

# NEWSLETTER



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*Per la ricerca degli articoli pubblicati nella letteratura scientifica nel trimestre in esame sono state consultate le banche dati Medline, Embase, utilizzando le seguenti parole chiave (o i loro sinonimi): 'Birth Cohort', 'Primary Care', 'Infant', 'Child', 'Human', 'Newborn', 'Pediatrician', 'General practice'. Sono qui riportate le referenze considerate rilevanti e pertinenti.*

1. Thorax 2021;76(2):116-125. doi:10.1136/thoraxjnl-2020-215422  
**ASSOCIATION OF ASTHMA SEVERITY AND EDUCATIONAL ATTAINMENT AT AGE 6-7 YEARS IN A BIRTH COHORT: POPULATION-BASED RECORD-LINKAGE STUDY.**  
*Evans A, Farewell D, Demmler J, Bandyopadhyay A, Powell CVE, Paranjothy S.*

**BACKGROUND:** There is conflicting research about the association between asthma and poor educational attainment that may be due to asthma definitions. Our study creates seven categories of current chronic and acute asthma to investigate if there is an association for poorer educational attainment at age 6-7 years, and the role of respiratory infections and school absence.

**METHODS:** This study used a population-based electronic cross-sectional birth cohort 1998-2005, in Wales, UK, using health and education administrative datasets. Current asthma or wheeze categories were developed using clinical management guidelines in general practice (GP) data, acute asthma was inpatient hospital admissions and respiratory infections were the count of GP visits, from birth to age 6-7 years. We used multilevel logistic regression grouped by schools to ascertain if asthma or wheeze was associated with not attaining the expected level in teacher assessment at Key Stage 1 (KS1) adjusting for sociodemographics, perinatal, other respiratory illness and school characteristics. We tested if absence from school was a mediator in this relationship using the difference method. Results There were 85 906 children in this population representative cohort with 7-year follow-up. In adjusted multilevel logistic regression, only asthma inpatient hospital admission was associated with increased risk for not attaining the expected level at KS1 (adjusted OR 1.14 95% CI (1.02 to 1.27)). Lower respiratory tract infection (LRTI) GP contacts remained an independent predictor for not attaining the expected level of education. Absence from school was a potential mediator of the association between hospital admission and educational attainment.

**CONCLUSIONS:** Clinicians and educators need to be aware that children who have inpatient hospital admissions for asthma or wheeze, or repeated LRTI, may require additional educational support for their educational outcomes.



2. Int J Obes (Lond) 2022;46(3):637-645. doi:10.1038/s41366-021-00975-3  
**DETERMINANTS OF CORD BLOOD ADIPOKINES AND ASSOCIATION WITH NEONATAL ABDOMINAL ADIPOSE TISSUE DISTRIBUTION.**  
*Tan K, Tint MT, Michael N, et al.*

**BACKGROUND:** Cord blood leptin and adiponectin are adipokines known to be associated with birth weight and overall infant adiposity. However, few studies

have investigated their associations with abdominal adiposity in neonates. We examined maternal factors associated with cord blood leptin and adiponectin, and the association of these adipokines with neonatal adiposity and abdominal fat distribution measured by magnetic resonance imaging (MRI) in an Asian mother-offspring cohort.

**METHODS:** Growing Up in Singapore Towards healthy Outcomes (GUSTO), is a prospective mother-offspring birth cohort study in Singapore. Cord blood plasma leptin and adiponectin concentrations were measured using Luminex and Enzyme-Linked Immunosorbent Assay respectively in 816 infants. A total of 271 neonates underwent MRI within the first 2-weeks after delivery. Abdominal superficial (sSAT), deep subcutaneous (dSAT), and intra-abdominal (IAT) adipose tissue compartment volumes were quantified from MRI images. Multivariable regression analyses were performed.

