











# The age of death in Japanese patients with type 2 and type 1 diabetes: A descriptive epidemiological study

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## Keywords

Administrative claims data, Age of death, Diabetes mellitus

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*J Diabetes Investig* 2022; 13: 1316–1320

doi: 10.1111/jdi.13802

## ABSTRACT

This study clarified the age of death in patients with or without diabetes using the largest health insurance database in Japan. This population-based retrospective cohort study was performed using the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) data. The ages of death between people with and without diabetes were compared. A total of 142,277,986 patients (74,488,962 women and 67,789,024 men) over 6 years, including 4,647,016 females, and 6,507,817 males with diabetes, were included. 2,786,071 females and 2,975,876 males died over 6 years, including 652,699 females and 954,655 males with diabetes. The average age of death in patients with diabetes was 2.6 years less than that of patients without diabetes. This descriptive epidemiological study illustrated the difference in age at death of patients with and without diabetes.

## INTRODUCTION

Diabetes is increasingly common in many countries<sup>1,2</sup>. Despite considerable information on the mortality of diabetes mellitus, less is known about the real trends for the age difference between those with diabetes and those without diabetes.

The National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) has enabled descriptive epidemiological studies of almost all people in Japan with a very small selection bias<sup>3</sup>. We have previously used the National Database to create retrospective sample cohorts of >100 million individuals with a very small selection bias, and thus, the National Database has satisfactory generalizability<sup>3</sup>. The National Database has been used to obtain real-world health-related evidence of global relevance<sup>4,5,6,7,8</sup>.

This study compared the trends in the age of death of people with diabetes with people without diabetes in Japan. Continuous quantification using descriptive epidemiology should help to remove the stigma associated with having diabetes.

## MATERIALS AND METHODS

### Data source

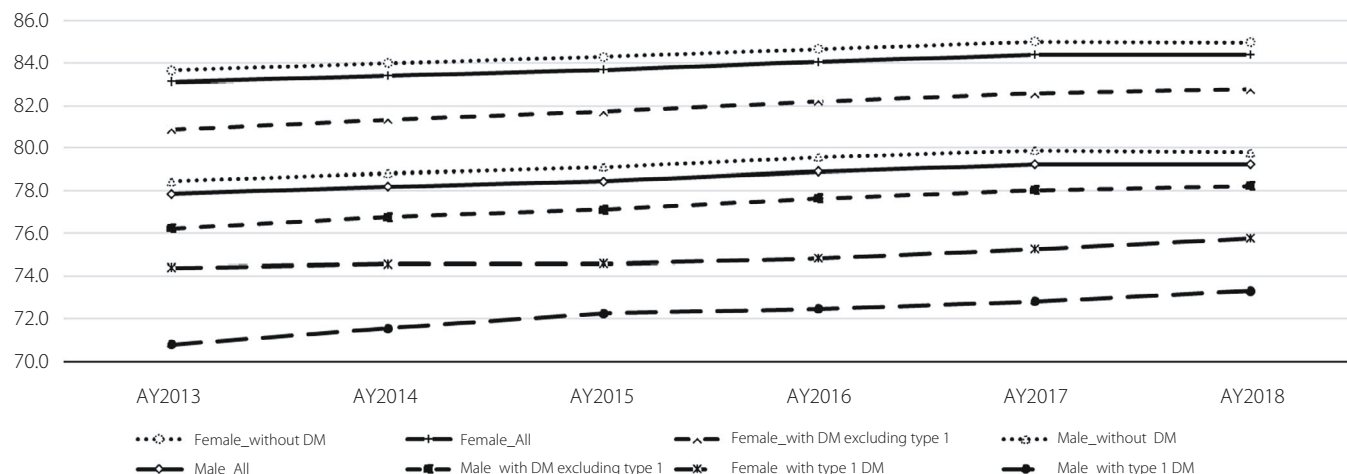
The study cohort comprised anonymized data of individuals enrolled in the NDB of the universal health coverage system of patients with any insurance program in Japan. The NDB data provided information on personal identifiers<sup>3</sup>, date, age group, sex, description of the procedures performed, World Health Organization International Classification of Diseases (ICD-10) diagnosis codes, medical care received, medical examinations conducted without the results, and prescribed drugs.

