

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. Ann Hum Biol 2021:1-4. doi:10.1080/03014460.2021.1951351
BODY SIZE AND COMPOSITION OF SAMOAN TODDLERS AGED 18-25 MONTHS IN 2019.

Oyama S, Duckham RL, Arslanian KJ, et al.

BACKGROUND: The “Foafoaga O le Ola (Beginning of Life)” study is a prospective birth cohort of n = 160 Samoan mother-infant dyads established in 2017-2018. A primary study aim is to explore how a missense variant at CREBRF rs373863828 impacts growth in early life, given its association with increased body size but lower risk of diabetes in adult Samoans. Here, we examine body size and composition by genotype among toddlers aged 18.7-24.5 months.

METHODS: Height, weight, head circumference, mid-upper-arm circumference, and abdominal circumference, as well as subscapular, triceps, iliac crest and thigh skinfold thickness were measured among 107 toddlers with known rs373863828 genotype; 42 of these toddlers completed dual-energy X-ray absorptiometry (DXA) scans from which body composition (total body less head fat mass, lean mass, bone mass, % fat mass and % fat-free mass) was estimated.

RESULTS: After controlling for sex and age, toddlers with at least one copy of the CREBRF minor allele (AA/AG) were 1.31 cm taller (SE = 0.64, p=0.045) than toddlers with the GG genotype.

CONCLUSION: Whether greater linear growth in early childhood could contribute to the metabolically protective effects associated with the CREBRF variant in adulthood should be explored in future studies.



2. J Clin Endocrinol Metab Published online June 18, 2021
doi:10.1210/clinem/dgab447

BROWN ADIPOSE TISSUE, ADIPOSITY AND METABOLIC PROFILE IN PRESCHOOL CHILDREN.

Tint MT, Michael N, Sadananthan SA, et al.

CONTEXT: An inverse relationship between brown adipose tissue (BAT) and obesity has previously been reported in older children and adults, but unknown in young children.

OBJECTIVE: We investigated the influence of BAT in thermoneutral condition on adiposity and metabolic profile in Asian preschool children.

DESIGN, SETTING AND PARTICIPANTS: A total of 198 children aged 4.5 years from a prospective birth cohort study, Growing Up in Singapore Towards healthy Outcomes (GUSTO) were successfully studied with water-fat magnetic resonance

imaging of the supraclavicular-axillary fat depot (FDSA). Regions within FDSA with fat-signal-fraction between 20% and 80% were considered BAT, and percentage BAT (%BAT), $(100 \times \text{BAT volume} / \text{FDSA volume})$ was calculated.

MAIN OUTCOME MEASURES: Abdominal adipose tissue compartment volumes, ectopic fat in the soleus muscle and liver, fatty liver index, metabolic syndrome scores and markers of insulin sensitivity. **RESULTS:** A one percent unit increase in %BAT was associated with lower body mass index, difference (95%CI), -0.08 (-0.10, -0.06) kg/m² and smaller abdominal adipose tissue compartment volumes. Ethnicity and sex modified these associations. In addition, each unit increase in %BAT was associated with lower ectopic fat at 4.5 years in the liver, -0.008 (-0.013, -0.003) %, soleus muscle, -0.003 (-0.006, -0.001) % of water-content and lower fatty liver index at 6 years.

CONCLUSIONS: Higher %BAT is associated with a more favorable metabolic profile. BAT may thus play a role in the pathophysiology of obesity and related metabolic disorders. The observed ethnic and sex differences imply that the protective effect of BAT may vary among different groups.



3. BMC Pregnancy Childbirth 2021;21(1):566. doi:10.1186/s12884-021-04036-5
COMPARATIVE EPIDEMIOLOGY OF GESTATIONAL DIABETES IN ETHNIC CHINESE FROM SHANGHAI BIRTH COHORT AND GROWING UP IN SINGAPORE TOWARDS HEALTHY OUTCOMES COHORT.
Loo EXL, Zhang Y, Yap QV, et al.