**RESULTS:** Indian or Malay ethnicity, female sex, and gestational age were positively associated with cord blood leptin and adiponectin concentrations. Maternal gestational diabetes (GDM) positively associated with cord blood leptin concentrations but inversely associated with cord blood adiponectin concentrations. Maternal pre-pregnancy body mass index (BMI) showed a positive relationship with cord blood leptin but not with adiponectin concentrations. Each SD increase in cord blood leptin was associated with higher neonatal sSAT, dSAT and IAT; differences in SD (95% CI): 0.258 (0.142, 0.374), 0.386 (0.254, 0.517) and 0.250 (0.118, 0.383), respectively. Similarly, each SD increase in cord blood adiponectin was associated with higher neonatal sSAT and dSAT; differences in SD (95% CI): 0.185 (0.096, 0.274) and 0.173 (0.067, 0.278), respectively. The association between cord blood adiponectin and neonatal adiposity was observed in neonates of obese mothers only.

**CONCLUSIONS:** Cord blood leptin and adiponectin concentrations were associated with ethnicity, maternal BMI and GDM, sex and gestational age. Both adipokines showed positive association with neonatal abdominal adiposity.



3. Environ Res 2022;205 doi:10.1016/j.envres.2021.112545  
**ENVIRONMENTAL POLLUTANT EXPOSURE ASSOCIATED WITH ALTERED EARLY-LIFE GUT MICROBIOME: RESULTS FROM A BIRTH COHORT STUDY.**  
*Naspolini NF, Meyer A, Moreira JC, Sun H, Froes-Asmus CIR, Dominguez-Bello MG.*

Emerging evidence shows that the gut microbiota interacts with environmental pollutants, but the effect of early exposure on the neonatal microbiome remains unknown. We investigated the association between maternal exposure to environmental pollutants and changes in early-life gut microbiome development. We surveyed 16S rRNA gene on meconium and fecal samples (at 1, 3, and 6 months) from the Brazilian birth cohort, and associated with levels of metals, perfluoroalkyl chemicals (PFAS), and pesticides in maternal and umbilical cord

blood. The results indicate that the magnitude of the microbiome changes associated with increasing pollutant exposure was bigger in cesarean-section (CS) born and CS-born-preterm babies, in relation to vaginally (VG) delivered infants. Breastfeeding was associated with a stronger pollutant-associated effect on the infant feces, suggesting that the exposure source could be maternal milk. Differences in microbiome effects associated with maternal or cord blood pollutant concentrations suggest that fetal exposure time - intrauterine or perinatal - may matter. Finally, despite the high developmental microbiota variability, specific microbionts were consistently affected across all pollutants, with taxa clusters found in samples from infants exposed to the highest toxicant exposure. The results evidence that perinatal exposure to environmental pollutants is associated with alterations in gut microbiome development which may have health significance.



4. J Atten Disord 2022;26(2):282-295. doi:10.1177/1087054720972790  
**EXAMINING THE EDUCATIONAL GAP FOR CHILDREN WITH ADHD AND SUBTHRESHOLD ADHD.**  
*Zendarski N, Guo S, Sciberras E, et al.*

**OBJECTIVE:** The present study examined the impact of Attention Deficit Hyperactivity Disorder (ADHD) on core educational outcomes in two large community cohorts of Australian school children.

**METHOD:** Academic (reading and numeracy) and non-academic (school engagement, attendance, peer victimization, and parental expectations) outcomes were compared between children with ADHD, subthreshold ADHD, and controls when children were in grade 5 (M age = 10.5). Data were drawn from the Longitudinal Study of Australian Children birth cohort (LSAC; N = 3,540) and the Children's Attention Project (CAP; N = 356).

**RESULTS:** Both subthreshold ADHD and ADHD groups had poorer outcomes on all measures, with medium effects sizes. Differences were not evident between subthreshold ADHD and ADHD groups.

**CONCLUSIONS:** Educational outcomes examined in this study highlight the educational risk for upperprimary school children with ADHD or subthreshold ADHD, in comparison to their peers. Monitoring these outcomes is necessary to inform policy, practice, and intervention.



