EPT and LPT had lower muscular fitness than controls, which
83 may predispose them to cardiometabolic and other chronic diseases. Adults born EPT also
84 perceived themselves less fit than controls.

85

86 **Introduction**

87 Every year approximately 14.9 million babies worldwide, 11% of all newborns, are born preterm
88 (<37 weeks of gestation).¹ Long-term follow-up studies have focused on those born smallest and
89 most immature, who have increased levels of cardiometabolic risk factors as adolescents or adults.
90 ^{2,3} However, the majority of preterm infants are born closer to full-term: in the U.S., for example,
91 70% of them are born late preterm, between 34 and 36 weeks of gestation.⁴ The adverse
92 consequences of preterm birth have also been suggested to be present in those born less preterm and
93 increase with the degree of prematurity.⁵

94 Adolescents and adults born preterm at very (<1500 g) or extremely (<1000 g) low birth weight
95 report undertaking less physical activity than those born at term,⁶⁻⁸ although these associations have
96 not been captured by studies using an objective measurement of physical activity (e.g.,
97 accelerometry).^{9,10} Lower muscular and cardiorespiratory fitness are also features of those born
98 preterm at extremely low birth weight.^{8,11} Few studies have assessed this in adolescents or adults
99 born less preterm; a study in Swedish male conscripts was consistent with a graded relationship
100 between lower length of gestation and lower maximal exercise capacity.¹² This question is
101 important because both cardiorespiratory and muscular fitness are independent predictors of
102 cardiometabolic and musculoskeletal health¹³⁻¹⁵ and lower late-life mortality.^{16,17}

103 We studied the association of early (<34 weeks) and late (34 to 36 weeks) preterm birth with
104 muscular, cardiorespiratory, and self-rated physical fitness among young adults. We further
105 examined the roles of prenatal and early life factors as potential confounders and current health
106 characteristics as mediators of fitness level.

107 **Methods**

108 **Participants**

109 The participants come from the ESTER Preterm Birth Study, which comprises 1890 young adults
110 (Supplemental Figure 1). They were recruited among the Northern Finland Birth Cohort 1986
111 (NFBC; 49.8%) born in 1985-1986 and among all children (50.2%) born from 1987 to 1989 in the
112 same geographical area, identified via the Finnish Medical Birth Register (FMBR).⁵ In 2009-2011,
113 750 individuals with adequately verified lengths of gestation participated in a clinical study at 23.3
114 (SD 1.2) years.¹⁸ Those who were pregnant (n=18) or reported cerebral palsy (n=6), mental
115 disability (n=7), and/or other severe physical disability (n=3) were excluded. This left us with 139
116 participants born early preterm, 247 late preterm, and 352 born after 37 completed weeks of
117 gestation (referred to as “at term”), who served as controls. Of those invited as born early preterm,
118 late preterm and as controls, 41.6%, 39.5%, and 35.9% participated, respectively. According to a
119 detailed non-participant analysis of the clinical examination, men were less likely to participate
120 among the late preterm and control groups; there was no difference in perinatal characteristics
121 between participants and non-participants in any of the groups. When we compared participants of
122 the clinical examination included in analyses of specific outcomes with those not included
123 (Supplemental Figure 1), early preterm participants were less likely to be included in analyses of
124 handgrip strength (p=0.04) and self-perceived fitness (p=0.01).

125 **Ethics**

126 The study was approved by the Coordinating Ethics Committee at Helsinki and Uusimaa Hospital
127 District. Participants provided written informed consent.

128 **Perinatal data**

129 Perinatal data for participants recruited through the NFBC came from the cohort database,
130 originally collected from hospital and maternal welfare clinic records.¹⁹ We collected corresponding
131 data for those invited through the FMBR. Length of gestation (determined by ultrasound in 62.7%
132 of preterm infants and 53.1% of controls, by last menstrual period in 36.8%/46.9%, and from
133 hospital records with no data on method of determination in 0.5%/0.0%, respectively)¹⁸ and
134 diagnoses of maternal gestational diabetes (GDM), hypertension (gestational or chronic), or
135 preeclampsia (including superimposed) according to prevailing criteria were confirmed by
136 reviewing original hospital records.^{20,21} Small for gestational age (SGA) was defined as birth weight
137 SD score < -2 SD and large for gestational age (LGA) as > 2 SD according to Finnish standards.²²

138 **Clinical examination**

139 Body weight and composition were assessed using segmental multi-frequency bioelectrical
140 impedance (InBody 3.0, Biospace Co., Seoul, Korea). Spirometry was performed before physical
141 fitness tests and repeated after inhalation of 400 µg salbutamol if it suggested airflow obstruction.²³⁻
142 ²⁵ The participants completed questionnaires on their medical history, including history of asthma,
143 medications, socioeconomic status, physical activity and daily smoking. Childhood socioeconomic
144 status was assessed as the educational attainment of the higher educated parent, . Physical activity
145 level was calculated in METh (metabolic equivalent hours) per week based on a questionnaire on 1)
146 light (assuming a value of 3 MET), 2) moderate to vigorous (5 MET), and 3) commuting physical
147 activity (4 MET).^{26,27}

148 **Outcomes**

149 As a measure of short-term endurance capacity of the upper body and the ability to stabilize the
150 trunk, the participants performed the 40 s modified push-up test. The participant lay prone on a mat,
151 clasped hands behind the back, performed a straight-leg push-up with the elbows completely

152 straight in the up position, touched one hand on the top of the supporting hand, and returned to the
153 prone position to repeat the cycle. The participants practiced one push-up cycle before the test.^{28,29}
154 For the handgrip test, the maximal isometric strength of the dominant hand was measured by a
155 dynamometer (Good Strength, IGS01, Metitur Oy, Jyväskylä, Finland) based on the strain-gauge
156 technique.^{29,30} Cardiorespiratory fitness was measured using the Åstrand-Ryhming step test,^{31,32}
157 during which the participant steps on and off a bench (33 cm high for women and 40 cm for men)
158 repeatedly for four minutes at 23 steps per minute, paced by a metronome. Heart rate was monitored
159 by a Polar monitor (RS800CX™ training computer and WearLink® W.I.N.D. transmitter, Polar
160 Electro Oy, Kempele, Finland) and recorded right after the test. Self-rated fitness was measured
161 with a question: “How do you consider your current physical fitness?” The response alternatives
162 were very good, quite good, fair, quite poor and very poor.³³ The scale was reversed (1=very poor,
163 5=very good) for clarity.