BACKGROUND: Gestational diabetes mellitus (GDM) has been associated with adverse health outcomes for mothers and offspring. Prevalence of GDM differs by country/region due to ethnicity, lifestyle and diagnostic criteria. We compared GDM rates and risk factors in two Asian cohorts using the 1999 WHO and the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria.

METHODS: The Shanghai Birth Cohort (SBC) and the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort are prospective birth cohorts. Information on sociodemographic characteristics and medical history were collected from interviewer-administered questionnaires. Participants underwent a 2-h 75-g oral glucose tolerance test at 24-28 weeks gestation. Logistic regressions were performed.

RESULTS: Using the 1999 WHO criteria, the prevalence of GDM was higher in GUSTO (20.8%) compared to SBC (16.6%) ($p = 0.046$). Family history of hypertension and alcohol consumption were associated with higher odds of GDM in SBC than in GUSTO cohort while obesity was associated with higher odds of GDM in GUSTO. Using the IADPSG criteria, the prevalence of GDM was 14.3% in SBC versus 12.0% in GUSTO. A history of GDM was associated with higher odds of GDM in GUSTO than in SBC, while being overweight, alcohol consumption and family history of diabetes were associated with higher odds of GDM in SBC.

CONCLUSIONS: We observed several differential risk factors of GDM among ethnic Chinese women living in Shanghai and Singapore. These findings might be due to heterogeneity of GDM reflected in diagnostic criteria as well as in unmeasured genetic, lifestyle and environmental factors.



4. Paediatr Perinat Epidemiol 2021;35(SUPPL 1):79. doi:10.1111/ppe.7-12779
DESCRIPTIVE EPIDEMIOLOGY OF NEONATAL VISITS TO EMERGENCY DEPARTMENTS IN ONTARIO, CANADA: A POPULATION-BASED RECORD LINKAGE STUDY.
Smith M, Weiss D, Langevin M, et al.

BACKGROUND: Infants and neonates present frequently to Emergency Departments (ED) for care, but there is relatively little research examining when and why ED visits occur in the neonatal period (first 28 days of life). Our objective was to determine the prevalence, incidence, timing, and reasons for neonatal ED visits using a large population-based cohort and record linkage across multiple databases.

METHODS: We extracted a one-year birth cohort (March 1, 2016 to February 28, 2017) from a population-based birth registry in Ontario, Canada. This cohort, representing all births in the province, was linked to national health administrative databases which capture all hospital admissions and ED visits. Prevalence and incidence rates of neonatal ED visits were calculated using standard techniques. ED visits were also characterized by age of neonate, access to primary care, maternal age, infant sex, and diagnosis code (assessed using the International Classification of Diseases 10th Revision).

RESULTS: 9.6% (13 190/136 967) of infants visited the ED in the neonatal period; 8.2% (n = 11 158) were single visits and 1.5% (n = 2032) visited 2+ times. In this period, the incidence rate of ED visits was twice as high in days 1-14 vs days 15-28, at 6.65 per 1000 days of follow-up (95% confidence interval 6.52, 6.78) and 2.99 (2.92, 3.07), respectively. The median age at first ED visit was 10 days old, but most occurred on the fourth day of life. Across all visits, the most frequent diagnosis was neonatal jaundice (19.0%), followed by parental fears in a healthy infant (5.0%). In most cases (88.2% of visits), parents reported having access to a family physician. Visit rates were higher among male infants and younger mothers (under 25 years) regardless of parity.

CONCLUSIONS: Approximately 10% of infants visit the ED in the neonatal period, most frequently in the first 14 days after birth. A large proportion of ED visits can be attributed to neonatal jaundice and parental concerns.



5. Urol Int. 2021;1-5. doi: 10.1159/000517268.
EVALUATION OF UNDESCENDED TESTES IN NEWBORNS: IT IS REALLY SIMPLE, JUST NOT EASY.

Promm M, Dittrich A, Brandstetter S, et al.

INTRODUCTION: The evaluation of the testicular position in newborns is important to ensure timely initiation of therapy. The aim of our study was to assess the reliability of a routinely performed screening examination.

PATIENTS AND METHODS: Newborns were examined by a pediatrician between 48 and 72 h after birth. Boys with suspected cryptorchidism were double-checked by a pediatric urologist within 24 h.

