

## Travel restrictions during an Alpha variant wave in Japan

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**Background :** Japan continued to implement border control measures throughout first three years of COVID-19 pandemic. Identifying Alpha variant (B.1.1.7) in the UK, December 2020, Japan first tightened entry screening among travelers with a recent history of staying in the UK stay and then extended the policy to passengers arriving from other origins. To retrospectively assess the effectiveness of initially targeting travelers with UK-stay history, we analyzed entry screening data of the fraction positives upon arrival testing, detection of Alpha variant, and the proportion of Alpha variant out of all variants during quarantine period.

**Methods/Results :** Alpha variant was first domestically detected via border quarantine in early December 2020, and the detection happened before late-December reinforcement for travelers with a UK-stay history. As the entry screening measures were broadened globally up to early January 2021, the time-dependent frequency of detecting Alpha variant by country during quarantine largely mirrored that of Alpha variant epidemic in countries of origin. Detection of Alpha variant was restricted to travelers with a UK-stay history.

**Discussion :** Travel restrictions plus pre-departure testing likely reduced arrival of infected individuals from multitudes of countries, but completely preventing an importation of variant was proven to be an extremely difficult task. Clarifying what we can expect to border control will inform more objective policies of entry screening and travel restriction in the future.

## Baseline serum carotene levels and risk of metabolic dysfunction-associated steatotic liver disease

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**Background :** Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by fatty liver in the presence of metabolic abnormalities. Oxidative stress contributes to MASLD development and progression; thus reducing oxidative stress is essential for its prevention. Carotenes, known as dietary antioxidants, may help mitigate oxidative stress, but longitudinal analyses of carotene levels for MASLD incident have not yet determined. This study aimed to investigate the associations of baseline serum carotene levels with MASLD incident among health checkup participants.

**Methods :** The study included residents of Yakumo Town, Hokkaido who underwent health checkup in 2015(baseline) and at least one between 2016 and 2023. Of 391 eligible participants, 210(73 men, mean age: 65.0) were included in our analysis after excluding those with no consent to the study, missing serum carotenoid or ultrasound data, had preexisting fatty liver disease, drink enough alcohol to have alcoholic liver disease, and those who developed alcoholic liver disease after 2016. Hepatic steatosis was diagnosed based on ultrasonographic examinations, and MASLD was defined according to a clinical guidelines by the American Association for the Study of Liver Diseases. Serum carotenes (lycopene,  $\alpha$ -carotene [aCA] and  $\beta$ -carotene [bCA]) were measured by high performance liquid chromatography and divided into tertiles in multivariable logistic regression analyses.

**Results :** A total of 59 participants were newly diagnosed with MASLD. Compared to the lowest tertile [T1], lower odds ratios (OR) of MASLD were observed in the middle [T2] (aCA: 0.42 [0.18–0.96] and bCA: 0.40 [0.17–0.93]) and the highest tertile [T3] (aCA: 0.29 [0.12–0.70] and bCA: 0.21 [0.08–0.52]). In lycopene, a lower OR of MASLD was found in T3 (0.30 [0.12–0.71]) compared to T1.

**Conclusions :** Our longitudinal study among rural residents showed that higher baseline carotene levels in serum may be involved in the prevention of MASLD.

## Method for Estimating Personal Healthy Life Expectancy

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**Background :** Healthy life expectancy is conventionally calculated at the population level, such as in countries or regions, from national population surveys that assess limitations in daily activities. However, there is no standardized approach for estimating it for individuals. This study aimed to develop a method for estimating personal healthy life expectancy using personal health record (PHR) data.

**Methods and Results :** We used the combined dataset of the Comprehensive Survey of Living Conditions and the National Health and Nutrition Survey conducted for randomly sampled general population in Japan, 2019. From the merged dataset, 5,552 respondents were included for the analysis. Machine learning models were constructed to predict activity limitation—a key determinant of healthy life expectancy—using age, sex, disease history, blood test results, and lifelog variables (blood pressure, body mass index, waist circumference, daily step counts, and sleep patterns). The prediction model achieved an area under the curve of 0.84. Personal healthy life expectancy was estimated using a derived equation in which an individual's probability of having no activity limitation, relative to their age group average, was scaled by the population healthy life expectancy.

