

## Epidemiological Analysis of a Measles Outbreak in Mie Prefecture in December 2018

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**Background :** An outbreak of measles primarily affecting teenagers and twenties occurred in Mie Prefecture from December 2018. Confirmed cases, including those in Mie and outside the prefecture, were reported up to January 16, 2019. The index case was a man in his twenties who had participated in a training seminar for teens, developing symptoms on December 28, yet still attended the seminar. Following the event, secondary community transmissions were reported. The aim of this study was to elucidate the epidemiological characteristics of secondary transmission during this outbreak.

**Methods :** We compiled patient data related to the outbreak based on publicly available reports from municipalities and public health centers in Mie and surrounding prefectures. The incubation period distribution was extracted from published evidence. We estimated the serial interval and the relative frequency of secondary infections by time of symptom onset. We then estimated the time-dependent effective reproduction number ( $R_t$ ).

**Results :** A total of 61 cases were reported, 29 of whom had participated in the training seminar, including the index case. Secondary infections were estimated to have occurred around two days before the index case developed symptoms during the seminar. The estimated  $R_t$  peaked during the training seminar period, declined following the report of the index case on December 30, but temporarily was above 1 again after schools started on January 7. After January 13,  $R_t$  continued to take the value below 1.

**Conclusion :** A large-scale secondary transmission event occurred in a closed setting where many unvaccinated susceptible individuals were clustered.

## Evaluating red and processed meat intake and colorectal cancer risk in Asian populations

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**Background :** While Western studies have linked higher intake of red and processed meat to increased colorectal cancer risk, evidence remains limited in Asia, where red and processed meat intake has generally been lower. We examined the association between red and processed meat intake and colorectal cancer risk in Asian cohorts through a systematic review and meta-analysis.

**Methods :** The protocol was registered in PROSPERO (CRD420251047573) as part of a comprehensive project evaluating the applicability of the 2018 World Cancer Research Fund (WCRF) recommendations in Asia. We conducted a literature search in PubMed from Jan 1990 to Jun 2025. The studies were screened by two independent reviewers. Relative risks (RRs) of colorectal cancer incidence with 95% confidence intervals (CIs) were extracted, and summary estimates calculated using random-effects models. Both categorical (highest vs. lowest) and dose-response analyses were conducted, with subgroup analyses by sex.

**Results :** We identified twelve cohort studies on red meat and seven on processed meat. Of these, seven red meat studies were included in the categorical analysis and six in the dose-response analysis, while three processed meat studies were included in each. Red meat intake was not significantly associated with colorectal cancer (categorical: RR 1.04, 95% CI: 0.92-1.19; dose-response per 100 g/day: RR 1.08, 95% CI: 0.98-1.19). Processed meat intake was associated with a higher risk in categorical analysis (RR 1.18, 95% CI: 1.06-1.32), with a dose-response per 50 g/day suggesting an increased risk among women (RR 1.29, 95% CI: 1.05-1.60).

**Conclusion :** This review provides preliminary evidence that, consistent with Western findings, processed meat intake may contribute to colorectal cancer risk in Asian populations. The limited number of Asian cohort studies remains a challenge, highlighting the need for further studies and supporting the evaluation of the applicability of current WCRF recommendations in Asia.

## Multi-Omics Integration Identifies Microbiota-Linked Metabolites for Early Prediction of Gestational Diabetes Mellitus

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**Background :** Gestational diabetes mellitus (GDM) poses significant maternal and neonatal risks, and current mid-pregnancy diagnostic approaches fail to enable early intervention. Emerging evidence suggests that gut microbiota-associated metabolites may play a role in GDM pathogenesis, but clinically validated early biomarkers remain scarce.

**Methods :** We conducted a multicenter, multi-cohort nested case-control and prospective study involving 2,693 pregnant women across five cohorts. Untargeted metabolomics and metagenomics were integrated to identify key early pregnancy biomarkers. A random forest-based prediction model was constructed using three consistently dysregulated metabolites (3-hydroxydecanoic acid,  $\gamma$ -Gly-Leu, and propionic acid) and validated in two external cohorts and one prospective cohort. Multi-omics correlation analyses were performed to explore microbiota-metabolite-clinical parameter interactions.

