

## Association between smoking status, amount, duration and epigenetic aging acceleration

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**Background :** Epigenetic age, estimated by DNA methylation-based clocks, is a promising biomarker that reflects inter-individual differences in biological aging. While GrimAge, a second-generation epigenetic clock, incorporates smoking history (e.g., pack-years) and has shown strong associations with age-related diseases and mortality, the potential reversibility of this acceleration through smoking cessation remains unclear, particularly in Japanese populations.

**Methods :** We analyzed data from 867 Japanese adults aged 40–69 years who participated in the Saga J-MICC Study between 2005 and 2007. Smoking-related variables included smoking status, amount, duration, and Brinkman Index. GrimAgeAccel was calculated as the residual from regressing GrimAge on chronological age. Associations between smoking indicators and GrimAgeAccel were evaluated using multivariable linear regression, adjusting for sex, array type, principal components of control probe intensities, BMI, education, lifestyle factors, chronic diseases, and medication use.

**Results :** Compared to never-smokers, both former and current smokers had elevated GrimAgeAccel (+2.25 years and +6.31 years, respectively) ( $p < 0.05$ ). Heavier or longer smoking exposure— $\geq 40$  cigarettes/day,  $\geq 20$  years of duration, or Brinkman Index  $\geq 800$ —was associated with marked increases in GrimAgeAccel (+7.65, +4.25, and +5.44 years, respectively). Notably, a longer duration since smoking cessation was associated with lower GrimAgeAccel, suggesting partial reversibility of epigenetic aging.

**Conclusion :** Although GrimAge is inherently sensitive to smoking exposure, this study highlights the potential mitigating effect of smoking cessation on EAA. The observed reduction in GrimAgeAccel among former smokers underscores the value of cessation interventions in promoting healthy aging and longevity. Further longitudinal studies are warranted to confirm these findings.

## COVID-19 Antibody Insights: Infection Control in Elderly Care Homes After Major Outbreak

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**Background :** Vaccination remains a key infection control strategy for COVID-19 in elderly care homes (ECH). Vaccine effectiveness depends on its properties and individuals' existing immune profiles.

This study aims to (i) determine the seroprevalence of BA.2 and BA.4/5 among residents shortly after an explosive Omicron surge, (ii) explore how the types and sequences of immunologic exposures shape neutralizing antibody (nAb) levels, (iii) measure the extent of cross-protection between BA.4/5 and BA.2, and (iv) determine the relative vaccine effectiveness against infection conferred by CoronaVac.

**Method :** A seroepidemiology survey was conducted in ECHs in Hong Kong in 2022. The surrogate virus neutralization test was used to determine the nAb level. Associated factors were identified by multilevel modeling, and Cox regression assessed CoronaVac's effectiveness among vaccinated residents.

**Result :** Of 679 residents, the median percentage inhibition of the nAb against BA.2 was 47%. Hybrid immunity elicited stronger nAb levels compared to vaccination alone or infection [I] alone in RCHes where CoronaVac [C] was predominant. A much higher nAb level was achieved by a recent infection than by an early one: CCCI and CCIC significantly boosted the nAb level by 53 units and 26 units more when compared to ICC. The level of nAb increased with the exposure interval for certain immune profiles. The extent of cross-protection between BA.2 and BA.4/5 was generally high, but diverged by residents' serostatus. The relative vaccine effectiveness of CoronaVac against infection was moderate (two-versus-one: 11%; three-versus-two: 36%).

**Discussion :** This study reinforces the need to understand the mechanisms which shape antibody responses to provide a scientific evidence for vaccination campaigns plan in ECHs. Tailoring the schedule of COVID-19 boosters according to the cross-reactivity and the pre-existing exposure interval of residents is advised.

## Impact of Sleep Quantity and Quality on Chronic Kidney Disease

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**Introduction :** Both short and long sleep durations, as well as poor sleep quality, are associated with adverse health outcomes. Sleep disorders and kidney disease have a bidirectional relationship. This study aimed to investigate the impact of sleep quantity and quality on chronic kidney disease (CKD) in the Korean population.

**Methods :** A total of 11,244 participants (4,545 men and 6,699 women) were included in this cross-sectional study. Sleep behaviors were assessed using interviewer-assisted questionnaires. Sleep duration was categorized into three groups: <6 hours/day (short sleep), 6–8 hours/day (reference) and  $\geq 9$  hours/day (long sleep). Sleep quality was classified based on the presence of obstructive sleep apnea (OSA) using the Berlin Questionnaire. CKD was defined as either a physician diagnosis or an estimated glomerular filtration rate  $< 60$  mL/min/1.73 m<sup>2</sup> according to the Kidney Disease Improving Global Outcomes guidelines. Multiple logistic regression models were used to examine the independent and combined associations of sleep patterns with CKD.

