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Incidence of lower limb amputation in people with and without diabetes: a nationwide 5-year cohort study in Japan

Fumika Kamitani,[1] Yuichi Nishioka,[1,2] Tatsuya Noda ,[2] Tomoya Myojin,[2] Shinichiro Kubo,[2] Tsuneyuki Higashino,[3] Sadanori Okada,[1] Yasuhiro Akai,[1,4,5] Hitoshi Ishii,[1,6] Yutaka Takahashi,[1] Tomoaki Imamura[2]

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For numbered affiliations see end of article.

Correspondence to
Dr Tatsuya Noda;
noda@naramed-u.ac.jp

ABSTRACT

Introduction This study was conducted to investigate the incidence and time trend of lower limb amputation (LLA) among people with and without diabetes.

Research design and methods This retrospective population-based cohort study was based on the national claims data in Japan, comprising a total population of 150 million. Data of all individuals who had LLA from April 2013 to March 2018 were obtained. We analysed the sex-adjusted and age-adjusted annual LLA rate (every fiscal year) in people with and without diabetes for major and minor amputation. To test for time trend, Poisson regression models were fitted.

Results In the 5-year period, 30 187 major and 29 299 minor LLAs were performed in Japan. The sex-adjusted and age-adjusted incidence of major and minor LLAs was 9.5 (people with diabetes, 21.8 vs people without diabetes, 2.3, per 100 000 person-years) and 14.9 (people with diabetes, 28.4 vs people without diabetes, 1.9, per 100 000 person-years) times higher, respectively, in people with diabetes compared with those without. A significant decline in the annual major amputation rate was observed ($p<0.05$) and the annual minor amputation rate remained stable ($p=0.63$) when sex, age and people with and without diabetes were included as dependent variables.

Conclusions This is the first report of the national statistics of LLAs in Japan. The incidence of major and minor LLAs was 10 and 15 times higher, respectively, in people with diabetes compared with those without. A significant decline in the major amputation rate was observed, and the annual minor amputation rate remained stable during the observation period. This information can help to create an effective national healthcare strategy for preventing limb amputations, which affect the quality of life of patients with diabetes and add to the national healthcare expenditure.

Strengths and limitations of this study

- This is the first report of the national statistics of lower limb amputations (LLAs) among people with and without diabetes.
- This retrospective cohort study was based on the National Database (NDB) in Japan, comprising almost all patients in Japan.
- Considering the definition of minor amputation, we could not distinguish between finger and toe amputations because of the coding system of the NDB.
- The detailed medical information and parameters of each patient, including glycated haemoglobin, body weight, smoking history and family history, could not be reviewed because of the nature of the database.
- However, NDB is a comprehensive survey and the likelihood of selection bias is relatively small; we adjusted for sex and age when comparing the LLA rates of people with and without diabetes.

INTRODUCTION

The objectives of diabetes management are to reduce the metabolic dysfunction that occurs because of hyperglycaemia, to prevent the development or progression of diabetes-related complications and conditions, and to enable the affected individuals to maintain their quality of life and life expectancy like healthy individuals.[1]

Vascular and neurological complications of diabetes can considerably influence lower limb amputation (LLA).[2–4] Previous studies have shown that diabetes increases the risk of LLA, although there were considerable variations in its incidence among people with diabetes.[5] It is important to understand the incidence rates of LLA in diabetic and non-diabetic populations to further improve the care of patients with diabetes and to avoid fatal outcomes, particularly regarding decisions associated with health policy and the economy.[4 5]

Among patients with diabetes, besides major LLAs (eg, amputation proximal to the ankle joint), there may be many minor LLAs (eg, amputation through the ankle joint and toe amputation).[6] Major amputations have severe detrimental impact on physical integrity, but minor amputations should also be prevented. Given the increasing incidence of diabetes, not only major LLAs but also minor LLAs impose a burden on the healthcare system. With significant ageing of the

population, the number of patients with diabetes in Japan continues to increase.[7] Therefore, it is important to understand the association of age with the total incidence of each major and minor LLA. However, no large-scale community-based surveys on the incidence of LLA among people with and without diabetes in Japan have been conducted. We aimed to investigate the incidence of LLAs in Japan and compare the age-adjusted incidence of LLA between people with and without diabetes. We also analysed the time trend based on data obtained from the National Database (NDB) of Health Insurance Claims in Japan. To the best of our knowledge, this study is the first to evaluate the LLA rate in Japan based on a nationwide dataset.

