

## Hobby engagement and subjective well-being in older adults with stroke survivors: JAGES-Home Care

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**Background :** Individuals with a history of stroke often face the risk of losing a range of social relationships and activities, including hobby engagement. While hobby engagement has been reported to contribute to well-being across cultures, its effects in individuals with a history of stroke are not well known. This study examined the association between hobby engagement and subjective well-being among older stroke survivors.

**Methods :** This cross-sectional study involved community-dwelling older adults who had a history of stroke, from the Japan Gerontological Evaluation Study-Home Care (JAGES-Home Care), a questionnaire survey of older adults receiving long-term care at home. The participants were asked about their engagement in 13 activities ("engaged" or "not engaged"). Additionally, their engagement numbers and engagement types (physical, cognitive, creative, and receptive engagement) were measured. Subjective well-being was assessed by the World Health Organization-Five Well-Being Index (WHO-5), with higher scores indicating higher well-being. We applied a multivariable linear regression analysis adjusted for the demographic factors, socioeconomic status, and caregiving status.

**Results :** Data from 411 stroke survivors were analyzed (mean age = 82.2; 51.4% females). Of the participants, 82.4% engaged in any hobbies. Multivariable analysis revealed that hobby engagement was associated with higher levels of subjective well-being ( $\beta = 0.69$ , 95% CI = 0.41 to 0.98). Individuals who engaged in a greater number of hobbies showed higher well-being. All hobby types were associated with higher well-being.

**Conclusions :** These findings suggest the positive role of hobby engagement, even if receptive, for the well-being of stroke survivors, highlighting the importance of promoting their engagement and removing its barriers.

## Reproductive Lifespan and CVD events Risk in Taiwanese Women: Results from a Nationwide Biobank

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**Background :** The duration of a woman's reproductive lifespan may affect long-term cardiovascular health, primarily due to its association with hormonal changes. However, the relationship between reproductive lifespan and the risk of cardiovascular disease (CVD), coronary artery disease (CAD), and stroke has not yet been established. Therefore, our study aimed to investigate the association between reproductive lifespan and the risk of these cardiovascular events in women.

**Method :** Data from a nationwide cohort, the Taiwan Biobank, which included 41,082 women aged 20 to 70 years, were investigated. Reproductive lifespan was defined as the duration between menarche and menopause, categorized into tertiles by length. Three cardiovascular outcomes—cardiovascular disease (CVD), coronary artery disease (CAD), and stroke—were ascertained via health-record linkage. Multivariable regression models were used to assess the association between reproductive lifespan and the risk of CVD, CAD, and stroke, with adjustments for age, education status, body weight, smoking history, intervention of hormone-based treatment, parity, and age at first birth.

**Results :** In fully adjusted models, when the Tertile with medium reproduction life span was compared, Population categorized in the last tertile had a increase risk of both CVD (OR: 1.29; 95% CI: 1.06, 1.57) and CAD (OR: 1.33; 95% CI: 1.04, 1.69), but not stroke or stroke (OR: 1.31; 95% CI: 0.94, 1.81). In contrast, those in the top tertile show no association with CVD (OR: 0.97; 95% CI: 0.81, 1.16), CAD (OR: 1.01; 95% CI: 0.81, 1.26), and stroke risk (OR: 0.94; 95% CI: 0.69, 1.27).

**Conclusion :** A Shorter reproductive lifespan but not a longer reproductive lifespan was associated with a higher risk for incident CVD and CAD.

**Keyword :** Reproductive Lifespan, Cardiovascular Diseases, Cohort Study, Taiwan Biobank

## Blood pressure, polygenic risk score, and cardiovascular mortality among 35,000 Japanese individuals

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**Background :** Although blood pressure (BP) control is a fundamental strategy to reduce cardiovascular disease (CVD) risk, BP control targets do not account for an individual's genetic predisposition in the clinical guidelines. Therefore, we examined joint associations of BP control and BP polygenic risk score (PRS) with CVD mortality in a Japanese population.

**Methods :** We obtained data from the Japan Multi-Institutional Collaborative Cohort (J-MICC) Study, a multicenter cohort study with 14 study areas throughout Japan. Of all study participants, more than 35,146 Japanese individuals (11,242 participants in subgroup #1 and 23,904 participants in subgroup #2) were genotyped and measured their BP. PRS for systolic blood pressure (SBP) and diastolic blood pressure (DBP) was calculated based on GWAS results from the Biobank Japan. Controlled BP was defined as SBP $\leq$ 140 mmHg or DBP $\leq$ 90 mmHg regardless of antihypertensive medications. From a baseline survey, participants were followed up until the end of 2019 or 2020. Date and cause of death were collected by research staff at each study site with permission from the Ministry of Health, Labor and Welfare. The mortality case with the ICD-10 code of I00-I99 was defined as CVD mortality in this study.