164 **Statistical methods**

165 All analyses were performed using SPSS, Versions 21.0 and 22.0 (IBM/SPSS, Chicago, Illinois,
166 USA). We compared descriptive characteristics by Student’s *t*-test and χ^2 -test, and the outcomes
167 using linear regression with a significance level of <0.05. We tested for interactions between two
168 variables (significance level $P < 0.01$) by including a product term together with these variables.
169 Categorical adjusting variables were entered as dummy variables, with a separate dummy for
170 missing values. In Model 1 we adjusted for sex, age, and cohort. In Model 2, we further adjusted for
171 parental and early life potential confounders: educational attainment of the higher educated parent,
172 maternal GDM and hypertension, and birth weight SD score. In Model 3 we additionally adjusted
173 for potential adult mediators that may differ between those born preterm and at term: self-reported
174 physical activity,^{6,7} diagnosed asthma,³⁴ height,^{6,7} body fat percentage⁵, and smoking.³⁵ For heart
175 rate after the step test, we also adjusted for whether the participant had received salbutamol in a
176 bronchodilation test. We identified specific covariates altering the associations by adding or

177 removing the variables step-wise. We reran the analyses after replacing the adjustment for body fat
178 percentage with lean body mass. As a sensitivity analysis, we also reran the analyses 1) after
179 exclusion of subjects with asthma and 2) after inclusion of subjects with a known chronic condition
180 affecting mobility who were excluded from the main analyses.

181 **Results**

182 Participant characteristics are shown in Table 1 and outcomes by exposure group in Table 2.
183 Correlations between the outcomes and associations between covariates and outcomes are shown in
184 Supplemental Files. There was no interaction between the association of sex and preterm birth
185 with the outcomes.

186 **Modified push-up test**

187 On average, women performed 10.4 (SD 2.0) push-ups in 40 seconds and men 14.4 (SD 3.7).
188 Participants born early and late preterm performed an average of 0.8 fewer push-ups than did the
189 controls. The difference remained similar when adjusted for socioeconomic status and pregnancy-
190 related factors but attenuated when adjusted for adult characteristics including body fat percentage
191 (Figure 1, Supplemental Table 1) or lean body mass instead.

192 **Hand grip strength**

193 The mean hand grip strength was 352.1 (SD 82.4) N among women and 643.1 (SD 145.7) N among
194 men. Those born early preterm had 23.8 N lower hand grip strength than controls, when adjusted
195 for sex, age and cohort. This difference attenuated after adjustment for socioeconomic status and
196 pregnancy-related factors, mainly because of adjustment for birth weight SD score. Further
197 adjustment for adult characteristics, including body fat percentage or lean body mass, had little
198 effect on the association. Those born late preterm had similar hand grip strength than controls
199 (Figure 1, Supplemental Table 1).

200 **Step test**

201 The mean heart rate after the step test was 160 (SD 14) beats/min among women and 153 (SD 16)
202 beats/min among men. There was no difference between either of the preterm groups and controls.
203 When further adjusted for adult characteristics, those born early preterm had 2 beats/min ($P=0.24$)
204 and those born late preterm 3 beats/min lower heart rate ($P=0.02$), indicating better
205 cardiorespiratory fitness. The change in the mean difference was mainly due to adjustment for adult
206 body fat percentage (Figure 1, Supplemental Table 1).

207 **Self-rated fitness**

208 The mean score for self-rated fitness on a scale ranging from one (very poor) to five (very good)
209 was 2.3 (SD 0.8) for women and 2.6 (SD 0.9) for men. Participants born early preterm scored 0.2
210 points lower than controls. Better self-rated fitness correlated with better measurements of physical
211 fitness. This correlation was weakest for hand grip strength, in particular among participants born
212 early preterm (Supplemental Table 2). The difference remained similar when adjusted for
213 socioeconomic status and pregnancy-related factors and attenuated when adjusted for adult
214 characteristics (Figure 1, Supplemental Table 1), mainly due to adjustments for body fat percentage
215 and physical activity level (not shown).

216 **Sensitivity analyses**

217 Participants with asthma had 23.0 N (95% CI 0.8; 45.3) weaker hand grip strength, 3 beats/min
218 (95% CI 0.2; 6.2) higher heart rate after the step test, 0.2 points (95% CI 0.0; 0.4) poorer self-
219 perceived fitness level, and a similar number of modified push-ups (0.2, 95% CI -0.5; 0.9)
220 compared with those with no asthma (adjusted for sex, age and cohort). We reran the analyses after
221 exclusion of participants with asthma. The results remained similar. We also reran the analyses to
222 include physically impaired participants excluded from the original analyses. Again, the results

223 remained. For the step-test, we excluded those who had inhaled salbutamol during spirometry
224 before the step test; the results remained.

225 **Pre- and neonatal factors**

226 As a continuous variable, one week longer length of gestation predicted 0.1 (95% CI 0.0-0.2) more
227 push-ups and 0.02 (0.01-0.04) higher scores in self-perceived fitness scale. One unit higher birth
228 weight SD score predicted 16.7 N (9.9-23.5) increase in hand grip strength. Participants born SGA
229 had 70.0 N (95% CI 36.4; 97.5) weaker hand grip strength than the remaining participants when
230 adjusted for sex, age, cohort, and stage of preterm birth. No difference was seen for the other
231 outcomes. When SGA-participants were excluded, the differences in hand grip strength between
232 groups attenuated and became statistically non-significant. Other results remained similar.

233 Of the participants born early preterm, 21 received supplementary oxygen for 28 days or longer
234 after birth. They had similar fitness as the remaining participants born early preterm.