**Design :** GDM patients exhibited early metabolic disturbances, including increased BMI, triglycerides, and platelet count. Untargeted metabolomics identified 14 metabolites with consistent alterations across both trimesters, enriched in pathways involving energy metabolism, oxidative stress, and amino acid biosynthesis. Gut metagenomic analysis revealed compositional shifts and disrupted co-occurrence networks. Key microbial genera/species showed strong correlations with GDM-related metabolites and clinical indicators. The metabolite-based predictive model achieved high AUCs: 0.854 (development), 0.804 and 0.819 (external), and 0.901 (prospective cohort), demonstrating robust generalizability.

**Conclusion :** Our findings support the early dysregulation of gut microbiota-associated metabolites in GDM pathogenesis. The constructed metabolite-based model offers a clinically applicable, interpretable, and scalable tool for early GDM risk stratification, with potential to inform personalized intervention strategies during pregnancy.

## Municipality-level temperature–mortality associations and vulnerable populations in Japan

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**Background :** Most studies of temperature-related health effects in Japan rely on prefecture- or city-level observations. Municipality-specific analyses, encompassing cities, towns, and villages, capturing temperature effect at smaller resolution remains limited.

**Objectives :** To estimate temperature-related excess deaths at municipality level across Japan, including age-, cause-, and sex-specific analysis.

**Methods :** Daily mean temperature and mortality data from 1,845 municipalities in Japan (2010–2019) were analyzed. Prefecture-specific temperature–mortality associations were estimated using distributed lag nonlinear models with a case time-series design, pooled through multivariate meta-analysis, and used to calculate municipality-level temperature-related excess mortality rates, which were then aggregated by urbanicity, climate zone and super-aged status, and separately by cause, age group (0–64, 65+), and sex.

**Results :** Heat contributed to 2.9 and cold to 86.0 excess deaths per 100,000 person per year (95% empirical Confidence Interval: 1.4–4.4 and 57.7–112.1, respectively). Towns and rural municipalities (<50,000 population) had the highest heat- and cold-related mortality, while island and subtropical areas had the lowest. Central Highland climate zone had the highest cold mortality and Hokkaido the highest heat mortality, whereas subtropical areas had the lowest for both. Super-aged municipalities ( $\geq 21\%$  elderly) and adults  $\geq 65$  years experienced higher mortality for both heat and cold. Circulatory diseases had higher temperature-related mortality than respiratory diseases, and males had higher mortality than females for both heat and cold.

**Conclusion :** Municipality-level analysis identifies vulnerable subgroups and regions, strengthening evidence of temperature-related mortality in Japan and informing targeted climate adaptation policies.

## Groundwater Arsenic Exposure and Kidney Function: Evidence from the Taiwan Biobank

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**Background :** Arsenic contamination in groundwater is a well-recognized environmental nephrotoxicant, linked to renal tubular damage, oxidative stress, and abnormal kidney biomarkers. Taiwan, a known arsenic-endemic area, provides a unique setting to investigate the population-level impact of arsenic exposure on kidney function.

**Methods :** This cross-sectional study included 53,347 adults aged 30–70 years from the Taiwan Biobank. Residential addresses were linked to the national groundwater arsenic potential map, which identifies areas with >75% probability of exceeding 0.025 mg/L. Participants were classified as exposed or non-exposed. Kidney function was assessed by blood urea nitrogen (BUN), uric acid, albumin-to-creatinine ratio (ACR), and estimated glomerular filtration rate (eGFR; CKD-EPI equation). Generalized linear models adjusted for demographics, lifestyle, and comorbidities were used to examine the associations.

**Results :** Compared with the non-exposed group, exposed participants had lower median BUN (12.7 vs. 13.1 mg/dL) and ACR (6.65 vs. 7.10 mg/g), but higher median uric acid (5.21 vs. 5.17 mg/dL) and eGFR (108.7 vs. 107.1 mL/min/1.73 m<sup>2</sup>). Regression analyses showed significant associations with reduced BUN ( $\beta = -0.0076$ , 95% CI: -0.0120, -0.0033), elevated uric acid ( $\beta = 0.0131$ , 95% CI: 0.0090, 0.0169), and decreased ACR ( $\beta = -0.1194$ , 95% CI: -0.1365, -0.1022). No significant association with eGFR was observed.

**Conclusions :** Groundwater arsenic exposure was associated with altered renal biomarkers, particularly uric acid and albuminuria, but not eGFR. These findings underscore the importance of continued monitoring in arsenic-endemic regions and highlight the need for longitudinal studies with refined exposure metrics to clarify causal pathways and guide preventive public health strategies.