RESULTS: 1,181/2,353 children included in the study between June 2015 and December 2017 were male. Eight hundred sixty-one boys could be included in this analysis; 5.8% (n = 50) were diagnosed with undescended testis (UDT) by the pediatrician. 30/50 boys were double-checked at the Department of Pediatric Urology. Forty percent (20/50) were lost to follow-up. In 43% (13/30), the diagnosis could be confirmed. Three former studies had shown a relevant discrepancy in the results of the diagnosis of UDT made by health care providers and urologists/pediatric surgeons. To our knowledge, this is the first study evaluating the testicular position in male newborns in such a large prospective birth cohort study by physicians with ranging expertise within 1 day.

CONCLUSION: Further treatment for UDT is based on clinical examination. Ours and previous studies can clearly show the various findings in boys suspected having UDT. Therefore, it is essential that the diagnosis is confirmed by a specialist before a therapy is initiated.



6. Sci Rep 2021;11(1):16435. doi:10.1038/s41598-021-95903-w
METABOLIC SIGNATURES IN THE CONVERSION FROM GESTATIONAL DIABETES MELLITUS TO POSTPARTUM ABNORMAL GLUCOSE METABOLISM: A PILOT STUDY IN ASIAN WOMEN.

Wang X-M, Gao Y, Eriksson JG, et al.

We aimed to identify serum metabolites related to abnormal glucose metabolism (AGM) among women with gestational diabetes mellitus (GDM). The study recruited 50 women diagnosed with GDM during mid-late pregnancy and 50 non-GDM matches in a Singapore birth cohort. At the 5-year post-partum follow-up, we applied an untargeted approach to investigate the profiles of serum metabolites among all participants. We first employed OPLS-DA and logistic regression to discriminate women with and without follow-up AGM, and then applied area under the curve (AUC) to assess the incremental indicative value of metabolic signatures on AGM. We identified 23 candidate metabolites that were associated with postpartum AGM among all participants. We then narrowed down

to five metabolites [p-cresol sulfate, linoleic acid, glycocholic acid, lysoPC(16:1) and lysoPC(20:3)] specifically associating with both GDM and postpartum AGM. The combined metabolites in addition to traditional risks showed a higher indicative value in AUC (0.92-0.94 vs. 0.74 of traditional risks and 0.77 of baseline diagnostic biomarkers) and R(2) (0.67-0.70 vs. 0.25 of traditional risks and 0.32 of baseline diagnostic biomarkers) in terms of AGM indication, compared with the traditional risks model and traditional risks and diagnostic biomarkers combined model. These metabolic signatures significantly increased the AUC value of AGM indication in addition to traditional risks, and might shed light on the pathophysiology underlying the transition from GDM to AGM.



7. Clin Exp Allergy 2019;49(2):199-206. doi:10.1111/cea.13245
SOLUBLE CD14 CONCENTRATION IN HUMAN BREAST MILK AND ITS POTENTIAL ROLE IN CHILD ATOPIC DERMATITIS: RESULTS OF THE ULM BIRTH COHORT STUDIES.
Logan CA, Weiss JM, Koenig W, et al.

BACKGROUND: Soluble CD14 (sCD14) is one of many factors in human breast milk which may influence programming of the immune response in the breastfed child. Although previous studies have mostly found little association between sCD14 concentration in breast milk and atopic outcomes, recent evidence continues to support a role of sCD14 in immune-related disease.

OBJECTIVE: We aimed to clarify whether an association exists between sCD14 concentration in human breast milk (m-sCD14) and child atopic dermatitis (AD) diagnosis by age 3 years within the context of two large birth cohorts.

METHODS: Data were obtained from the Ulm Birth Cohort Study (UBCS) and the Ulm SPATZ Health Study, methodologically similar birth cohort studies, each consisting of approximately 1000 newborns and their mothers recruited from the general population shortly after delivery in Ulm, Southern Germany, respectively, from 11/2000 to 11/2001 and 04/2012 to 05/2013. sCD14 concentrations were measured by different ELISAs (UBCS: IBL, SPATZ: R&D) in breast milk samples collected at 6 weeks post-delivery in both studies and additionally at 6 months and 1 year in SPATZ. Children's AD diagnosis was assessed using parent and paediatrician reports at 1, 2 and 3 years of age.