235 **Discussion**

236 Our main finding was that young adults born early and late preterm performed fewer modified
237 push-ups and those born early preterm had lower hand grip strength in comparison with the control
238 group. Cardiorespiratory fitness was, however, not lower. Young adults born early preterm rated
239 themselves less fit than controls.

240 **Muscular fitness**

241 In the modified push-up test, young adults born early or late preterm performed on average one
242 push-up less than controls. For comparison, 17-year-olds born at 800 g or less performed 5–6 fewer
243 push-ups and exhibited lower performance in other tests measuring muscular fitness than controls.⁸
244 The difference in our study was not explained by socioeconomic status, pregnancy-related factors,
245 or the level of current physical activity and lean body mass. An exception was adjustment for body

fat percentage, which attenuated the associations. This suggests that the higher adiposity of adults born preterm may in part explain their lower performance in the modified push-up test as the test requires supporting one's body weight.

Hand grip strength is a well-established predictor of future physical function, disease risk, and mortality.^{16,17,36-38} Low birth weight is consistently associated with reduced hand grip strength in children, adolescents, and adults. A meta-analysis reported age-adjusted results with approximately 2 kg (20 N) higher muscle strength per kilogram higher birth weight.³⁹ Our findings show a 2.4 kg (23.8 N) difference in hand grip strength between the early preterm group and controls. This difference was largely explained by the lower birth weight SD score of those born early preterm.. An approximate estimate of its consequences is provided by a meta-analysis reporting an overall summary hazard ratio of 0.93 for mortality associated with a 2.5 kg increase in hand grip strength.¹⁶

Cardiorespiratory fitness

Against our hypothesis, cardiorespiratory fitness measured by step test was not lower among young adults born preterm. The confidence interval extended no further than 0.27 SD from zero, indicating we could exclude all but small differences between groups. Several, although not all,⁴⁰ studies have shown lower cardiorespiratory fitness among children and young people born extremely (<28 weeks) or very (<32 weeks) preterm or at extremely or very low birth weight using a maximal exercise test^{10,11,40-43} or a submaximal test^{8,41} as in our study. A study in 218,820 Swedish male conscripts showed that among those born 32 to 36 weeks maximal exercise capacity was 0.10 SD lower than among term-borns¹²; such a small difference would not have been detected in the present study. Together with these studies ,our study suggests that lower levels of cardiorespiratory fitness are not present across the whole range of preterm births at least at any meaningful level.⁴⁴⁻⁴⁶

268 **Self-rated fitness**

269 Correlations between self-rated and objectively measured cardiorespiratory fitness were similar to
270 those previously observed.⁴⁷ They were also similar within groups, indicating that adults born
271 preterm and at term estimate their fitness equally well. This was also true for the modified push-up
272 test, whereas correlations between self-rated fitness and hand grip strength were weak. We are
273 aware of one previous study reporting that young adults born with extremely low birth weight
274 expressed less physical self-confidence.⁴⁸ The difference we found between early preterm and
275 control groups was relatively weak—0.2 points lower scores . The association was not explained by
276 socioeconomic status or pregnancy-related factors. However, adjustment for adult characteristics
277 such as physical activity and body fat percentage attenuated the results, suggesting a mediating role
278 in the association of early preterm birth and self-perceived fitness. The role of leisure time physical
279 activity and body mass index in determining self-perceived health and fitness has been shown
280 earlier ⁴⁹ and is also supported by our results .

281 **Implications**

282 Lower muscular fitness is associated with early and possibly also late preterm birth. This may
283 predispose people born preterm to cardiometabolic diseases in concert with other risk factors,
284 including higher blood pressure and impaired glucose regulation.^{2,3} Low muscular fitness is also
285 associated with other health disadvantages including poorer bone health¹⁵ and is a well-established
286 predictor of mortality in later adulthood.^{16,17} Lower muscular fitness may partly be a consequence
287 of previously observed lower conditioning physical activity levels among young adults born
288 preterm,⁶⁻⁸ which in turn could originate from poorer motor skills or reduced pulmonary function.⁵⁰
289 Our findings ³ emphasize promotion of physical activity, in particular activity to enhance muscular
290 fitness, across the whole range of preterm birth from early childhood onwards .⁵¹ A healthy
291 lifestyle adopted in childhood is likely to carry on into adulthood.⁵² In addition to these practical

292 implications, our results concur with the large body of evidence from human and animal studies
293 suggesting that individual differences in physical activity and fitness originate from early life.⁵³

294 **Strengths and limitations**

295 The strengths of our study include measurement of muscular fitness, assessed in two ways, and
296 cardiorespiratory fitness, and a study population enabling the evaluation of physical fitness across
297 the full range of preterm birth. A detailed non-participation analysis⁵ raised little concern over
298 participation bias. Participants of the clinical examination who could not be included in analyses of
299 handgrip and self-perceived fitness were more likely to be born early preterm; this would be
300 expected to result in more conservative estimates. We had access to reliable and diverse perinatal
301 data, including verified length of gestation. However, an accurate estimation of cardiorespiratory
302 fitness would require maximal exercise testing with a direct measurement of oxygen uptake.

303 **Conclusions**

304 We found that young adults born preterm have lower muscular fitness, as individuals born either
305 early preterm or late preterm performed fewer modified push-ups and those born early preterm had
306 lower hand grip strength. No difference existed in cardiorespiratory fitness. Young adults born early
307 preterm perceived themselves to be less fit than did the controls. The differences we found may
308 increase the risk of chronic adult disease in later life. For pediatricians and allied health
309 professionals, they call for promotion of physical activity in children born both early and late
310 preterm, with a particular focus on promoting physical activity that enhances muscular fitness.

311 **References**

- 312 1. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller A-B, Narwal R, et al. National, regional,
313 and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for
314 selected countries: a systematic analysis and implications. *Lancet*. 2012;379(9832):2162-2172.

