

## Associations of physiques among three-generational families: The TMM BirThree Cohort Study

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**Background :** Examining an intergenerational association of height, weight, and body mass index (BMI) along family lines helps to understand its hereditary mechanism. However, few studies have analyzed three-generational families.

**Objective :** To evaluate the association of parents' and grandparents' height, weight, and BMI with those of neonates.

**Methods :** Three-generational families that participated in the Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study (TMM BirThree Cohort Study) were analyzed; neonate at birth (n=20,115), mother (n=19,937), father (n=6,926), maternal grandmother (MGM) (n=3,148), maternal grandfather (MGF) (n=1,287), paternal grandmother (PGM) (n=1,018), and paternal grandfather (PGF) (n=653). The inter-generational association of height was analyzed in three steps as follows. i) Association between each family members' and neonatal height was examined using a simple linear regression model. ii) Multiple linear regression analysis was performed to explain the neonatal height using all family members' heights. iii) The association confirmed in ii) was verified using the random family method (RFM) with 5,000 iterations. The same steps were done for weight and BMI.

**Results :** Mother's (coefficient=0.052), father's (0.040), MGM's (0.022), and MGF's (0.018) heights ( $p<0.05$ ) were associated with neonatal height in step i). In steps ii) and iii), the association between mothers' and neonates' heights was verified (coefficient=0.067,  $p=0.0068$ ,  $p$  for RFM=0.040). No intergenerational association was verified for neonatal weight in steps ii) and iii). Mother's (0.039), father's (0.013), and MGF's (0.026) BMI ( $p<0.05$ ) were associated with neonatal BMI in step i). In steps ii) and iii), the association of mother's BMI (coefficient=0.033,  $p=0.023$ ,  $p$  for RFM=0.013) and of MGF's BMI (0.032, 0.036, 0.032) with neonatal BMI was verified.

**Conclusion :** Grandparental generation can be a considerable factor for neonatal BMI.

## Assessing the association between floods and dengue incidence in Vietnam: A time series study

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**Background :** Dengue is a neglected tropical disease with a substantial rise in cases over the past few decades. Flooding is known to worsen vector-borne diseases, particularly mosquito-borne transmission. Climate change and urbanization increase both flooding and dengue risks, especially in low- and middle-income countries. However, evidence on the timing and strength of the flood-dengue association remains limited, particularly in Vietnam, where flood and dengue burden are both high.

**Objectives** To assess the association between flood presence and dengue incidence in Vietnam (national level) and Ho Chi Minh City (provincial level).

**Methods :** This ecological study used a time series design. The study included all 63 provinces of Vietnam and 24 districts of HCMC. A generalized additive mixed model with a negative binomial distribution was used. A cross-basis function was applied to model both the cumulative and lagged effects. The model also included temporal and spatial terms, mean temperature, precipitation, and population size. The analysis was also conducted by seasons (dry and rainy season). Socioeconomic and land use features were considered in sensitivity analysis.

**Results :** Exposure to flooding is associated with an increased risk of dengue in Vietnam. Dengue risk was 28.9% higher during flood-affected periods compared to non-flood periods at the national level (95% CI: 4.2–59.5) and 10.4% higher in HCMC (95% CI: 3.3–18.0). The highest increase in risk was observed in the second month following flood exposure (RR=1.14; 95% CI: 1.06–1.22). Flooding increased dengue risk nationally during the rainy season, while in HCMC, it was linked to reduced risk.

**Conclusion :** A significant association between flooding and increased dengue risk was identified, with delayed effects emerging around five weeks, or one month, after flooding. The impact varies by season and administrative levels. The study provides new insights into the flood-dengue association.

## Hygienic Behaviors and Pediatric Infectious Diseases in 11–12-Year-Olds in the post-COVID-19 era

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**Background :** The impact of hygienic behaviors, including handwashing and mask-wearing, on pediatric infectious diseases in the post-COVID-19 era (defined as  $\geq$  May, 2023 in Japan) remains poorly understood. This study aimed to examine these associations using an additional survey conducted within the Hokkaido Regional Unit Center of the Japan Environment and Children's Study (JECS).

