

## Nutritional risk assessment and clinical outcome among older adults: The role of body composition

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**Background :** Current evidence lacks investigation of body composition's modifying effects on dietary pattern-health associations in aging populations. This study examines associations between diverse nutritional patterns and clinical outcomes among middle-aged and older adults, investigating body composition as an effect modifier.

**Method :** This retrospective longitudinal cohort study used 1999 Taiwan Longitudinal Study on Aging data, following participants for 12 years. Participants aged  $\geq 50$  years were included. Latent Class Analysis categorized dietary patterns from food frequency questionnaires. Body composition analyses used BMI ( $<24$  vs  $\geq 24$   $\text{kg}/\text{m}^2$ ) and calf circumference ( $<34\text{cm}$  men/ $<33\text{cm}$  women vs  $\geq 34\text{cm}$  men/ $\geq 33\text{cm}$  women). Outcomes included mortality, incident hypertension, and diabetes. Multivariate logistic regression analyzed associations between dietary patterns and outcomes across body composition subgroups.

**Result :** Among 1,624 participants, LCA identified four patterns: "least diverse" (n=441), "legumes, dairy, fruits, vegetables" (n=253), "fish and meat" (n=627), and "most diverse" (n=303). The "most diverse" group showed significantly lower mortality (aOR=0.66, 95%CI:0.46-0.95, p=0.03) and hypertension risks (aOR=0.57, 95%CI:0.38-0.86, p<0.01). Among BMI $<24$   $\text{kg}/\text{m}^2$  participants, "most diverse" pattern reduced mortality (aOR=0.62, 95%CI:0.39-0.97, p=0.04) and hypertension (aOR=0.48, 95%CI:0.28-0.81, p<0.01). In adequate calf circumference groups, "most diverse" pattern reduced mortality (aOR=0.56, 95%CI:0.34-0.91, p=0.02) and hypertension (aOR=0.55, 95%CI:0.33-0.91, p=0.02).

**Conclusion :** The "most diverse" dietary pattern demonstrates protective associations with mortality and hypertension, supporting dietary diversity in aging strategies. Body composition modifies these effects, suggesting individualized nutrition counseling based on body composition for optimal cardiometabolic risk reduction.

## Social capital and coronary artery calcification

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**Introduction :** Little is known about the relationship between social capital and atherosclerosis. Therefore, we examined this relationship in a general population using data from the prospective cohort study called the Fukuoka Epidemiological Study of Atherosclerosis (FESTA).

**Method :** FESTA is a prospective cohort study conducted in Fukuoka City, Nakagawa City (Fukuoka Prefecture), and Iki City (Nagasaki Prefecture), starting in 2019. Chest CT scans were performed to detect coronary artery calcification (CAC). The eligible population included men aged 40 years or older and women aged 60 years or older. The Agatston score was used to assess CAC, with a score of 100 or higher indicating significant coronary artery calcification. Individual and community levels of civic participation, social cohesion, and reciprocity were used as indices of social capital. This study was approved by the Institutional Review Board (2018M078).

**Results :** Out of a total of 719 participants, we identified 535 as study subjects by excluding those without an Agatston score. The mean age of the participants was 68.0 years, with 50.5% being men, and 112 individuals (20.9%) having significant calcification. The results of the multilevel logistic regression indicated that individual civic participation among women tended to be associated with a lower risk of atherosclerosis (adjusted odds ratio, 0.41; 95% confidence interval, 0.16 to 1.10), although this finding was not statistically significant. For other individual and community-level social capital factors, no significant relationship with atherosclerosis was observed.

**Discussion :** The results regarding the relationship between social capital and atherosclerosis were inconclusive. We recommend continuing the FESTA study to clarify the association between social capital and atherosclerosis.

## Cultural Adaptation and Pilot Validation of Adherence Tools for Japanese Breast Cancer Patients

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**Purpose :** Adherence to long-term endocrine therapy is essential for achieving optimal outcomes in patients with breast cancer. This pilot study evaluated the content validity and internal consistency of the Japanese versions of the Beliefs about Medicines Questionnaire (BMQ) and the Medication Adherence Rating Scale (MARS) to develop a culturally appropriate adherence assessment tool for Japanese patients with breast cancer.