2. Johansson S, Iliadou A, Bergvall N, Tuvemo T, Norman M, Cnattingius S. Risk of high blood pressure among young men increases with the degree of immaturity at birth. *Circulation*. 2005;112(22):3430-3436.
3. Kajantie E, Hovi P. Is very preterm birth a risk factor for adult cardiometabolic disease? *Semin Fetal Neonatal Med*. 2014;19(2):112-117.
4. Martin JA, Osterman MJ. Preterm births - United States, 2006 and 2010. *MMWR Surveill Summ*. 2013;62(Suppl 3):136-138.
5. Sipola-Leppanen M, Vaarasmäki M, Tikanmäki M, Matinlinna HM, Miettola S, Hovi P, et al. Cardiometabolic Risk Factors in Young Adults Who Were Born Preterm. *Am J Epidemiol*. 2015; First published online May 5, 2015 doi:10.1093/aje/kwu443
6. Kajantie E, Strang-Karlsson S, Hovi P, Raikonen K, Pesonen AK, Heinonen K, et al. Adults born at very low birth weight exercise less than their peers born at term. *J Pediatr*. 2010;157(4):610-616, 616 e611.
7. Kaseva N, Wehkalampi K, Strang-Karlsson S, Salonen M, Pesonen AK, Raikonen K, et al. Lower conditioning leisure-time physical activity in young adults born preterm at very low birth weight. *PLoS One*. 2012;7(2):e32430.
8. Rogers M, Fay TB, Whitfield MF, Tomlinson J, Grunau RE. Aerobic capacity, strength, flexibility, and activity level in unimpaired extremely low birth weight (≤ 800 g) survivors at 17 years of age compared with term-born control subjects. *Pediatrics*. 2005;116(1):e58-65.
9. Kaseva N, Martikainen S, Tammelin T, Hovi P, Järvenpää A-L, Andersson S, et al. Objectively measured physical activity in young adults born preterm at very low birth weight. *J Pediatr*. 2015;166(2):474-476.
10. Welsh L, Kirkby J, Lum S, Odendaal D, Marlow N, Derrick G, et al. The EPICure study: maximal exercise and physical activity in school children born extremely preterm. *Thorax*. 2010;65(2):165-172.
11. Burns YR, Danks M, O'Callaghan MJ, Gray PH, Cooper D, Poulsen L, et al. Motor coordination difficulties and physical fitness of extremely-low-birthweight children. *Dev Med Child Neurol*. 2009;51(2):136-142.
12. Svedenkrans J, Henckel E, Kowalski J, Norman M, Bohlin K. Long-Term Impact of Preterm Birth on Exercise Capacity in Healthy Young Men: A National Population-Based Cohort Study. *PLoS One*. 2013;8(12):e80869.
13. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*. 2009;301(19):2024-2035.
14. Artero EG, Lee D-c, Lavie CJ, España-Romero V, Sui X, Church TS, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev*. 2012;32(6):351-358.
15. Smith JJ, Eather N, Morgan PJ, Plotnikoff RC, Faigenbaum AD, Lubans DR. The health benefits of muscular fitness for children and adolescents: a systematic review and meta-analysis. *Sports Med*. 2014;44(9):1209-1223.
16. Cooper R, Kuh D, Hardy R, Mortality Review Group. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ*. 2010;341(c4467).
17. Rantanen T. Muscle strength, disability and mortality. *Scand J Med Sci Sports*. 2003;13(1):3-8.
18. Sipola-Leppänen M, Vääräsmäki M, Tikanmäki M, Hovi P, Miettola S, Ruokonen A, et al. Cardiovascular Risk Factors in Adolescents Born Preterm. *Pediatrics*. 2014;134(4):e1072-1081.
19. Järvelin MR, Hartikainen-Sorri AL, Rantakallio P. Labour induction policy in hospitals of different levels of specialisation. *Br J Obstet Gynaecol*. 1993;100(4):310-315.
20. Miettola S, Hartikainen AL, Vaarasmäki M, Bloigu A, Ruokonen A, Jarvelin MR, et al. Offspring's blood pressure and metabolic phenotype after exposure to gestational hypertension in utero. *Eur J Epidemiol*. 2013;28(1):87-98.
21. Vääräsmäki M, Pouta A, Elliot P, Tapanainen P, Sovio U, Ruokonen A, et al. Adolescent Manifestations of Metabolic Syndrome Among Children Born to Women With Gestational Diabetes in a General-Population Birth Cohort. *Am J Epidemiol*. 2009;169(10):1209-1215.