5. Front Psychol 2021;12:781602. doi:10.3389/fpsyg.2021.781602  
**IS MOTOR MILESTONE ASSESSMENT IN INFANCY VALID AND SCALED EQUALLY ACROSS SEX, BIRTH WEIGHT, AND GESTATIONAL AGE? FINDINGS FROM THE MILLENNIUM COHORT STUDY.**  
*de Almeida Maia D, Bardid F, Koch T, et al.*

Is the assessment of motor milestones valid and scaled equivalently for all infants? It is not only important to understand if the way we use gross and fine motor scores are appropriate for monitoring motor milestones but also to determine if these scores are confounded by specific infant characteristics. Therefore, the aim of the study is to investigate the latent structure underlying motor milestone assessment in infancy and measurement invariance across sex, birth weight, and gestational age. For this study, the birth cohort data from the United Kingdom Millennium Cohort Study (MCS) was used, which includes the assessment of eight motor milestone tasks from the Denver Developmental Screening Test in 9-month-old infants (N = 18,531), depicting early motor development of the first children of generation Z. Confirmatory factor analyses showed a better model fit for a two-factor structure (i.e., gross and fine motor development) compared to a one-factor structure (i.e., general motor development), and multiple indicators multiple causes modeling revealed no differential item functioning related to sex, birth weight, and gestational age. The study provides support for the use of gross and fine motor scores when assessing motor milestones in infants-both boys and girls with different birth weights and of varying gestational ages. Further investigation into widely adopted assessment tools is recommended to support the use of valid composite scores in early childhood research and practice.



6. Eur Spine J 2022;31(2):248-257. doi:10.1007/s00586-021-07054-1  
**SPINOPELVIC ALIGNMENT AND LUMBAR VERTEBRAL SHAPE IN CHILDREN: ASSOCIATIONS WITH STRUCTURAL SPINAL ABNORMALITIES AND BODY COMPOSITION IN THE GENERATION R STUDY.**  
*van den Heuvel MM, Griffioen NE, Achterberg HC, et al.*

**PURPOSE:** To investigate the spinopelvic alignment and vertebral shape in children, and associations with body composition and structural spinal abnormalities on magnetic resonance imaging (MRI).

**METHODS:** We performed a cross-sectional study embedded in the Generation R Study, a prospective population-based birth cohort. Pelvic incidence and vertebral concavity ratios for each lumbar level were determined on sagittal MRI images in 9-year-old children, and structural spinal abnormalities were scored semi-quantitatively. The BMI-SD score was calculated, and body composition was assessed using DXA scans. Associations of pelvic incidence and vertebral concavity ratios with structural abnormalities and body composition measures were assessed using (multilevel) regression analyses.

**RESULTS:** This study included 522 participants (47.7% boys), aged 9.9 years (IQR 9.7-10.0). The mean pelvic incidence was 36.6° (SD 8.0). Vertebral concavity ratios ranged from 0.87 to 0.90, with significantly lower ratios for boys compared to girls. Associations were found for a larger pelvic incidence with decreased disc height [OR 1.03 (95% CI 1.02-1.05)], and a pelvic incidence in the lowest tertile with less disc bulging [OR 0.73 (95% CI 0.56-0.95)]. Increased vertebral concavity ratio was associated with decreased disc height [OR 14.16 (95% CI 1.28-157.13)]. Finally, increased fat-free mass index was associated with a smaller pelvic incidence [adjusted OR 0.85 (95% CI 0.07-1.63)].

**CONCLUSION:** The mean pelvic incidence of 9-year-old children is 36.6° on supine MRI images, and a slightly concave shape of the lumbar vertebrae is seen. Spinopelvic alignment is associated with structural spinal abnormalities, and might itself be influenced by the children's body composition.