METHODS

Study design and population

The use of NDB dataset was approved by the Ministry of Health, Labour and Welfare, and the need for informed consent was waived in view of the study design. In this study, not only patients with LLA, but also the general public are included. All civilian and patient data were anonymised before an analysis.

The study cohort comprised individuals enrolled in the NDB; all civilian and patient data were anonymised. Japan has a universal public healthcare system, and the NDB includes almost all patients in Japan. However, people whose family names changed due to marriage or divorce and people whose insurance changed due to social circumstances are also counted as other individuals. Approximately 2% of the people on welfare were not included in this study because they were not covered by the insurance programme. The NDB data provided information on personal identifiers,[8] date, age group, sex, description of the medical procedures conducted, the WHO International Classification of Diseases diagnosis codes, medical care received, medical examinations conducted (not including test results) and prescribed drugs, which were independent of the doctor's or patient's reports.[9] Drug information included the prescription amount, brand name, generic name, dosage and the number of days for which the medicine was prescribed. The age recorded in this study was age at the time of the last treatment during the study period or the patient's age when LLA was performed.

We designed this cohort study to include all the data of LLA patients collected between April 2013 and March 2018 in the analysis.

Criteria for diagnosing diabetes

We defined patients with diabetes as individuals who had any of the diagnosis codes associated with diabetes and those who were prescribed diabetes medication at least once in the past 5 years. The diagnosis and medicine codes for diabetes are the same as those reported previously[9] and are presented in online supplemental tables S1 and S2, respectively. We included all patients with any type of diabetes. In Japan, the indication for metformin is limited to type 2 diabetes patients, and prescriptions for obese people and for women with polycystic ovary syndrome patients are not permitted. Patients on dietary or exercise management without antidiabetic medication were excluded.

Definition of LLA

The medical procedure receipt codes (as LLA codes) are shown in online supplemental table S3. We defined major LLAs as the use four medical procedure receipt codes proximal to the ankle joint, as follows: above-knee/transfemoral amputation, below-knee/transtibial amputation, hindquarter amputation/hip disarticulation and through-knee amputation. In the Japanese medical code, the amputation of fingers and toes is indicated by the same code, and it is impossible to distinguish between them. Therefore, we defined minor LLA as through-foot amputation, transmetatarsal amputation and Lisfranc disarticulation, finger and toe amputation, and finger and toe joint disarticulation. The primary outcome was the first occurrence of each major or minor LLA in the study period. If the first major LLA occurred during the observation period, its observation was terminated at that time. Similarly, if the first minor LLA occurred during the observation period, its observation was terminated at the time. Therefore, even when the major and minor LLAs occurred many times in the same person during the 5-year study period, we counted only the first major and minor LLAs. Moreover, even if a minor LLA occurred, the major LLA observation was continued such that the incidence of the major LLA was not underestimated.

Statistical analyses

We defined the duration between the first occurrence of the medical treatment code or drug code and the last occurrence as the risk period. To calculate the incidence of LLA, the denominator included all the observation populations of each group, extracted from the NDB dataset. LLA rates are presented as the number of amputations per 100 000 person-years. To compare the LLA incidence rates between people with and without diabetes, the incidence rates were evaluated after adjusting for sex and age using the direct method, that is, the sex and age structure of Japan's national census in 2015 (online supplemental table S4). We included age-adjusted standardised incidence of LLA for all ages. Furthermore, the relative risk (RR) of LLA among people with diabetes was calculated by dividing amputation rates among people with diabetes by amputation rates among those without diabetes.

We used Microsoft SQL Server for our data processing and univariate analysis, and used IBM SPSS for Windows (V.25.0; IBM) for our multivariate analysis.