- 367 22. Pihkala J, Hakala T, Voutilainen P, Raivio K. [Characteristic of recent fetal growth curves in Finland].
368 *Duodecim*. 1989;105(18):1540-1546.
- 369 23. Sovijärvi A, Piirilä P, Korhonen O, Louhiluoto E, Pekkanen L. Spirometria- ja PEF-mittausten suoritus
370 ja arviointi. Suomen klinisen fysiologian yhdistyksen ja Suomen keuhko-lääkäriyhdistyksen suositus
371 [Performing and evaluating spirometry and PEF measurements. Recommendation by the Finnish
372 Society of Clinical Physiology and Finnish Society of Pulmonary Medicine]. *Moodi*. 2003;4(113).
- 373 24. Viljanen AA, Halttunen PK, Kreus KE, Viljanen BC. Spirometric studies in non-smoking, healthy
374 adults. *Scand J Clin Lab Invest Suppl*. 1982;159():5-20.
- 375 25. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for
376 lung function tests. *Eur Respir J*. 2005;26(5):948-968.
- 377 26. Kantomaa MT, Stamatakis E, Kankaanpää A, Kaakinen M, Rodriguez A, Taanila A, et al. Physical
378 activity and obesity mediate the association between childhood motor function and adolescents'
379 academic achievement. *Proc Natl Acad Sci U S A*. 2013;110(5):1917-1922.
- 380 27. Tammelin T, Ekelund U, Remes J, Nayha S. Physical activity and sedentary behaviors among Finnish
381 youth. *Med Sci Sports Exerc*. 2007;39(7):1067-1074.
- 382 28. Suni JH, Oja P, Laukkanen RT, Miilunpalo SI, Pasanen ME, Vuori IM, et al. Health-related fitness test
383 battery for adults: aspects of reliability. *Arch Phys Med Rehabil*. 1996;77(4):399-405.
- 384 29. Suni JH RM, Ruiz JR. Retest Repeatability of Motor and Musculoskeletal Fitness Tests for Public
385 Health Monitoring of Adult Populations. *J Nov Physiother*. 2014;4(1):1000194.
- 386 30. Stenholm S, Härkänen T, Sainio P, Heliövaara M, Koskinen S. Long-term Changes in Handgrip
387 Strength in Men and Women—Accounting the Effect of Right Censoring Due to Death. *J Gerontol A*
388 *Biol Sci Med Sci*. 2012;67(10):1068-1074.
- 389 31. Åstrand PO, Ryhming I. A nomogram for calculation of aerobic capacity (physical fitness) from pulse
390 rate during sub-maximal work. *J Appl Physiol*. 1954;7(2):218-221.
- 391 32. Tammelin T, Nayha S, Rintamäki H. Cardiorespiratory fitness of males and females of northern
392 Finland birth cohort of 1966 at age 31. *Int J Sports Med*. 2004;25(7):547-552.
- 393 33. Pulkkinen KR, Mäkinen T, Valkeinen H, Prattala R, Borodulin K. Educational differences in self-rated
394 physical fitness among Finns. *BMC Public Health*. 2013;13(163).
- 395 34. Jaakkola JJ, Ahmed P, Ieromnimon A, Goepfert P, Laiou E, Quansah R, et al. Preterm delivery and
396 asthma: a systematic review and meta-analysis. *J Allergy Clin Immunol*. 2006;118(4):823-830.
- 397 35. Strang-Karlsson S, Räikkönen K, Pesonen A-K, Kajantie E, Paavonen E, Lahti J, et al. Very Low
398 Birth Weight and Behavioral Symptoms of Attention Deficit Hyperactivity Disorder in Young
399 Adulthood: The Helsinki Study of Very-Low-Birth-Weight Adults. *Am J Psychiatry*.
400 2008;165(10):1345-1353.
- 401 36. Rantanen T, Guralnik JM, Foley D, et al. Midlife hand grip strength as a predictor of old age
402 disability. *JAMA*. 1999;281(6):558-560.
- 403 37. Silventoinen K, Magnusson PKE, Tynelius P, Batty GD, Rasmussen F. Association of body size and
404 muscle strength with incidence of coronary heart disease and cerebrovascular diseases: a
405 population-based cohort study of one million Swedish men. *Int J Epidemiol*. 2009;38(1):110-118.
- 406 38. Gale CR, Martyn CN, Cooper C, Sayer AA. Grip strength, body composition, and mortality. *Int J*
407 *Epidemiol*. 2007;36(1):228-235.
- 408 39. Dodds R, Denison HJ, Ntani G, Cooper R, Cooper C, Sayer AA, et al. Birth weight and muscle
409 strength: A systematic review and meta-analysis. *J Nutr Health Aging*. 2012;16(7):609-615.
- 410 40. Clemm H, Roksund O, Thorsen E, Eide GE, Markestad T, Halvorsen T. Aerobic capacity and exercise
411 performance in young people born extremely preterm. *Pediatrics*. 2011;129(1):e97-e105.
- 412 41. Smith LJ, van Asperen PP, McKay KO, Selvadurai H, Fitzgerald DA. Reduced Exercise Capacity in
413 Children Born Very Preterm. *Pediatrics*. 2008;122(2):e287-e293.
- 414 42. Vrijlandt EJLE, Gerritsen J, Boezen HM, Grevink RG, Duiverman EJ. Lung Function and Exercise
415 Capacity in Young Adults Born Prematurely. *Am J Respir Crit Care Med*. 2006;173(8):890-896.
- 416 43. Kilbride HW, Gelatt MC, Sabath RJ. Pulmonary function and exercise capacity for ELBW survivors in
417 preadolescence: effect of neonatal chronic lung disease. *J Pediatr*. 2003;143(4):488-493.

- 418 44. Ridgway CL, Ong KK, Tammelin T, Sharp SJ, Ekelund U, Jarvelin MR. Birth size, infant weight gain,
419 and motor development influence adult physical performance. *Med Sci Sports Exerc.*
420 2009;41(6):1212-1221.
- 421 45. Boreham CA, Murray L, Dedman D, Smith GD, Savage JM, Strain JJ. Birthweight and aerobic fitness
422 in adolescents: the Northern Ireland Young Hearts Project. *Public Health.* 2001;115(6):373-379.
- 423 46. Salonen MK, Kajantie E, Osmond C, Forsen T, Yliharsila H, Paile-Hyvarinen M, et al. Developmental
424 origins of physical fitness: the Helsinki Birth Cohort Study. *PLoS One.* 2011;6(7):e22302.
- 425 47. Germain JL, Hausenblas HA. The Relationship Between Perceived and Actual Physical Fitness: A
426 Meta-Analysis. *J Appl Sport Psychol.* 2006;18(4):283-296.
- 427 48. Saigal S, Stoskopf B, Boyle M, Paneth N, Pinelli J, Streiner D, et al. Comparison of current health,
428 functional limitations, and health care use of young adults who were born with extremely low birth
429 weight and normal birth weight. *Pediatrics.* 2007;119(3):e562-573.
- 430 49. Okano G, Miyake H, Mori M. Leisure Time Physical Activity as a Determinant of Self-Perceived
431 Health and Fitness in Middle-Aged Male Employees. *J Occup Health.* 2003;45(5):286-292.
- 432 50. Saarenpaa HK, Tikanmaki M, Sipola-Leppanen M, Hovi P, Wehkalampi K, Siltanen M, et al. Lung
433 Function in Very Low Birth Weight Adults. *Pediatrics.* 2015;
- 434 51. Peykari N, Eftekhari MB, Tehrani FR, Afzali HM, Hejazi F, Atoofi MK, et al. Promoting Physical
435 Activity Participation among Adolescents: The Barriers and the Suggestions. *Int J Prev Med.*
436 2015;6(12).
- 437 52. Telama R, Yang X, Leskinen E, Kankaanpaa A, Hirvensalo M, Tammelin T, et al. Tracking of physical
438 activity from early childhood through youth into adulthood. *Med Sci Sports Exerc.* 2014;46(5):955-
439 962.
- 440 53. Gardner DS, Rhodes P. Developmental origins of obesity: programming of food intake or physical
441 activity? *Adv Exp Med Biol.* 2009;646(83-93).