RESULTS: Complete exposure and outcome data were available for 659 UBCS and 489 SPATZ children. In both cohorts, sCD14 concentration was significantly associated with breastfeeding frequency ($P < 0.01$). We observed no association between m-sCD14 concentration and child AD diagnosis in either study.

CONCLUSIONS: Our results do not support an association between sCD14 concentration in mature breast milk and AD among breastfed children.



8. *Pediatr Pulmonol.* 2021;10.1002/ppul.25592. doi:10.1002/ppul.25592
THE ASTHMA PREDICTIVE INDEX AS A SURROGATE DIAGNOSTIC TOOL IN PRESCHOOLERS: ANALYSIS OF A LONGITUDINAL BIRTH COHORT.
Castro-Rodriguez JA, Forno E, Padilla O, Casanello P, Krause BJ, Borzutzky A.

Diagnosing asthma in preschool children remains an unsolved challenge, at a time when early identification would allow for better education and treatment to prevent morbidity and lung function deterioration. Objective: To evaluate if the asthma predictive index (API) can be used as surrogate for asthma diagnosis in preschoolers. Methods: Birth cohort of 339 pregnant women enrolled at delivery and their offspring, who were followed for atopy, wheezing, and other respiratory illnesses through 30 months of age. The API was determined at 30 months of age by the researchers; and examined its association with physician-diagnosed asthma during the first 30 months, made independently by the primary care physician not involved in the study. Results: Among 307 offspring with complete follow-up, 44 (14.3%) were API+. Maternal body mass index, maternal education, past oral contraceptive use, birthweight, placenta weight, age of daycare at 12 m, gastroesophageal reflux disease at 12 m, acute otitis media at 18 m, bronchiolitis, croup and pneumonia, cord blood adiponectin were all associated with API+. In the multivariable analysis, API+ was associated with almost sixfold odds of asthma diagnosis (adjusted OR = 5.7, 95% CI [2.6–12.3]), after adjusting for the relevant covariates above including respiratory infections like bronchiolitis and pneumonia. The API sensitivity was 48%, specificity 92%, 61% PPV, 88% NPV, 6.4 LR+, 0.56 LR–, 0.84 diagnosis accuracy. The adjusted odds for asthma was 11.4. Conclusions: This longitudinal birth cohort suggests, for first time, that API (a structured definition for asthma), could be used as a diagnostic tool, not only as a prognostic tool, in toddlers and preschoolers.



9. *Int J Obes (Lond)* 2021;45(9):1995–2005. doi:10.1038/s41366-021-00864-9
THE LONGITUDINAL ASSOCIATION BETWEEN EARLY-LIFE SCREEN VIEWING AND ABDOMINAL ADIPOSITY-FINDINGS FROM A MULTIETHNIC BIRTH COHORT STUDY.
Padmapriya N, Tint M-T, Sadananthan SA, et al.

IMPORTANCE: Screen viewing in adults has been associated with greater abdominal adiposity, with the magnitude of associations varying by sex and ethnicity, but the evidence is lacking at younger ages. We aimed to investigate sex- and ethnic-specific associations of screen-viewing time at ages 2 and 3 years with abdominal adiposity measured by magnetic resonance imaging at age 4.5 years.

METHODS: The Growing Up in Singapore Towards healthy Outcomes is an ongoing prospective mother-offspring cohort study. Parents/caregivers reported the time their child spent viewing television, handheld devices, and computer screens at

ages 2 and 3 years. Superficial and deep subcutaneous and visceral abdominal adipose tissue volumes were quantified from magnetic resonance images acquired at age 4.5 years. Associations between screen-viewing time and abdominal adipose tissue volumes were examined by multivariable linear regression adjusting for confounding factors.