**Methods :** Between July 2023 and March 2025, we conducted a questionnaire survey among children aged 11–12 years and their parents participating in the additional JECS school-age survey in Hokkaido (residing in or near Sapporo and Kitami city). We applied logistic regression to assess the associations between hygienic behaviors (handwashing frequency, mask-wearing) and pediatric infectious diseases (COVID-19 and pertussis), adjusted for vaccination history. Written informed consent was obtained from all participants.

**Results :** A total of 803 children aged 11–12 years were analyzed. Overall, 24.6% reported always washing their hands and 70.0% reported always wearing a mask. In logistic regression with COVID-19 infection as the outcome, handwashing (always vs. less than always) was not associated with infection (univariable OR = 0.95, 95% CI 0.62–1.42; multivariable OR = 1.10, 95% CI 0.65–1.83). By contrast, always wearing a mask was associated with lower odds of infection (univariable OR = 0.56, 95% CI 0.38–0.83; multivariable OR = 0.61, 95% CI 0.41–0.92). Pertussis analyses showed no statistically significant associations.

**Conclusions :** Frequent handwashing did not provide significant protection, whereas consistent mask-wearing was strongly associated with a reduced risk of common pediatric infectious diseases in the post-COVID-19 era.

## Association of circulating metabolites and polygenic risk score with incident hyperuricemia

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**Objective :** This study aimed to identify plasma metabolites linked to hyperuricemia incidence and to examine whether these metabolites mediate the association between genetic risk and hyperuricemia.

**Methods :** This prospective study included 13,132 Japanese participants aged  $\geq 20$  years (mean  $\pm$  SD:  $60.2 \pm 10.9$  years; 69.4% women) free of hyperuricemia at baseline. Nuclear magnetic resonance spectroscopy quantified 43 metabolites, including amino acids, ketone bodies, and glycolytic metabolites. A polygenic risk score (PRS) for hyperuricemia was constructed from uric acid loci identified in a genome-wide association study. Hyperuricemia was defined as uric acid  $\geq 7.0$  mg/dl or self-reported history. The association between PRS and hyperuricemia was examined using modified Poisson regression, PRS-metabolite associations by linear regression, and mediation analysis to assess metabolite effects.

**Results :** During 4.3 years of median follow-up, 407 incident cases were ascertained. Higher PRS was associated with increased risk of hyperuricemia (RR 1.93, 95%CI 1.55–2.41). Six metabolites were associated with higher and six with lower risk. Carnitine and creatinine were positively correlated with PRS, while tryptophan and tyrosine were negatively correlated. Creatinine mediated the PRS-hyperuricemia association by 2% (95%CI 0.03–6.0).

**Conclusion :** Creatinine partly mediated the genetic risk of hyperuricemia. These findings improve understanding of metabolic pathways underlying genetic susceptibility to hyperuricemia.

## Heterogeneity in the association between heat exposure and cognitive decline in older urban adults

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**Introduction :** Heat exposure may increase the risk of cognitive decline in older adults. However, vulnerability has rarely been assessed across multiple domains simultaneously. We examined heterogeneity in the association between exposure to extreme heat and cognitive decline among urban-dwelling older adults in Japan.

**Methods :** We surveyed older adults ( $\geq 65$  years) in 2010 who resided in a municipality in Aichi Prefecture and ascertained incident cognitive decline through March 2023 from the national Long-Term Care Insurance database. A monthly heat index was constructed as the within-month sum of daily wet bulb globe temperature exceedances above the 85th percentile during the study period, then lag weights derived from a distributed lag non-linear model for months 10–21 were applied to compute a weighted sum. Heterogeneity was assessed using generalized random forests (GRF), adjusting for 55 baseline covariates and potential effect modifiers.

**Results :** Among 13,613 participants, 3,731 (27.4%) developed cognitive decline during follow-up. The heat index was associated with cognitive decline (Relative risk 1.16, 95% Confidence Interval 1.11-1.20). The Shapley value indicated vulnerable factors in the following order: aged  $\geq 75$  years, no hobbies, unemployment, a small number of friends seen in the past month, and divorced/bereaved.

**Conclusion :** Heat exposure was associated with a higher risk of incident cognitive decline, with greater susceptibility among the oldest and socially disengaged or unsupported individuals. These findings suggest that heat-health adaptation and dementia prevention should explicitly incorporate multi-domain vulnerability, prioritizing outreach, social participation supports, and access to cooling for these high-risk subgroups.