442

443

Figure 1. Mean differences (95 % CIs, error bars) in preterm groups compared with controls (zero line). Adjustments: Model 1 (sex, age, cohort, bronchodilation [step test]), Model 2 (Model 1 + parental education, maternal smoking, gestational diabetes, hypertensive disorder), Model 3 (Model 2 + physical activity, asthma, height, body fat percentage, smoking).

Table 1. Perinatal, neonatal, and current characteristics of the young adults born preterm and of the control group born at term.

	Early Preterm, <i>n</i> =139			<i>P</i> value ^a	Late Preterm <i>n</i> =247			<i>P</i> value ^a	Controls, <i>n</i> =352			Missing
	No.	%	Mean (SD)		No.	%	Mean (SD)		No.	%	Mean (SD)	
Men	65	46.8		0.93	120	48.6		0.90	168	47.7		0/0/0
NFBC member	49	35.3		<0.001	110	44.5		<0.001	213	60.5		0/0/0
Peri- and neonatal												
Multiple pregnancy	32	23.0		<0.001	33	13.4		<0.001	4	1.1		0/0/0
Maternal hypertension ^b	18	12.9		0.48	36	14.6		0.14	36	10.2		0/0/0
Maternal pre-eclampsia ^c	33	23.7		<0.001	29	11.7		0.002	16	4.5		0/0/0
Maternal gestational diabetes	4	2.9		0.64	11	4.5		0.08	6	1.7		0/0/0
Maternal smoking during pregnancy	21	15.1		1.00	47	19.0		0.41	57	16.2		0/0/0
Cesarean section	84	60.4		<0.001	70	28.3		<0.001	41	11.6		0/0/0
Gestational age, weeks			31.8 (2.0)	<0.001			35.8 (0.8)	<0.001			40.1 (1.2)	0/0/0
Birth weight, g			1784 (486)	<0.001			2668 (514)	<0.001			0.0 (1.0)	0/0/0
Birth weight SD score (SD)			-0.7 (1.4)	<0.001			-0.6 (1.3)	<0.001			0.0 (1.2)	0/0/0
Small for gestational age	23	16.5		<0.001	31	12.6		<0.001	7	2.0		0/0/0
Large for gestational age	4	2.9		1.00	5	2.0		0.45	11	3.1		0/0/0
Respirator treatment	68	48.9		<0.001	30	12.1		<0.001	2	0.6		0
Duration of respirator treatment, days ^e			24.1 (50.7)	0.55				0.51			2.5 (0.7)	
Supplementary oxygen	101	72.7		<0.001	97	39.3		<0.001	7	2.0		0
Duration of supplementary oxygen, days ^f			16.5 (14.6)	<0.001			14.2 (62.5)	0.65			3.4 (1.5)	
Current												
Age (SD), y			23.1 (1.4)	<0.001			23.1 (1.3)	<0.001			23.6 (1.1)	0/0/0
Height (SD), cm												0/0/0
Men			178.6 (7.0)	0.33			177.7 (6.7)	0.94			177.6 (7.0)	
Women			163.3 (5.1)	0.44			164.6 (5.7)	0.35			163.9 (5.9)	
Body mass index (SD), kg/m ²												0/0/0
Men			24.2 (4.0)	0.88			25.2 (4.6)	0.06			24.3 (3.3)	
Women			24.2 (5.7)	0.22			23.6 (4.2)	0.66			23.4 (4.4)	
Body fat percentage (SD), %												5/5/10
Men			17.6 (6.5)	0.82			19.5 (7.5)	0.01			17.4 (5.7)	
Women			30.8	0.009			28.9	0.25			27.9	

		(7.9)		(6.9)		(7.5)			
Lean body mass (SD), kg		63.2 (8.8)		63.4 (8.4)		63.1 (8.7)		5/5/10	
		44.2 (7.2)		45.1 (5.8)		44.5 (5.4)			
Parental education		0.46		0.58				1/5/4	
Basic or less	13	9.4		20	8.3		20	5.7	
Secondary	83	59.7		138	57.0		213	61.2	
Lower-level tertiary	14	10.1		31	12.8		45	12.9	
Upper-level tertiary	28	20.1		53	21.9		70	20.1	
Self-reported physical activity, METh/wk		23.5 (13.7)		24.9 (14.6)		25.7 (13.9)		4/7/10	
Daily smoking	39	28.1	0.14	54	21.9	0.95	75	21.3	0/0/0
Use of beta blockers ^g	0	0	1.000	0	0	0.52	2	0.6	0/0/0
Asthma	29	20.9	0.21	40	16.2	0.94	55	15.6	0/0/0
Bronchodilation test performed ^h	58	41.7	0.002	78	31.6	0.23	94	26.7	0/0/0

1) Abbreviations: METh/wk, metabolic equivalent hours per week.

^a *P* values refer to comparisons between preterm groups and controls, using Student's *t*-test or Pearson's chi-square test with Yates's continuity correction for 2-by-2 tables (and Fisher's exact test for use of beta blockers).

Level of statistical significance *P* value <0.05.

^b Gestational or chronic hypertension.

^c Includes superimposed pre-eclampsia.

^d Subjects whose mother's gestational diabetes data are missing include those whose mothers did not undergo an oral glucose tolerance test despite risk factors and thus have uncertain gestational diabetes status.

^e Mean (SD) duration of respirator treatment among those treated in respirator.

^f Mean (SD) duration of supplementary oxygen among those treated with supplementary oxygen.

^g During the day before clinical visit.

^h During clinical visit.

Table 2. Mean (SD) values of fitness measures in early preterm (< 34 weeks), late preterm (34-36 weeks) and control (≥ 37 weeks) group by sex.