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Received 20 January 2022; revised 17 March 2022; accepted 5 April 2022

**Table 1** | The descriptive statistics divided by sex and diabetes status in Japan

Number	Sex	Target population	Year	Number of population at risk of death in Japan	Number of death	Mean Age at death	SD as death	Percentile (Age at death)										
								0.5	2.5	5.0	10.0	25.0	50.0	75.0	90.0	95.0	97.5	99.5
01	All	All	6 years	14,227,986	57,61,947	81.2	12.6	29	50	59	66	75	84	90	94	97	99	102
02	Female	All	6 years	7,448,8962	27,86,071	83.8	12.5	31	52	60	68	79	87	92	96	98	100	103
03	Male	All	6 years	6,777,89,024	29,75,876	78.7	12.2	26	50	57	64	73	81	87	91	94	96	100
04	All	with DM	6 years	1,11,54,833	16,07,354	79.3	11.1	39	54	60	65	73	81	87	92	94	96	100
05	Female	With DM	6 years	46,47,016	6,52,699	82.0	11.3	38	55	62	68	77	84	90	94	96	98	101
06	Male	With DM	6 years	65,07,817	9,54,655	77.4	10.6	39	53	59	64	71	79	85	89	92	94	98
07	All	With type 1 DM	6 years	1,83,033	13,247	73.3	12.3	31	44	50	57	67	75	82	87	90	92	96
08	Female	With type 1 DM	6 years	1,05,505	5,233	75.0	13.2	28	43	50	57	68	77	84	90	92	94	98
09	Male	With type 1 DM	6 years	77,528	8,014	72.2	11.5	34	45	51	57	66	74	80	85	88	90	94
10	All	With DM excluding type 1	6 years	1,09,71,800	15,94,107	79.3	11.1	39	54	60	66	73	81	87	92	94	96	100
11	Female	With DM excluding type 1	6 years	45,41,511	6,47,466	82.0	11.2	38	55	62	68	77	84	90	94	96	98	101
12	Male	With DM excluding type 1	6 years	64,30,289	9,46,641	77.5	10.6	39	53	59	65	71	79	85	89	92	94	98
13	All	Without DM	6 years	13,11,23,153	41,54,593	81.9	13.0	25	49	58	66	76	85	91	95	97	99	103
14	Female	Without DM	6 years	6,98,41,946	21,33,372	84.4	12.8	29	51	60	68	80	87	93	96	99	101	104
15	Male	Without DM	6 years	6,12,81,207	20,21,221	79.3	12.8	21	48	56	64	73	82	88	92	94	97	100



**Figure 1** | Average age of death by year for people with/without diabetes.

### Definition of death

Although most information on death in NDB is recorded, some may not be recorded or may be given mistakenly. Therefore, we used death identification logic in NDB as described previously<sup>9</sup>; with 92.9% sensitivity and 99.7% specificity of mortality information<sup>9</sup>.

### Study population

The data of individuals who died between April 2013 and March 2019 were used. The number of people at risk of death in Japan was also used as the number of people who used insurance at least once.

### Definition of diabetes

A validated algorithm was used to define diabetes in NDB. The algorithm (74.6% sensitivity and 88.4% predictive value) for detecting people with diabetes had three elements: the diagnosis-related codes for diabetes without the 'suspected' flag, the medication codes for diabetes, and these two codes on the same record<sup>10</sup>. (Patients were classified as having or not having diabetes based on the specific health checkups records, according to the Japanese guideline<sup>11</sup>).

### Definition of type 1 diabetes

The validated algorithm (72% sensitivity and 68% positive predictive value) was used to define type 1 diabetes in NDB, including individuals diagnosed with type 1 diabetes, prescribed insulin, and advised to self-monitor their blood glucose. (The gold standard was the algorithm used in the previous study, which required that most diabetes diagnosis codes are type 1 codes<sup>12</sup>.)

### Statistical analysis

The age of death was compared between people with and without diabetes. The average age, standardized difference of the ages, and percentile values of the ages were calculated. Thus, if the age distribution of populations with and without diabetes differs, the average age at death would differ. Mortality rates by age group in each group with and without diabetes are also shown as supplemental material. Statistical analyses were performed using the Microsoft SQL Server 2017 Standard (Microsoft Corp., Redmond, WA, USA).

### RESULTS

Table 1 shows the number of people at risk of death, the number of deaths, and their descriptive statistics divided by sex and diabetes status. The average age of death in people with diabetes was 2.6 years younger than those without diabetes. Figure S1 shows the histograms corresponding to the line numbers or Table 1. Table S1 also shows the mortality by age from April 2014 to March 2019 of non-diabetics and those in the diabetes categories.

