

## 論文の内容の要旨

論文題目 Comparative Analysis of Trends in Underlying Cause of Death Assignment of  
Diabetes-Attributable Deaths in the United States  
(米国の糖尿病関連死における原死因の傾向に関する比較研究)

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**Background:** Cause-of-death assignment as the underlying cause of death (UCD) is led by limitations of and variations in skills of the certifiers, health technology, or access to health facilities, that are heterogeneous between sociodemographic variation among individuals. Quantification of differences between levels of sociodemographic factors that influence cause-of-death assignment, and estimation of adjusted cause-specific mortality profiles based on these differentials referenced to levels with high validity (hereafter, “adjusted assignment”) is needed. In addition, identification of temporal trends in UCD assignment is significant, given that we know cause-of-death assignment with respect to sociodemographic factors change over time. Therefore, a comprehensive assessment of the role of sociodemographic factors on UCD assignment to cardiovascular disease, neoplasms, and other diseases, among diabetes-attributable deaths is needed, for preventive actions to be taken towards adjusted assignment among diabetes-attributable deaths in the United States (US).

**Objectives:** This study quantified the effect of sociodemographic factors on cause-of-death assignment to International Classification of Disease and Related Health Problem (ICD) disease clusters, and estimated the adjusted probability of cause-specific mortality and described temporal trends in UCD assignment by sociodemographic factors among diabetes-attributable deaths in the US between 1999 and 2017.

**Methods:** The nationally representative Multiple Cause of Death data covering all states and districts in the US was provided by the Centers for Disease Control and Prevention (CDC). Adult diabetes-attributable deaths were included in this study, for all years during the ICD-10 implementation. A multinomial loglinear regression analysis via neural network was used for prediction to estimate the effect of sociodemographic factors on UCD assignment to cardiovascular disease, neoplasms, other non-communicable disease, and communicable disease, relative to diabetes. The adjusted probability and number of UCD assignment were estimated using quantified effects of sociodemographic factors on UCD relative to its levels with high validity of cause of death assignment. A simulation was conducted via

nonparametric bootstrapping algorithm to quantify uncertainty of the estimates. The observed and adjusted probabilities of UCD assignment were calculated for each disease cluster and predictor level. Based on the adjusted UCD assignment, temporal trend in probability of UCD assignment were plotted by 1) age, sex, and race, and 2) age, race, and autopsy status.

**Results:** There were 4,472,917 diabetes-attributable deaths, equivalent to 9.4% of all-cause mortality between 1999-2017. Age was a key contributor for UCD assignment among cardiovascular disease, neoplasms, other NCDs, and communicable disease, in relations to diabetes UCD assignment. Between 1999-2017, there was an increase in the probability of UCD assignment to cardiovascular disease among ages 70-74 (relative risk ratio (RRR): 1.08 (95% confidence intervals (CI): 1.07 – 1.08)), ages 75-79 (RRR: 1.15 (95% CI: 1.14 – 1.15)), 80-84 (RRR: 1.22 (95% CI: 1.21 – 1.23)), and 85 and over (RRR: 1.33 (95% CI: 1.32 – 1.33)) compared to 60-69. For neoplasms relative to diabetes, compared to ages 60-69, the RRR of UCD assignment was higher among ages 70-74 (1.14 (95% CI: 1.13 – 1.14)) and ages 75-79 (1.07 (95% CI: 1.06 – 1.07)), whereas it was lower among other age groups under 60 and over 80. Compared to whites, blacks had decreased probability of UCD assignment to cardiovascular disease (RRR: 0.88 (95% CI: 0.88 – 0.89)), neoplasms (RRR: 0.85 (95% CI: 0.84 – 0.85)), other NCDs (RRR: 0.65 (95% CI: 0.65 – 0.66)), and communicable disease (RRR: 0.89 (95% CI: 0.89 – 0.89)), compared to diabetes. For cardiovascular disease UCD assignment, compared to diabetes, being outpatient (RRR: 1.15 (95% CI: 1.14 – 1.15)) and dead arrival at hospital (RRR: 1.11 (95% CI: 1.11 – 1.11)) increased its probability, relative to inpatient deaths. The trend was opposite for neoplasms, with decreased probability of UCD assignment to neoplasms compared to diabetes among the outpatient deaths (RRR: 0.23 (95% CI: 0.23 – 0.23)) and those dead arrival at hospital (RRR: 0.21 (95% CI: 0.21 – 0.21)) compared to inpatients. Between 2003-2017, of which information on autopsy was available, there was a general decline among assignment to cardiovascular diseases, with an increase in assignment to other NCDs among all race and age subgroups. Increased probability of UCD over-assignment of diabetes-attributable death to neoplasm among those without autopsy as compared to those with autopsy was found after 2005.

**Conclusion:** Better quality of autopsy performance and quality training of clinicians regarding UCD cause-of-death assignment in relations to sociodemographic factors, especially age, race, and place of death, may contribute to improving cause-of-death assignment among diabetes-attributable deaths. More resources need to be allocated to digitalization of multiple cause of death records for other countries to facilitate the generation of cross-country evidence needed in the development of future version of the ICD. Findings

of this study will help to identify priorities for improvement in cause-of-death assignment, as well as evidence-based resource allocation to the correct knowledge domain and sociodemographic group according to the levels of adjusted assignment. The evidence will as well inform preventive actions to be taken towards diabetes-attributable true causes of death in the country and other advanced economies.