Supplementary Online Content

Zhong W, Mao Y. Daily insulin dose and cancer risk among patients with type 1 diabetes. *JAMA Oncol.* Published online July 28, 2022. doi:10.1001/jamaoncol.2022.2960

eMethods.

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

The variables analyzed in this study included both time-independent and time-dependent variables. The time-independent variables included were: 1) design factors: primary or secondary prevention cohorts, and intensive or conventional treatment groups; 2) demographic factors at baseline: age, sex, adult status at type 1 diabetes (T1D) diagnosis, weight, body mass index (BMI), smoking, alcohol drinking, exercising habit, and family history of hypertension, T1D, type 2 diabetes, and myocardial infarction; 3) traditional metabolic risk factors measured at baseline: blood pressures, pulse, hypertension status, lipid levels (total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and hyperlipidemia status; 4) diabetes-related factors measured at baseline: duration of diabetes, stimulated C-peptide, hemoglobin A1c (HbA1c), and albumin excretion rate (AER).

The time-dependent variables were those measured multiple times at subsequent visits and were 1) demographic factors: weight, BMI, smoking, alcohol drinking, exercising habit; 2) traditional metabolic risk factors: blood pressures, pulse, hypertension status, lipid levels (total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, and hyperlipidemia status; 3) medications (angiotensin-converting enzyme (ACE) inhibitor, Angiotensin II receptor blocker (ARB), beta blockers, calcium channel blockers, and lipid lowering drugs); 4) diabetes-related factors measured at baseline: daily insulin dose, HbA1c, estimated glucose disposal rate (eGDR), AER, estimated glomerular filtration rate (eGFR), and hypoglycemic episodes (coma/seizure or requiring assistance).

The association of risk factors with cancer incidence was evaluated using Cox proportional hazards models. The baseline measurements as well as the time-dependent measurements were fitted into the model individually adjusting for baseline age and sex. Those variables that were statistically significant in the age and sex adjusted models were included in multivariable models for further assessments.

All statistical tests were two-sided and P-values of less than 0.05 were considered statistically significant. Statistical analyses were performed by using SAS version 9 software (Cary, NC, USA).