**Results :** During the follow-up period (median: 12.0 years), a total of 381 CVD deaths were observed. Compared with controlled BP, HRs (95% CI) of CVD mortality were 1.98 (1.37 to 2.88) for uncontrolled SBP and 2.41 (1.66 to 3.49) for uncontrolled DBP. Compared to controlled BP in the lowest PRS tertile, HRs (95% CI) of CVD mortality in the highest PRS tertile were 2.28 (1.17 to 4.43) for SBP and 3.08 (1.61 to 5.91) for DBP even though BP was controlled. These associations in the subgroup #1 were replicated in the subgroup #2.

**Conclusion :** Our findings highlight the importance of BP PRS in detecting a hidden CVD risk stratum in addition to BP measurements.

## Adherence to “Lifelong Health Support 10” and Cardiovascular Disease Prevention: The Saita Study

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**Background :** Comprehensive management is important for cardiovascular disease (CVD) prevention. Lifelong Health Support 10 (LHS10) is a healthy lifestyle guidance developed at the national center, consisting of lifestyle and dietary recommendations. We investigated the association between adherence to LHS10 and CVD risk in Japan urban population.

**Methods :** We recruited 5,280 participants aged 30-90 years who completed food-frequency questionnaires for the Saita study. The main exposures were obtained from the LHS10 guidelines. We made the score based on the LHS10 guidelines of no smoking, BMI<25 kg/m<sup>2</sup>, stair climbing>60% of time, alcohol consumption <46 g/day, and having “healthy diets”. Each component was assigned 1 point if the criterion was met, and 0 otherwise. The total score ranged from 0-5 and categorized into 3 categories: low, moderate, and high adherence (score ≤2, 3, and ≥4, respectively). “Healthy diets” was calculated from food intake: participants received 1 point if their intake of fish, fiber, fruit, vegetables and soy products was higher than the sex-specific median intake, and 1 point if their intake of saturated fatty acid, processed red meats, salt, sugary drinks, and sweets was less than the sex-specific median intake (healthy diet score (HDS)= 0-10). "Healthy diets" accounted for 1 point when HDS ≥4. We used multivariable-adjusted Cox regression to calculate the hazard ratios with 95% confidence intervals (CIs) for the incidence of CVD and ischemic heart disease (IHD).

**Results :** During a median follow-up of 15.6 years, we observed 429 CVD and 197 IHD incidences. Compared with individuals in the low adherence, the HR (95%CI) of total CVD in the high adherence group were 0.71 (0.53-0.96). There was an inverse association of the healthiest group with risk of IHD (HR=0.64; 95%CI (0.43-0.95)).

**Conclusions :** Our findings provide evidence supporting the importance of adherence to the LHS10 in CVD prevention in Japan.

## Proteomics linking SGLT2 inhibitors with atrial fibrillation and heart failure: A genetic study

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**Background :** Randomized controlled trials show sodium-glucose cotransporter 2 (SGLT2) inhibitors reduce heart failure and atrial fibrillation risk although this cannot be solely explained by its glycemic properties. The use of genomics and proteomics can inform the putative mechanisms related to its cardiovascular effect and hence our understanding of its drug action.

**Methods :** Based on the 25 proteins associated with SGLT2 inhibitor use in a published randomized trial, we conducted a cis-Mendelian randomization study. We identified strong ( $p < 5 \times 10^{-8}$ ) and independent ( $r^2 < 0.01$ ) cis variants from these proteins from a genome wide associations study of proteins (N: 54,219). We applied these cis variants as instruments to genetic summary statistics of atrial fibrillation (AF) (N: 1,650,345) and heart failure (HF) (N: 1,946,349). Wald ratio was used as the main analysis, with genetic colocalization as the sensitivity analysis. We also included relevant Magnetic Resonance Imaging (MRI)-measured traits as secondary outcomes. Bonferroni correction was used to correct for multiple testing.

**Results :** Amongst 20 proteins with cis-variants, OTU domain-containing ubiquitin aldehyde-binding protein 1 (OTUB1) was associated with lower risk of atrial fibrillation (OR: 0.79 per SD, 95% CI: 0.73 to 0.86) after Bonferroni correction, with support by genetic colocalization (PP.H4 = 0.983). OTUB was also associated with lower PR interval ( $\beta$ : -0.082 SD per SD, 95% CI: -0.122 to -0.042), with moderate evidence of genetic colocalization (PP.H4 = 0.636). Other proteins were not associated with AF or HF risk.

**Conclusions :** OTUB1 likely explains part of the protective effect of SGLT2 inhibitor use in AF risk, which can help guide corresponding drug development for reposition in AF prevention.