		Early preterm		Late preterm		Controls	
		Mean (SD)	n	Mean (SD)	n	Mean (SD)	n
Modified push-ups/40 s	Men	13.9 (4.0)	62	13.7 (4.0)	115	14.8 (3.2)	157
	Women	10.2 (3.0)	68	10.3 (2.8)	112	10.8 (3.3)	169
	All	12.0 (3.9)	130	12.0 (3.8)	227	12.7 (3.8)	326
Hand grip strength (N)	Men	609.8 (150.4)	65	627.5 (145.7)	118	653.5 (135.7)	163
	Women	336.6 (66.8)	74	351.6 (90.8)	127	350 (81)	183
	All	464.3 (177.7)	139	484.5 (183.1)	245	492.9 (187.5)	346
Heart rate after step test (beats/min)	Men	155 (16)	62	153 (16)	115	153 (15)	160
	Women	161 (14)	70	160 (15)	117	160 (14)	168
	All	158 (15)	132	156 (16)	232	157 (15)	328
Self-perceived fitness (scale 1-5)	Men	2.4 (1.0)	62	2.5 (0.9)	117	2.7 (0.8)	163
	Women	2.2 (0.9)	73	2.5 (0.8)	123	2.4 (0.8)	179
	All	2.3 (0.9)	135	2.5 (0.8)	240	2.5 (0.8)	342

SupplementalTable 1. Modified push-ups/40s, hand grip strength (N), heart rate after step test (beats/min) and self-perceived fitness (scale 1-5, 1=very poor, 5=very good) in preterm groups compared with term-born controls.

	Controls		Model ^a	Early preterm		<i>P</i> value ^b	Late preterm		<i>p</i> value ^b	Total N
	Mean(SD)	n		Mean difference (95% CI)	n		Mean difference (95% CI)	n		
Modified push-ups/40 s		326			130			227		
	12.7 (3.8)		1	-0.8 (-1.5; -0.1)		0.02	-0.8 (-1.4; -0.3)		0.005	683
			2	-0.9 (-1.6; -0.1)		0.03	-0.8 (-1.4; -0.2)		0.008	683
			3	-0.4 (-1.1; 0.4)		0.33	-0.4 (-1.0; 0.1)		0.12	654
Hand grip strength (N)		346			139			245		
	492.9 (187.5)		1	-23.8 (-46.8; -0.9)		0.04	-9.1 (-28.1; 9.9)		0.35	730
			2	-10.7 (-35.0; 13.7)		0.39	3.4 (-16.2; 23.0)		0.73	730
			3	-13.1 (-37.6; 11.5)		0.30	-2.0 (-21.5; 17.6)		0.84	692
Heart rate after step test (beats/min)		328			132			232		
	157 (15)		1	0 (-3; 3)		1.00	-1 (-4; 2)		0.43	692
			2	0 (-4; 3)		0.89	-1 (-4; 2)		0.41	692
			3	-2 (-5; 1)		0.24	-3 (-5; 0)		0.02	659
Self-perceived fitness (scale 1-5)		342			135			240		
	2.5 (0.8)		1	-0.2 (-0.4; 0.0)		0.02	0.0 (-0.2; 0.1)		0.61	717
			2	-0.2 (-0.4; 0.0)		0.03	0.0 (-0.2; 0.1)		0.91	717
			3	-0.1 (-0.2; 0.1)		0.40	0.1(0.0; 0.2)		0.22	697

^aModel 1: sex, age, cohort, and for step test: bronchodilation at clinical visit.

Model 2:Model 1+ SES, maternal smoking, gestational diabetes and hypertensive disorder during pregnancy, birth weight SD score.

Model 3:Model 2 + self-reported physical activity, diagnosed asthma, adult body size: height, body fat percentage, smoking.

^bLevel of statistical significance *P* value <0.05.

Supplemental Table 2. Correlations between the outcomes among study participants.

		Hand grip strength (N)			Heart rate after step test (beats/min)			Self-perceived fitness (scale 1-5) ^a		
		Correlation coefficient	<i>P</i> value	No.	Correlation coefficient	<i>P</i> value	No.	Correlation coefficient	<i>P</i> value	No.
Modified push-ups/40s	All	0.268	<0.001	681	-0.210	<0.001	661	0.311	<0.001	666
	Early preterm	0.152	0.088	130	-0.207	0.021	126	0.300	0.001	126
	Late preterm	0.301	<0.001	226	-0.216	0.001	218	0.330	<0.001	221
	Controls	0.288	<0.001	325	-0.214	<0.001	317	0.288	<0.001	319
Hand grip strength (N)	All				-0.124	<0.001	692	0.150	<0.001	712
	Early preterm				-0.141	0.108	132	0.069	0.431	135
	Late preterm				-0.090	0.173	231	0.153	0.018	239
	Controls				-0.150	0.007	329	0.167	0.002	338
Heart rate after step test (beats/min)	All						691	-0.361	<0.001	678
	Early preterm							-0.380	<0.001	128
	Late preterm							-0.392	<0.001	226
	Controls							-0.337	<0.001	324

Correlations were adjusted for sex and age.

^a Self-perceived fitness scale 1-5, with 1=very poor, 5=very good.

Supplemental Table 3. Covariates in association with the outcomes among study participants. Mean differences (95% CI) of the outcomes compared with the reference group or one unit higher value adjusted for sex, age and cohort selection.