RESULTS: In the overall sample (n = 307), greater total screen-viewing time and handheld device times were associated with higher superficial and deep subcutaneous adipose tissue volumes, but not with visceral adipose tissue volumes. Interactions with child sex were found, with significant associations with superficial and deep subcutaneous and visceral adipose tissue volumes in boys, but not in girls. Among boys, the increases in mean (95% CI) superficial and deep subcutaneous and visceral adipose tissue volumes were 24.3 (9.9, 38.7), 17.6 (7.4, 27.8), and 7.8 (2.1, 13.6) mL per hour increase in daily total screen-viewing time, respectively. Ethnicity-specific analyses showed associations of total screen-viewing time with abdominal adiposity only in Malay children. Television viewing time was not associated with abdominal adiposity.

CONCLUSION: Greater total screen-viewing time (and in particular, handheld device viewing time) was associated with higher abdominal adiposity in boys and Malay children. Additional studies are necessary to confirm these associations and to examine screen-viewing interventions for preventing excessive abdominal adiposity and its adverse cardiometabolic consequences.



10. Public Health Nutr 2021:1-24. doi:10.1017/S1368980021003621

THE ROLE OF EDUCATION AND MIGRATION BACKGROUND IN EXPLAINING DIFFERENCES IN FOLIC ACID SUPPLEMENTATION INTAKE IN PREGNANCY: RESULTS FROM A GERMAN BIRTH COHORT STUDY.

Miani C, Ludwig A, Doyle I-M, et al.

OBJECTIVE: Official German recommendations advise women to start taking folic acid supplementation (FAS) before conception and continue during the first pregnancy trimester to lower the risk of birth defects. Women from lower socioeconomic background and ethnic minorities tend to be less likely to take FAS in other European countries. As little is known about the determinants of FAS in Germany, we aimed to investigate the association between FAS and formal education and migration background, adjusting for demographic factors.

DESIGN: We used data (2013-2016) on nutrition and socioeconomic and migration background from the baseline questionnaire of the BaBi cohort study. We performed multivariate regressions and mediation analyses. **SETTING:** Bielefeld, Germany.

PARTICIPANTS: 947 women (pregnant or who had given birth in the past two months).

RESULTS: 16.7% of the participants (158/947) didn't use FAS. Migration-related variables (e.g. language, length of stay) were not associated with FAS in the

adjusted models. FAS was lower in women with lower level of formal education and in unplanned pregnancies. Reasons given by women for not taking FAS were unplanned pregnancy and lack of knowledge of FAS.

CONCLUSIONS: Health practitioners may be inclined to see migrant women as an inherently at-risk group for failed intake of FAS. However, it is primarily women who did not plan their pregnancy, and women of lower formal education level, who are at risk. Different public health strategies to counter low supplementation rates should be supported, those addressing the social determinants of health (i.e. education) and those more focussed on family planning.

1. Eur J Endocrinol 2021;185(2):279-288. doi:10.1530/EJE-20-1462
BIOCHEMICAL SIGNS OF POLYCYSTIC OVARY SYNDROME IN YOUNG WOMEN BORN PRETERM.

Paalanne M, Vääräsmäki M, Mustaniemi S, et al.

OBJECTIVE: It has been suggested that adverse early life exposures increase the risk of developing polycystic ovary syndrome (PCOS) in later life. We hypothesized that women born preterm would have more biochemical and clinical signs of PCOS than women born at term.

DESIGN: The ESTER Preterm Birth Study participants were born in Northern Finland and identified from the Northern Finland Birth Cohort and the Finnish Medical Birth Register. Altogether, 74 women born very or moderately preterm (<34 gestational weeks, VMPT), 127 born late preterm (at 34-36 weeks, LPT), and 184 born full term (≥37 weeks, controls) were included in the analysis (mean age: 23.2 years).

METHODS: We measured serum total testosterone and sex hormone-binding globulin (SHBG) and calculated the free androgen index (FAI). PCOS according to the clinical and biochemical signs was defined either as hirsutism and oligoamenorrhea (via questionnaire) or as oligoamenorrhea and elevated testosterone levels (>2.4 nmol/L).