7. BMC Med 2022;20(1):20. doi:10.1186/s12916-021-02217-9

**VARIABILITY IN NEWBORN TELOMERE LENGTH IS EXPLAINED BY INHERITANCE AND INTRAUTERINE ENVIRONMENT.**

*Chen L, Tan KML, Gong M, et al.*

**BACKGROUND:** Telomere length (TL) and its attrition are important indicators of physiological stress and biological aging and hence may vary among individuals of the same age. This variation is apparent even in newborns, suggesting potential effects of parental factors and the intrauterine environment on TL of the growing fetus.

**METHODS:** Average relative TLs of newborns (cord tissue, N = 950) and mothers (buffy coat collected at 26-28 weeks of gestation, N = 892) were measured in a birth cohort. This study provides a comprehensive analysis of the effects of heritable factors, socioeconomic status, and in utero exposures linked with maternal nutrition, cardiometabolic health, and mental well-being on the newborn TL. The association between maternal TL and antenatal maternal health was also studied.

**RESULTS:** Longer maternal TL ( $\beta = 0.14$ ,  $P = 1.99E-05$ ) and higher paternal age ( $\beta = 0.10$ ,  $P = 3.73E-03$ ) were positively associated with newborn TL. Genome-wide association studies on newborn and maternal TLs identified 6 genetic variants in a strong linkage disequilibrium on chromosome 3q26.2 (Tag SNP-LRRC34-rs10936600:  $P(\text{meta}) = 5.95E-08$ ). Mothers with higher anxiety scores, elevated fasting blood glucose, lower plasma insulin-like growth factor-binding protein 3 and vitamin B12 levels, and active smoking status during pregnancy showed a higher risk of giving birth to offspring with shorter TL. There were sex-related differences in the factors explaining newborn TL variation. Variation in female newborn TL was best explained by maternal TL, mental health, and plasma vitamin B12 levels, while that in male newborn TL was best explained by paternal age, maternal education, and metabolic health. Mother's TL was associated with her

own metabolic health and nutrient status, which may have transgenerational effects on offspring TL.

**CONCLUSIONS:** Our findings provide a comprehensive understanding of the heritable and environmental factors and their relative contributions to the initial setting of TL and programming of longevity in early life. This study provides valuable insights for preventing in utero telomere attrition by improving the antenatal health of mothers via targeting the modifiable factors.

TRIAL REGISTRATION: ClinicalTrials.gov, NCT01174875. Registered on 1 July 2010.

1. J Gerontol A Biol Sci Med Sci 2022: glac007. doi:10.1093/gerona/glac007  
**EARLY LIFE FACTORS AS PREDICTORS OF AGE-ASSOCIATED DEFICIT ACCUMULATION ACROSS 17 YEARS FROM MIDLIFE INTO OLD AGE.**  
*Haapanen MJ, Jylhävä J, Kortelainen L, et al.*

**BACKGROUND:** Early life exposures have been associated with the risk of frailty in old age. We investigated whether early life exposures predict the level and rate of change in a frailty index (FI) from midlife into old age.

**METHODS:** A linear mixed model analysis was performed using data from three measurement occasions over 17 years in participants from the Helsinki Birth Cohort Study (n=2000) aged 57-84 years. A 41-item FI was calculated on each occasion. Information on birth size, maternal body mass index (BMI), growth in infancy and childhood, childhood socioeconomic status (SES), and early life stress (wartime separation from both parents), was obtained from registers and healthcare records.

**RESULTS:** At age 57 years the mean FI level was 0.186 and the FI levels increased by 0.34 percent/year from midlife into old age. Larger body size at birth associated with a slower increase in FI levels from midlife into old age. Per 1kg greater birth weight the increase in FI levels per year was -0.087 percentage points slower (95% CI=-0.163, -0.011; p=0.026). Higher maternal BMI was associated with a higher offspring FI level in midlife and a slower increase in FI levels into old age. Larger size, faster growth from infancy to childhood, and low SES in childhood were all associated with a lower FI level in midlife but not with its rate of change.

**CONCLUSIONS:** Early life factors seem to contribute to disparities in frailty from midlife into old age. Early life factors may identify groups that could benefit from frailty prevention, optimally initiated early in life.



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