Figure 1 shows the average age of death by group. Even if annual comparisons may not always be appropriate, the order was unchanged for 6 years. Figures S1–S4 show the 10th, 25th, 50th, 75th, and 90th percentiles of the age of death divided among 47 prefectures in Japan, ordered by the median value. Figures S1–S4 identify all people, people with diabetes excluding type 1, and people with type 1 diabetes, respectively.

### DISCUSSION

This study showed the quantitative numbers of age at death. This is the first real-world descriptive epidemiological study that has divided the entire population into people with and without diabetes. This study shows that the lifetime hazard

would be even greater, and excess risk would be higher for persons in whom diabetes develops in early adult life rather than in later adult life, especially in type 1 diabetes. Diabetes confers an approximately two-fold excess risk for a wide range of vascular diseases, independent of other conventional risk factors<sup>13,14</sup>.

This study has several limitations. First, we could not control for confounders. Despite this, our study shows the actual age of death of people with diabetes compared with those without diabetes. Second, we could not detect all the deaths. Deaths that do not result in an insurance claim at the time of death cannot be identified, such as suicides, accidental deaths, and other deaths discovered at a later time. Table S1 showed the 2015 mortality comparison between vital statistics and NDB, with the limitation that NDB is based on insurance claims and does not capture some deaths. Third, the proportion of death in childhood affected the average age. The median and percentile values were evaluated in our study. Fourth, if the group without diabetes has a larger proportion of some disease than those with diabetes, the difference in age at death between groups may be small. Finally, some people may have died undiagnosed with diabetes, despite having diabetes, especially in the cases of sudden death, resulting in an underestimation of age at death among patients with diabetes and an overestimation of age at death among patients without diabetes if the age at death among the non-diabetic population was less than the average.

In conclusion, our study objectively shows the difference in age at death in people with and without diabetes; continuous quantification using descriptive epidemiology should enable the demystification of stigma associated with diabetes. Further continuous studies on the age of death are needed to ensure that the difference is shrinking due to the treatment of diabetes.

## FUNDING

This study was supported by Health Science and Labor Research Grants (HSLRG) (Grant Number: 211A1006) of the Ministry of Health, Young Researcher Grants (2021) from the Japan Diabetes Society, and Japan Society for the Promotion of Science KAKENHI (grant numbers: JP18K17390, JP18H04126, and JP21K10451).

## DISCLOSURE

YN received consultant fees from Novo Nordisk. SO received speaker fees from Ono, Mitsubishi Tanabe, Daiinippon Sumitomo, Eli Lilly Japan, Takeda, AstraZeneca, Novartis Pharmaceuticals, Novo Nordisk, Mochida Pharmaceutical, Kyowa Kirin, Terumo. HI received lecture fees and consultant fees from Takeda, Eli Lilly Japan, Sanofi, Merck & Co., Astellas, Mitsubishi Tanabe, Daiichi Sankyo, Ono, AstraZeneca, Taisho Toyama, Shionogi, Kowa, Boehringer Ingelheim, Novo Nordisk, Sumitomo Daiinippon, and Kyowa Hakko Kirin. YT received consultant fees from Novo Nordisk, Otsuka, and Recordati, and speaker fees from Novo Nordisk, Sumitomo Daiinippon, Eli Lilly, Ono, Novartis, Nippon Boehringer Ingelheim,

AstraZeneca, and Kyowa Kirin. The other authors declare that they have no conflict of interest.

Approval of the Research Protocol: The Ethics Committee of Nara Medical University (approval no. 1123–6, October 8th, 2015).

Informed consent: N/A.

Approval date of registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S1** | Age distribution of deaths corresponding to Table S1 | (vertical axis: percentage, horizontal axis: age).

**Figure S2** | Distributions of ages of death by prefecture (all death people).

**Figure S3** | Distributions of ages of death by prefecture (death people with diabetes excluding type 1).

**Figure S4** | Distributions of ages of death by prefecture (death people with type 1 diabetes). Distributions are shown as box-and-whisker plots; 25, 50, and 75 percentiles of age by prefecture are shown as boxes, sorted by the median ages, whereas institutional-level distributions of ages by prefecture are shown as whiskers, representing the 10th and 90th percentiles.

**Table S1** | Five year mortality by age class

**Table S2** | Comparison age-specific mortality rate among overall population in NDB with those from the vital statistics in 2015.