# Association of Serum Irisin Levels with Obesity Indices in a General Population of Japanese Men

**Naotsugu Akashi** (1)
Keiko Kondo (1), Aya Kadota (1), Sayuki Torii (1), Sayaka Kadowaki (1), Itsuko Miyazawa (2), Chiaki Sekine (1)
Takashi Hisamatsu (3), Akiko Harada (1), Akira Fujiyoshi (4), Katsuyuki Mirua (1)

1 : NCD Epidemiology Research Center (NERC), Shiga University of Medical Science
2 : Department of Medicine, Shiga University of Medical Science
3 : Department of Public Health, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences
4 : Department of Hygiene, Wakayama Medical University

**Background** : Irisin is an exercise-induced myokine secreted mainly from skeletal muscle into the circulation, which is known to improve glucose/lipid metabolism abnormalities in obesity and promotes lipolysis. However, the relationship between serum irisin levels and obesity indices in the general population has not been fully elucidated. We aimed to examine the association of serum irisin levels with fat deposition and anthropometric measures in a general population of Japanese men.

**Methods** : From 2006–2008, we conducted a cross-sectional study in a population-based sample of Japanese men aged 40 through 79 years. We measured serum irisin levels using an enzyme-linked immunosorbent assay, and calculated areas of visceral adipose tissue (VAT) , subcutaneous adipose tissue (SAT), and total adipose tissue (TAT) in abdomen using computed tomography. The adjusted means of obesity indices according to the quartiles of irisin were calculated, using analysis of covariance. Covariates included age, BMI (excluded when analyzed as outcome), 7-day average step count, drinking status, and smoking status.

**Results** : We analyzed 1031 men (mean age and body mass index [BMI], 64.0 years and 23.6 kg/m$^2$, respectively). Higher serum irisin levels were associated with higher HDL cholesterol (P = <0.001) and associated with lower LDL cholesterol and triglyceride (P = 0.004, <0.001, respectively). Higher serum irisin levels were associated with lower BMI, waist circumferences, abdominal SAT area and TAT area (all P for trend <0.001), and VAT area (P for trend = 0.016) in unadjusted model. The associations with BMI and SAT area remained significant after adjustment for covariates, whereas those with waist circumference, VAT area and TAT area were not.

**Conclusions** : Higher serum irisin levels were significantly associated with lower BMI and SAT area, independent of confounders, including age and step count, in general Japanese men.

# Drug Prescriptions in Duchenne Muscular Dystrophy and Becker Muscular Dystrophy in Japan

**Naohiro Yonemoto** (1)

1 : Department of Biostatistics, University of Toyama

**Introduction** : Muscular dystrophy (MD) is a group of genetic disorders that cause progressive weakness and loss of muscle mass. There are different types of muscular dystrophy, including Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD), which vary in severity and the muscles affected. Aims: The study objective is to describe the prescribing status of DMDs and BMDs in Japan.

**Methods** : The study design employed a cross-sectional and cohort approach, utilizing health claims data from January 2005 to June 2017. We described prescriptions for steroids, cardiovascular drugs, and neuropsychiatric drugs by DMD and BMD.

**Results** : The subjects were 95 patients with DMD and 63 patients with BMD. The mean age at the date of first diagnosis was 16 years (SD 10.3). The median follow-up period was 45.5 months (interquartile range: 21.75 -60.0) from the first diagnosis. 27.4% of DMD and 4.8% of BMD were prescribed steroid, prednisolone. 42.1% of DMD and 15.9% of BMD were beta-blockers (ATC code: C07). 35.8 % of DMD and 28.6 % of BMD were psycholeptics drugs (ATC code: N05).

**Conclusions** : We have identified the prescribing status of DMDs and BMDs in Japan. New drugs for DMDs are being developed. We hope that our findings will be useful for future discussions on drug prescribing in MD.

# Association between periconceptional omega-6 and omega-3 fatty acid intake and postpartum depression

**Kenta Matsumura** (1,2,3)
Kei Hamazaki (2,3,4), Akiko Tsuchida (2,3), Hidekuni Inadera (2,3)

1 : Aomori University of Health and Welfare / Graduate School of Health Sciences / Department of Epidemiology and Nutritional Psychiatry
2 : University of Toyama / Faculty of Medicine / Department of Public Health
3 : University of Toyama / Toyama Regional Center for Japan Environment and Children's Study
4 : Gunma University / Graduate School of Medicine / Department of Public Health

**Background** : Dietary intake of omega-3 polyunsaturated fatty acids (PUFAs) has favorable effects on the prevention of postpartum depression, but fish, the principal source of omega-3 PUFAs, are becoming a depleted resource.

**Objective** : We examined whether lower periconceptional intake of omega-6 PUFAs—whose metabolic pathways are antagonistic to those of omega-3 PUFAs—is associated with lower prevalence of postpartum depression, while simultaneously considering omega-3 PUFA intake.

**Methods** : The participants were 92,595 mothers involved in an ongoing nationwide birth cohort of the Japan Environment and Children's Study (JECS). Periconceptional intakes of omega-6 and omega-3 PUFA were measured using a food frequency questionnaire (FFQ). Postpartum depression was identified at 1 month postpartum based on an Edinburgh Postnatal Depression Scale (EPDS) score of ≥9. Generalized additive mixed model analysis was used to draw contour plots of postpartum depression on a plane with omega-6 and omega-3 PUFA intakes on the x- and y-axes, respectively.