	Modified push-ups/40s (N=683)			Hand grip strength (N) (N=730)			Heart rate after step test (beats/min) (N=692)			Self-perceived fitness; scale 1 (lowest) to 5 (highest) (N=717)		
	Mean difference (95% CI)	P value	No.	Mean difference (95% CI)	P value	No.	Mean difference (95% CI)	P value	No.	Mean difference (95% CI)	P value	No.
Sex												
Male	3.7 (3.2; 4.2)	<0.001* **	334	287.9 (271.0; 304.4)	<0.001 ***	346	-7 (-8; -4)	<0.001* **	337	-0.2 (-0.3; -0.1)	0.001* **	342
Female	Referent		349	Referent		384	Referent		355	Referent		375
Age	0.0 (-0.3; 0.3)	0.84	683	0.8 (-8.5; 10.1)	0.86	730	0 (-2; 1)	0.49	692	0.0 (0.0; 0.1)	0.18	717
Cohort												
FMBR	Referent		341	Referent		363	Referent		346	Referent		354
NFBC	-0.2 (-0.9; 0.5)	0.50	342	17.0 (-6.3; 40.3)	0.15	367	-2 (-5; 1)	0.27	346	0.0 (-0.2; 0.2)	0.90	363
Bronchodilation test ^a	-0.3 (-0.8 ; 0.3)	0.30	683	-7.3 (-25.4; 10.7)	0.43	730	4 (2; 7)	<0.001* **	692	-0.1 (-0.3; 0.0)	0.03*	717
Parental educational level												
Basic or less	-1.7 (-2.8; -0.6)	0.003**	47	4.2 (-32.0; 40.5)	0.82	52	2 (-3; 7)	0.37	49	-0.3 (-0.6; -0.0)	0.03	51
Secondary	-1.0 (-1.7; -0.4)	0.002**	402	0.7 (-20.7; 22.1)	0.95	431	2 (0; 6)	0.06	404	-0.2 (-0.4; -0.1)	0.007	427
Lower-level tertiary	-0.8 (-1.7; 0.2)	0.10	85	1.3 (-28.7; 31.4)	0.93	90	1 (-3; 5)	0.563	87	0.0 (-0.3; 0.2)	0.77	88
Upper-level tertiary	Referent		142	Referent		149	Referent		145	Referent		150
Missing	-2.0 (-4.6; 0.6)	0.12	7	-83.4 (-165.1; -1.6)	0.05*	8	4.5 (-7; 16)	0.43	7	-1.6 (-3.3 ;0.1)	0.06	1
Maternal smoking during pregnancy												
No	Referent		557	Referent		588	Referent		558	Referent		578
Yes	-0.9 (-1.6; -0.2)	0.008**	112	-6.8 (-29.1; 15.5)	0.55	125	0 (-3; 3)	0.94	118	-0.1 -0.2; 0.1)	0.45	122
Missing	1.5 (-0.3; 3.3)	0.10	14	-11.7 (-67.3; 44.0)	0.68	17	-3 (-10; 4)	0.43	16	0.2 (-0.2; 0.6)	0.35	17
Maternal gestational diabetes						730						717
No GDM	Referent		614	Referent		655	Referent		622	Referent		53
GDM	-0.9 (-2.5; 0.6)	0.24	19	-37.2 (-87.1; 12.8)	0.14	21	3 (-4; 10)	0.45	18	-0.4 (0.8; 0.0)	0.03*	644
Missing	-0.7 (-1.7; 0.3)	0.18	50	-7.9 (-41.1; 25.3)	0.64	54	-3.5 (-8; 1)	0.12	52	0.1 (-0.2; 0.3)	0.69	20
Maternal hypertensive disorder during pregnancy												717
No maternal hypertensive disorder	Referent		517	Referent		553	Referent		521	Referent		544
Maternal hypertension ^b	-0.4 (-1.2; 0.4)	0.34	84	-10.8 (-36.5; 14.8)	0.41	89	2 (-2; 5)	0.34	85	-0.1 (-0.3; 0.1)	0.17	88

Maternal pre-eclampsia ^c	-0.4 (-1.2; 0.54)	0.36	73	-34.6 (-61.8; -7.4)	0.01*	78	4 (0; 7)	0.05	76	-0.1 (-0.3; 0.1)	0.52	75
Missing	-0.5 (-2.7; 1.8)	0.67	9	20.5 (-51.1; 92.1)	0.57	10	-6 (-15; 4)	0.23	10	0.5 (-0.1; 1.0)	0.08	10
Birth weight SD score	0.0 (-0.3; 0.2)	0.67	683	16.7 (9.9; 23.5)	<0.001***	730	-0 (-1; 1)	0.68	692	0.0 (0.0; 0.1)	0.16	717
Self-reported physical activity, METh/wk	0.1 (0.0; 0.1)	<0.001**	666	0.6 (0.0; 1.2)	0.04*	712	0 (0; 0)	<0.001**	676	0.03 (0.02;-0.03)	<0.001***	717
Asthma												
Yes	0.2 (-0.5; 0.9)	0.53	111	-23.0 (-45.3; -0.8)	0.04*	123	2 (-1; 5)	0.19	115	-0.2 (-0.4; 0.0)	0.01*	123
No	Referent		572	Referent		607	Referent		577	Referent		594
Height (cm)	0.0 (0.0; 0.0)	0.91	683	6.0 (4.8; 7.3)	<0.001***	730	0 (0; 0)	0.20	692	0.8 (-0.2; 1.8)	0.13	717
Body fat percentage, %	-0.2 (-0.2; -0.2)	<0.001**	671	-2.9 (-4.1; -1.7)	<0.001***	710	1 (1; 1)	<0.001**	675	-0.047 -0.055;-0.038)	<0.001***	697
Lean body mass, kg	0.0 (0.0-0.1)	0.233	671	6.7 (5.6; 7.7)	<0.001***	710	0 (0; 0)	0.63	675	0.003 (-0.005; 0.012)	0.47	697
Daily smoking												
Yes	-0.8 (-1.4; -0.2)	0.01*	150	-1.2 (-21.1; 18.6)	0.91	167	-3 (-5; 0)	0.03*	158	-0.3 (-0.5;-0.2)	<0.001***	162
No	Referent		533	Referent		563	Referent		692	Referent		555

1) Abbreviations: CI, confidence interval; FMBR, Finnish Medical Birth Register; METh/wk, metabolic equivalent hours per week; NFBC, Northern Finland Birth Cohort.

^aDuring clinical visit.

^bGestational or chronic hypertension.

^cIncludes superimposed pre-eclampsia.

*One person can have more than one reason for exclusion

**During the day before clinical visit.