**Conclusion :** We developed a novel method for estimating personal healthy life expectancy from PHR data, incorporating both lifelog data and blood biomarkers, by machine-learning and mathematical approach. The application of this individualized health metric may advance personalized medicine, preventive health strategies, and tailored health guidance, while serving as a behavioral nudge to promote healthier lifestyles. Integration of datasets from countries with shorter healthy life expectancy may enhance the generalizability and applicability of this framework.

## An education tool to improve dietary Na/K ratio for prevention of hypertension, Na/K questionnaire

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**Background :** The beneficial effects of a low dietary Na/K ratio in preventing hypertension (HTN) have been reported. Dietary instruction method that encourages a decrease in dietary Na/K is necessary. Based on the simple dietary questionnaire applicable for evaluating dietary habits related to CVDs, we developed a Na/K questionnaire (NaKq), in which food consumptions of foods that contribute to Na and K intake are asked. We conducted the NCS among local health checkup participants.

**Methods :** We surveyed people aged 20-74 who received health checkups in N City in 2024 and 2025, using a questionnaire that included NaKq. Urinary Na, K, and Cr were measured using spot urine. The NaKq asked about the frequency of consumption of vegetables, fruits, potatoes, tofu, milk/yogurt as sources of K, and salted fish, fish cakes, pickles, miso soup, discretionary use of soy sauce and salt, and noodles as sources of salt. Dietary K scores (Ksc), Na scores (Nsc), and Nsc/Ksc ratio were calculated using consumption frequency. Participants were grouped into quartiles according to urinary Na/K ratio (UNaK, mmol/mmol) and mean Ksc and Nsc were compared using analysis of variance.

**Results :** A total of 2563 residents who received the health checkups, answered the questionnaire, with no missing values were analyzed (1095 men and 1468 women, mean age 60.8 years). Mean  $\pm$  SD UNaK was higher in men ( $4.96 \pm 2.67$ ) than in women ( $4.67 \pm 2.62$ ). Mean  $\pm$  SD for Ksc, Nsc, and Nsc/Ksc ratio were  $39.5 \pm 36.0$ ,  $36.3 \pm 32.5$ , and  $1.24 \pm 0.92$ , respectively. The mean Ksc was lower and the mean Nsc was higher in the higher UNaK quartile. Furthermore, the mean Nsc/Ksc ratio was also significantly higher in the high urinary Na/K ratio quartile ( $1.08 \pm 1.08$  for Q1 and  $1.44 \pm 1.34$  for Q4,  $P < 0.001$ ).

**Conclusion :** The dietary Nsc/Ksc ratio obtained from NaKq positively associated with UNaK. Encouraging people to increase Ksc and decrease Nsc using NaKq would be useful in dietary education to prevent hypertension.

## Loneliness and diabetes risk: a prospective cohort study in Japanese adults

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**Background :** Diabetes prevention is an important public health priority, and identifying its social determinants is essential. While several studies have investigated the association between loneliness and diabetes risk using conventional statistical approaches, modern causal inference methods have yet to be applied.

**Methods :** From 114,054 Japanese aged 40-75 years old recruited between 2009 and 2017 in the Japan Public Health Center-based Prospective Study for the Next Generation (JPHC-NEXT), 61,356 individuals who were registered with available insurance data without self-reported diabetes at study participation were analyzed. We used loneliness as an exposure variable assessed by a direct question. Diabetes occurrence was derived from the claim data defined by ICD-10 codes starting from “E11-14” and diabetes drug prescriptions. We applied targeted minimum loss-based estimation (TMLE) to evaluate the association between loneliness and diabetes risk from baseline through the median follow-up, adjusting for sociodemographic characteristics, medical factors, and family history of diabetes. For comparison, we also conducted a Cox proportional hazard model over the entire study period.

**Findings :** The mean age of participants was 61.1 years (standard deviation: 8.8) and 54.6% were females. A total of 2471 (4%) reported high loneliness. During the median follow-up time of 7.7 years (up to 8 years), 3558 new cases of diabetes were identified. Compared with those reporting low loneliness, participants with high loneliness had a higher risk of diabetes (risk ratio: 1.23 [95%CI: 1.04, 1.42]). The Cox proportional hazards model yielded a similar estimate of TMLE. (hazard ratio: 1.20 [95%CI: 1.02-1.40]).

**Conclusions :** By applying advanced causal inference methods, we observed the association between loneliness and an increased risk of diabetes among Japanese adults, highlighting the significance of addressing loneliness as a modifiable risk factor.