

## Comparing Old and New Definitions of Rare Cancers using the Japan Cancer Patient Experience Survey

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**Purpose :** Patients with rare cancers face unique challenges compared with those with more common cancers, including delays in diagnosis and treatment initiation and, in some cases, the absence of established standard therapies. Rare cancers collectively account for about 20% of all cancer incidence, but precise list of rare cancers were not available in Japan, so surveys of rare cancers targeted rather conservative list of rare cancers, i.e, only those that are obviously rare. In 2025, a new classification was proposed to rare cancers. This study aimed to apply the new classification to the nationwide Cancer Patient Experience Survey (CPES) and to compare it with the previous narrower definition, to clarify the situation of rare cancer patients and to provide implications for future surveys.

**Method :** We analyzed data from 11,247 participants in the CPES. Patients were classified as having rare cancers according to both the old definition (n=626) and the new classification (n=2,478). Patient characteristics and survey responses were compared to examine differences in demographic and clinical profiles between the two definitions.

**Results :** The new classification identified a larger proportion of female patients (54.4% vs. 43.8%), largely reflecting the inclusion of breast and gynecological cancers. This reclassification also resulted in reducing the relative proportion of oral and testicular cancers. Nevertheless, survey responses suggest that rare cancer patients continue to face particular difficulties in diagnosis, treatment decisions, and daily life compared with those with more common cancers.

**Conclusion :** The new classification revealed notable differences in the characteristics of patients categorized as having rare cancers. We recommend adopting this classification in future CPES to more accurately reflect the realities of rare cancer patients and to strengthen the evidence base for policy and clinical practice.

## Association of Intramuscular Fat in Thigh and Trunk Muscles with Insulin Resistance in Japanese

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**Objective** : Ectopic fat in skeletal muscles may play a key role in insulin resistance. However, it is unknown whether the association differs between different muscles and whether muscle fat is related with insulin resistance independent of visceral and hepatic fat.

**Methods** : In a cross-sectional study of 1,495 non-diabetic Japanese men (n=915) and women (n=580), we used computed tomography (CT) to measure muscle attenuation (MA) within four muscle groups: anterior thigh (rectus femoris), posterior thigh (biceps femoris and semitendinosus), psoas, and paraspinous muscles. Intra-abdominal fat area (IAFA) as an estimate of visceral adiposity and liver-to-spleen (L/S) ratio to assess hepatic steatosis were also done by CT. Insulin resistance was defined as the natural logarithm of HOMA-IR in multiple linear regression analysis, and as the highest quartile of HOMA-IR ( $\geq 1.56$ ) in logistic regression analysis.

**Results** : In multiple linear and logistic regression models, lower CT attenuation in the four muscles was significantly related to elevated HOMA-IR levels independent of age, alcohol consumption, smoking status, and regular physical exercise in both sexes. After further adjusting for IAFA and L/S ratio, multiple linear regression analysis showed that anterior thigh MA was significantly associated with HOMA-IR in men ( $\beta' = -0.113$ ,  $p < 0.001$ ) and women ( $\beta' = -0.107$ ,  $p = 0.009$ ). Similarly, logistic regression analysis revealed that lower anterior thigh MA (per 1-SD decrease) was associated with insulin resistance in men ( $OR = 1.29$ , 95% CI: 1.05-1.57) and women ( $OR = 1.43$ , 95% CI: 1.06-1.92). In both analyses, no significant association was found for posterior thigh, psoas, or paraspinous MA in either sex.

**Conclusions** : Lower anterior thigh MA was related to insulin resistance, independent of both visceral and liver fat. This association was not observed in the posterior thigh, psoas, or paraspinous muscles.

## Visceral adiposity, hepatic steatosis, and future elevated liver enzymes in Japanese men

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**Background:** Serum levels of gamma-glutamyltransferase (GGT) and alanine aminotransferase (ALT) are risk factors for cardiometabolic diseases. While the "portal theory" suggests that abdominal visceral fat and liver fat are closely linked via the portal vein, it is not known whether visceral adiposity and hepatic steatosis contribute independently to future increases in GGT and ALT.