RESULTS: Women born VMPT/LPT exhibited 33.0% (8.7, 62.8)/16.4% (-2.0, 38.1) higher testosterone, 28.5% (5.3, 45.9)/24.1% (5.6, 38.9) lower SHBG levels, and 64.6% (19.4, 127.1)/42.5% (11.1, 82.9) higher FAI than controls after adjusting for age and recruitment cohort, maternal BMI, smoking, and pregnancy disorders, parental education, history of hypertension, diabetes, myocardial infarction or stroke, and subject's birth weight s.d. Odds ratios for having PCOS were 1.67 (0.44, 6.23)/3.11 (1.26, 7.70).

CONCLUSIONS: Women born preterm have a more hyperandrogenic hormonal profile, and those born LPT are approximately three times more likely at risk to have PCOS compared to women born at term.



2. Prim Care Diabetes 2021;15(3):561-566. doi:10.1016/j.pcd.2021.02.001
GLUCOSE REGULATION AND PAIN IN OLDER PEOPLE-THE HELSINKI BIRTH COHORT STUDY.

Åström MJ, von Bonsdorff MB, Haanpää M, Salonen MK, Kautiainen H, Eriksson JG.

AIMS: To assess if individuals with diabetes or prediabetes report more pain or have increased use of pain medication compared to normoglycaemic individuals.

METHODS: Using cross-sectional data, we studied 928 men and 1075 women from

the Helsinki Birth Cohort Study in 2001-2004 at a mean age of 61.5 years. Glucose regulation was assessed with a 2-h 75 g oral glucose tolerance test, and applying World Health Organization criteria, participants were defined as having normoglycaemia, prediabetes (impaired fasting glucose or impaired glucose tolerance), newly diagnosed diabetes or previously diagnosed diabetes. Self-reported pain intensity and interference during the previous 4 weeks was estimated using the RAND 36-Item Health Survey 1.0. Information on use of pain medication during the past 12 months was obtained from the Social Insurance Institution of Finland.

RESULTS: There was no difference in pain intensity or interference between glucose regulation groups for neither men nor women after adjusting for covariates (age, body mass index, education years, Beck Depression Inventory and physical activity). In addition, use of pain medication was similar between glucose regulation groups.

CONCLUSIONS: Although pain is a common symptom in the general population, impairments in glucose regulation alone does not seem to increase pain among older individuals.



3. Aust N Z J Public Health Published online July 26, 2021 doi:10.1111/1753-6405.13146

USE OF MEDICAL SERVICES BY OLDER AUSTRALIAN WOMEN WITH DEMENTIA: A LONGITUDINAL COHORT STUDY.

Byles J, Cavenagh D, Bryant J, et al.

OBJECTIVE: To assess the use of Medicare-subsidised health services by women with and without dementia.

METHODS: Data from women of the 1921-26 birth cohort of the Australian Longitudinal Study on Women's Health were linked to various administrative datasets to ascertain dementia diagnosis. The use of subsidised general practitioner (GP) services (75+ health assessments [HAs], chronic disease management meetings [CDMs], multidisciplinary case conferences [MCCs]) and specialist and allied health services between 2000 and 2013 for these women was analysed using longitudinal GEE models.

RESULTS: A total of 9,683 women were included with 1,444 (15%) women identified as having dementia. Compared to women with no dementia indication, women with dementia had more yearly non-emergency GP attendances (short [<30 minutes] IRR=1.11 [1.07, 1.13]; long [>30 minutes] IRR=1.11 [1.04, 1.19]) and fewer specialist attendances (IRR=0.91 [0.85, 0.97]) and were more likely to have an emergency GP attendance (OR=2.29 [2.05, 2.57]). There were no significant differences in the odds of having either a HA or CDM or using allied health services for women with and without dementia indicators.

CONCLUSIONS: The overall use of services designed to improve the prevention and coordination of the care of older people with chronic conditions was low. Women

with dementia were no more likely to access these services. Implications for public health: There is underuse of some primary and allied healthcare services designed for people with complex chronic conditions. These could be better used by women with dementia to improve the management of complex comorbidities (e.g. CDMs), to prevent the onset of disability (e.g. physiotherapy), and enhance needs assessment and service access (e.g. HAs).

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