**Results** : The adjusted prevalence ranged from 11.0% to 26.3% within the respective 1$^{st}$ to 99$^{th}$ percentile intake ranges and decreased monotonically with lower omega-6 PUFA intake. In contrast, the prevalence decreased with higher omega-3 PUFA intake, but this trend plateaued above 2 g/day.

**Conclusions** : Our results highlight the potential importance of focusing on omega-6 PUFAs, as well as omega-3 PUFAs, prior to conception to reduce the risk of postpartum depression.

# Regional differences in subjective well-being: A comparative study of the Hida and Hokuriku regions

**Manae Uchibori** (1)
Shuhei Nomura (2,3), Hisateru Tachimori (1), Anna Kubota (1), Yoshiaki Kanamori (1)

1 : Keio University
2 : Keio University Global Research Institute, Tokyo, Japan
3 : International University of Health and Welfare, Tokyo, Japan

**Background :** Subjective well-being (SWB), especially life satisfaction, is a widely used indicator of population health and quality of life. However, evidence from Japan's regional areas remains limited, despite their diverse demographic and socioeconomic conditions. This study compares SWB and its socio-demographic determinants between two contrasting regions—Hida, a depopulating mountainous area, and Hokuriku, a more urbanized region. By identifying shared and region-specific factors, we aim to inform targeted well-being policies.

**Methods :** We analyzed data from two cross-sectional surveys: Hida (2022): 1,249 residents aged 20–89 across four municipalities—Hida, Takayama, Gero, and Shirakawa (response rate: 35.7%) and Hokuriku (2023): 5,813 residents aged 13–69 from Toyama, Ishikawa, and Fukui prefectures, collected via online survey (first-come, first-served; no response rate applicable). Life satisfaction was assessed using an 11-point scale (0 = worst possible life, 10 = best possible life). We examined its associations with age, gender, household income, and educational attainment. Age-stratified sensitivity analyses were conducted.

**Results :** In Hida, the mean life satisfaction score was 6.4, increasing with age and peaking in the 70s, followed by a slight decline in the 80s. In contrast, Hokuriku's average score was 5.7, with the highest satisfaction among teens and people in their 20s, and the lowest among those in their 40s. In both regions, SWB was higher among women and positively associated with higher income and education.

**Conclusions :** Age-related patterns of life satisfaction varied by region. Findings highlight the need for region- and age-sensitive policies that support well-being across the life course—particularly for young people in depopulating rural areas and middle-aged adults in regional urban settings.

# Estimating the cardioprotective mechanism of SGLT2 inhibitors using causal mediation analysis

**Akari Kawai** (1)
Yukio Kitajima (2), Masanori Ozawa (2), Atsushi Aminaka (2), Arisa Kobayashi (3,4), Shingo Fukuma (3,5), Masataka Taguri (1)

1 : Department of Health Data Science, Tokyo Medical University, Tokyo, Japan
2 : EPS corporation, Tokyo, Japan
3 : Human Health Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan
4 : Division of Nephrology and Hypertension, Department of Internal Medicine, The Jikei University School of Medicine, Tokyo, Japan
5 : Department of Epidemiology Infectious Disease Control and Prevention, Hiroshima University Graduate school of Biomedical and Health Sciences, Hiroshima, Japan

**Introduction :** Sodium–glucose cotransporter-2 inhibitor (SGLT2i) is glucose-lowering agent by increasing urinary glucose excretion in type 2 diabetes. Beyond glycemic control, recent trials have shown reductions in cardiovascular (CV) and renal events across broad patient populations. However, the mechanisms behind CV benefits are not fully understand. We aimed to quantify the extent to which the SGLT2i–CV association is mediated by changes in HbA1c and/or eGFR using causal mediation analysis.

**Methods :** We conducted a retrospective cohort study using the Real-World Data database (Real World Data Co., Ltd., Japan), a nationwide database. Adults with newly diagnosed type 2 diabetes who initiated an SGLT2i, another glucose-lowering drug (oGLD), or combination therapy between April 2014 and October 2021 were included. Using the multistate modeling for stochastic interventions on a time-to-event mediator, we decomposed the total effect on CV events into direct and indirect effects via time-updated HbA1c and eGFR. Effects were defined as differences in the cumulative incidence (event probabilities) at time t under hypothetical interventions on the mediators using the CMAverse package by R.

**Results :** Among 19,018 eligible patients, 683 initiated SGLT2i, 17,320 initiated oGLD, and 1,015 received combination therapy; 1,428 CV events occurred during follow-up. Crude event rates were lower with SGLT2i than oGLD (p=0.23). Estimation of adjusted hazard ratios, direct/indirect effects, and the proportion mediated via HbA1c and eGFR will be reported at the congress.

**Conclusions :** In this real-world study, SGLT2i initiation is associated with fewer CV events than oGLD. Forthcoming mediation analyses will quantify the degree to which changes in glycemia and kidney function account for this benefit versus pathways independent of HbA1c and eGFR.