**Results :** Compared with the reference group, participants with long sleep duration and those with OSA had a 2.02-fold and 1.75-fold higher risk of CKD, respectively, in the fully adjusted model. Furthermore, participants who had both conditions showed a markedly increased risk of CKD (adjusted odds ratio: 3.97; 95% confidence interval: 2.83–5.56). However, short sleep duration was not significantly associated with CKD.

**Conclusion :** These findings support an adverse effect of long sleep duration and poor sleep quality on CKD. As sleep habits are modifiable lifestyle factors, their improvement may help reduce the risk of kidney dysfunction.

## A novel inflammatory food score and its association with cardiovascular disease in a Japanese cohort

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**Background :** Most existing dietary inflammatory indices are not readily applicable in practice. We therefore aimed to develop a novel inflammatory food score (IFS) for practical use and examined its association with cardiovascular disease (CVD).

**Methods :** We used data from the Japan Multi-Institutional Collaborative Cohort Study. Food intakes (22 items) were estimated using a food frequency questionnaire at the baseline survey. The IFS was developed in a group of participants (N = 13,969) using least absolute shrinkage and selection operator (LASSO) regression, with log-transformed daily food intakes as exposures and log-transformed serum high-sensitivity C-reactive protein (hsCRP) at baseline as the outcome. Scores for each food were assigned based on the LASSO coefficients. The IFS was externally validated against the log(hsCRP) in another group (cross-sectional design, N = 5,989). Finally, associations of IFS with CVD incidence (N = 20,723, median follow-up: 15.3 years) and mortality (N = 81,343, median follow-up: 13.5 years) were examined using Cox proportional hazard model with adjustment for covariates (cohort design).

**Results :** LASSO regression retained 21 of the 22 food items as predictors of hsCRP. In the external validation, the IFS was positively associated with hsCRP (multivariable-adjusted correlation coefficient: 0.04 [95% CI: 0.01–0.07]). Exponentiated coefficients (95% CIs) for the 2nd, 3rd, and 4th quartiles of IFS were 1.03 (0.95–1.12), 1.09 (1.01–1.18), and 1.12 (1.03–1.21), respectively. While no association was found between IFS and myocardial infarction/stroke incidence (559 cases, hazard ratio [HR] for the 4th quartile: 1.10 [0.85–1.42]) and mortality (326 cases, HR for the 4th quartile: 1.17 [0.84–1.62]), IFS was associated with higher risk of total CVD mortality (674 cases, HR for the 4th quartile: 1.31 [1.04–1.65]).

**Discussion :** Our IFS could validly assess the inflammatory potential of a diet and was associated with total CVD mortality.

## Impact of Lifestyle Behaviors on Glycemic Deterioration in Diabetes: Longitudinal Analysis, 2011-2021

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**Background :** Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to insufficient insulin action. Sustained hyperglycemia can lead to serious complications such as nephropathy, reducing quality of life and increasing the burden on healthcare systems. Identifying risk factors for glycemic deterioration is essential to prevent severe outcomes. However, few studies have longitudinally assessed risk factors for glycemic worsening among individuals with DM using large-scale health check-up data. This study aimed to identify lifestyle behaviors associated with glycemic deterioration using 11 years of longitudinal health check-up data.

**Methods :** We analyzed Specific Health Checkup data from 2011 to 2021. Individuals who met the criteria for DM ( $HbA1c \geq 6.5\%$  or use of glucose-lowering medication) and participated in the following year's checkup were included. Glycemic deterioration was defined as  $HbA1c$  increase  $\geq 0.5\%$  or initiation of hypoglycemic medication within one year. Ten lifestyle behaviors were included as explanatory variables. Multivariable logistic regression analyses were adjusted for age, sex, BMI, medication status, and laboratory values. Odds ratios and 95% confidence intervals were calculated. Significance was set at  $p < 0.05$ . Analyses used Python 3. Approved by the university ethics committee (Approval No. HS2023-137).

**Results :** Of 1,589,781 individuals, 37,683 met inclusion criteria. Analysis showed that current smoking (OR=1.12, 95%CI=1.04-1.22), slow walking speed (1.09, 1.02-1.15), fast eating speed (1.09, 1.02-1.16), and eating before bedtime (1.08, 1.00-1.16) were risk factors.

**Conclusion :** This longitudinal study identified lifestyle behaviors associated with glycemic worsening in DM. Behavioral modifications such as smoking cessation, improving physical activity as reflected by walking speed, slower eating, and avoiding late-night meals may improve early glycemia and prevent severe complications.