**Patients and methods :** The BMQ and MARS were first translated into Japanese and then subsequently assessed for grammatical errors. To investigate content validity, a pilot survey was conducted with 50 Japanese patients with breast cancer undergoing adjuvant endocrine therapy to investigate content validity. The internal consistency of the BMQ and MARS was examined using item-total and item-rest correlations and Cronbach's alpha. Items with low correlations were flagged for revision or removal. Oncology experts further reviewed the flagged items for clinical relevance and cultural appropriateness.

**Results :** Several items, particularly those inconsistent with the Japanese healthcare context, showed low relevance, as assessed by the physicians. Specifically, Q6 ("This medicine is a mystery to me") and Q14 ("Natural remedies are safer than medicines") of the BMQ had low item-rest correlations ( $r = 0.079$  and  $0.075$ , respectively), indicating weak associations with other items. In MARS, four items (Q3, Q4, Q5, and Q9) were redundant, thereby warranting consolidation.

**Conclusion :** The findings of this study demonstrate the need for the cultural adaptation of the two adherence assessment tools. Revising or removing culturally incongruent, as well as redundant, items would improve the relevance and reliability of the BMQ and MARS for Japanese patients with breast cancer.

## Principal stratification-based interpretation of selection-related immortal time bias

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Structural descriptions of immortal time bias identified two mechanisms that can lead to this inferential problem: one relates to selection into analysis (or definition of eligibility) after treatment assignment; and the other, to misclassification of follow-up time due to post-eligibility treatment assignment. Selection-related immortal time bias is thought to affect fewer epidemiologic studies compared to the misclassification-related type; perhaps for this reason, there have been only a few studies on the former. In this study, we describe selection-related immortal time bias using the principal stratification framework. In particular, we use the concept of principal strata (that is, strata of the population defined by joint potential outcomes of a post-treatment variable [here, selection]) to characterize the non-comparability of treatment arms (or exposure groups) linked to post-treatment selection (that is, to conditioning on eligibility after treatment assignment). We show that the estimand that conditions on observed eligibility after time zero of follow-up, which is associated with selection-related immortal time bias, can be interpreted as a comparison of groups that only partially overlap in their principal strata. Moreover, we consider scenarios where time (relative to treatment assignment and start of follow-up) of eligibility definition varies and progressively approaches time zero. We present both numerical examples and derivations that show that probabilities of the outcome among individuals selected into the analysis monotonically approach unconditional (in absence of selection) expected potential outcomes under different treatment levels. Further, when eligibility coincides with time zero, effect estimates can be unbiased. This work puts forward a potential outcomes-based description of selection-related immortal time bias, and suggests that principal effects might be useful causal estimands for some studies affected by this bias.

## Impact of bioactive vitamin D levels on the immunogenicity of COVID-19 vaccine in a Japanese cohort

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**Background/Objectives :** Blood vitamin D levels have been linked to COVID-19 severity; however, the effects of unsupplemented vitamin D levels in the serum on vaccine immunogenicity remain limited. This study evaluated the impact of baseline serum 1  $\alpha$ , 25-(OH)<sub>2</sub> vitamin D, a bioactive form with steady blood concentrations, on vaccine response.

**Methods :** From June to September 2021, we measured active vitamin D levels in 88 Japanese workers and students before vaccination with BNT162b2 or mRNA-1273. We assessed SARS-CoV-2 spike protein S1 IgG and IgM levels and antigen-specific INF-  $\gamma$  -releasing cells from pre-vaccination up to 8 months post-second dose.

**Results :** Active vitamin D levels ranged from 33.7 to 99.8 pg/mL; 45.5% exceeded the Japanese standard limit of 60 pg/mL. No subjects had values below the lower limit of the reference range (20 pg/mL). In a mixed model accounting for repeated measures and sub-cohort random effects and following fixed effects, vaccine type, weeks post-vaccination, age, sex, *ALDH2* gene polymorphism, height, smoking, ethanol intake, exercise, stress, steroid use, allergies, dyslipidemia, active vitamin D was negatively associated with anti-S1 IgG and IgM ( $p < 0.001$ ) but positively with INF-  $\gamma$  -releasing cell counts ( $p = 0.003$ ).

**Conclusions :** The humoral and cellular immunogenicity of the SARS-CoV-2 vaccine is associated with baseline active vitamin D levels, oppositely. Considering the larger role of cellular immunity in defending against a SARS-CoV-2 infection, as well as the independence of viral mutations,[MT1] higher levels of active vitamin D than those in the reference range may be advantageous. However, despite the growing interest in deficiency, we failed to examine the association with low vitamin D levels.