**Methods :** A total of 572 and 559 Japanese men aged 28–77 years without diabetes and without elevated GGT or ALT levels, respectively, were enrolled. Intra-abdominal fat area (IAFA); abdominal, thoracic and thigh subcutaneous fat areas (SFA); and liver-to-spleen (L/S) ratio measured by computed tomography. Elevated GGT and ALT were defined as levels at or above the 75th percentile of these values in the baseline population:  $\geq 67$  IU/L and  $\geq 32$  IU/L, respectively. Discrete-time model was used to estimate odds ratios for future elevated GGT and ALT in relation to exposures. Multivariable models included IAFA, L/S ratio, age, smoking habit, regular physical activity, daily alcohol consumption, and fasting immunoreactive insulin.

**Results :** During the 8 years of follow-up, we confirmed 91 cases of future elevated GGT, and 144 cases of future elevated ALT. Greater IAFA and lower L/S ratio were associated with an increased risk for future elevated GGT and ALT. For future elevated GGT, the multiple-adjusted odds ratios were 1.30 (95% CI, 0.68-2.49) and 2.67 (1.34-5.32) for the middle and highest IAFA tertiles, respectively, versus the lowest; and 2.91 (1.17-7.22) for L/S ratio  $< 0.8$  and 1.00 (0.54-1.84) for 0.8 to  $< 1.1$  versus  $\geq 1.1$ . These associations remained significant after adjustment for abdominal SFA or total SFA, none of which were significant. Similar results were observed for ALT.

**Conclusion :** Greater visceral adiposity and hepatic steatosis independently increased the risk of elevated GGT and ALT.

## Temperature-related Dengue Risk and Socio-economic factors: A Multi-Province Study in Southeast Asia

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**Background :** While several local-level studies have shown that socio-economic factors can modify the effect of temperature on dengue transmission, few inter-regional studies have examined this relationship. To address this gap, we employed a novel approach by integrating diverse data sources—including household-level surveys and gridded data—to investigate whether province-level socio-economic conditions influence temperature-related dengue risk across select Southeast Asia locations.

**Method :** As part of the Southeast Asia Research on Climate change and Dengue (SEARCD) project, we conducted a two-stage analysis for 147 provinces in the Philippines, Indonesia, and Cambodia. We collected monthly dengue cases and mean temperature data. Thereafter, we derived socio-economic indicators by aggregating household demographic survey data and processing openly available gridded data. In the first stage, we used distributed lag non-linear models to estimate province-specific relative risk at high temperatures. In the second stage, we pooled these estimates by a random-effects meta-analysis, and assessed effect modification by a meta-regression analysis.

**Results :** The pooled RR of dengue at 90th, 95th and 99th temperature percentile with respect to the 50th were 1.07[95%CI:1.02, 1.12], 1.10[1.03,1.17] and 1.12[1.00,1.26] respectively. In the meta-regression analysis, while socio-economic variables of GDP per capita, population density, coverage of improved drinking water source or improved toilet facility and educational attainment were significantly associated with relative risk at 95th temperature,  $I^2$  did not decrease.

**Discussion :** Socio-economic indicators were associated with relative risk but did not explain the between-province heterogeneity in temperature-related risk. These findings suggest that unmeasured factors drive risk variation and interventions aimed at mitigating temperature-driven dengue risk should be implemented not only in specific regions but also nationwide.

## Evaluating the population impact of mask-wearing on COVID-19 transmission during pre-vaccine period

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**Background & aims :** Multiple non-pharmaceutical interventions (NPIs) were carried out across the globe during the COVID-19 pandemic, with mask-wearing being one of the key aerosol transmission prevention strategies before the COVID-19 vaccine rollout. The present study aimed to estimate the population effectiveness of mask-wearing before vaccine roll-out.

**Methods :** We analyzed data from March 2020 to March 2021 across Europe, Asia, and Oceania. Collected datasets included age-stratified daily incidence of cases, monthly or yearly number of confirmed deaths, and mask-wearing coverage in public spaces. First, we estimated the effective reproduction numbers and reproduced the observed epidemic curve. Subsequently, we constructed epidemic curves under counterfactual scenarios assuming pre-pandemic mask-wearing levels. The cumulative incidence and deaths counts were compared between the observed and counterfactual scenarios.

**Results :** Mask-wearing coverage increased substantially in all countries. Analysis revealed significant relative reductions in effective reproduction numbers associated with observed mask-wearing coverage. The counterfactual scenarios demonstrated that maintaining pre-pandemic mask-wearing levels would have resulted in substantially higher case and death counts across all countries.

**Conclusions :** Mask-wearing recommendations and mandates significantly reduced COVID-19 transmission and mortality. Individual-level preventive measures have proved highly effective for epidemic control in populations lacking vaccine-induced immunity.