Annual standardised major and minor LLAs were analysed from 2013 to 2016 fiscal year. Year 2017 was excluded because the observation period in 2017 was shorter than other years, and the denominator was smaller, which could overestimate the LLA rate. To test for time trends,

Table 1 Characteristics of the NDB study population categorised into people with and without diabetes

Age groups, years	Total	People with diabetes, n (%)	People without diabetes, n (%)
Total	150 328 339	9 962 459 (6.6)	140 365 880 (93.4)
Men, total	70 958 283	5 838 320 (8.2)	65 119 963 (91.8)
Men, age groups, years			
0–44	35 317 225	301 772 (0.9)	35 015 453 (99.1)
45–64	17 572 798	1 709 991 (9.7)	15 862 807 (90.3)
65–74	9 134 765	1 849 566 (20.2)	7 285 199 (79.8)
75–84	6 152 042	1 458 566 (23.7)	4 693 476 (76.3)
≧85	2 781 453	518 425 (18.6)	2 263 028 (81.4)
Women, total	79 370 056	4 124 139 (5.2)	75 245 917 (94.8)
Women, age groups, years			
0–44	37 492 073	212 476 (0.6)	37 279 597 (99.4)
45–64	18 906 831	792 993 (5.7)	18 113 838 (94.3)
65–74	9 860 220	1 154 454 (11.7)	8 705 766 (88.3)
75–84	7 538 821	1 191 531 (15.8)	6 347 290 (84.2)
≧85	5 572 111	772 685 (13.9)	4 799 426 (86.1)

NDB, National Database.

we fitted Poisson regression models for major or minor amputation rate using year of outcome (difference from the first fiscal year 2013 as an ordinal variable), age and sex, and the population with and without diabetes as independent variables. All models were adjusted for overdispersion using a dispersion parameter.

RESULTS

Population included in the NDB and the diabetic population

Of the 150 328 339 people (186 819 100 972 person-days) included in the NDB, 9 962 459 had diabetes, which accounted for 6.6% of the total sample (table 1). In the subgroups of men and women, the proportion of diabetic patients was higher in the elderly group (age ≥65 years).

Incidence of LLAs

Major LLAs occurred in 30 187 people, whereas minor LLAs occurred in 29 299 people in the 5-year period. In Japan, a new major and minor LLA occurred in approximately 6000 individuals per year. Table 2 shows the characteristics of LLA patients stratified into subgroups of people with and without diabetes. Figure 1A,B shows the sex and age composition of the patient population with major and minor LLAs. In the overall study population, the incidence of LLA was higher among men than in women. Patients with diabetes accounted for 58% and 66% of the total major and minor LLAs, respectively; the highest number of LLAs in men were performed around 65–84 years of age, whereas, in women, the number was significantly associated with age. Therefore, most amputations occurred in the elderly population.

Age-adjusted incidence rate

Throughout the observation period, the major amputation risk was 9.5 times higher in people with diabetes compared with people without diabetes (people with diabetes, 21.8 vs people without diabetes, 2.3, per 100 000 person-years); the minor amputation risk was also 14.9 times higher among people with diabetes (people with diabetes, 28.4 vs people without diabetes, 1.9, per 100 000 person-years) (table 3). This difference was particularly pronounced in minor amputations than major amputations. Additionally, the RR was higher in men than in women.

Time trend

We observed a significant decrease in the major amputation rate in the general population, from 5.5 per 100 000 person-years in 2013 to 4.4 in 2016 ($p<0.05$, for time trend, Poisson model). The major amputation rate decreased among people with (2013:22.8; 2016:20.0) and without diabetes (2013:2.6; 2016: 2.1). In detail, there was a little change among men with diabetes and a decreasing trend in women with diabetes for major amputation. Furthermore, both men and women without diabetes showed a decreasing trend.

In contrast, the minor amputation rate remained stable in the general population, from 5.6 per 100 000 person-years in 2013 to 4.7 in 2016 ($p=0.63$, for time trend, Poisson model). The minor amputation rate remained stable among people with (2013:29.0; 2016:28.9) and without diabetes (2013 2.1; 2016: 1.7) (table 4, figure 2).

Patient and public involvement

No patient involved.

Table 2 Patients with lower limb amputations according to diagnosis of diabetes, sex, age

Age groups, years	Major LLA			Minor LLA		
	Total	People with diabetes, n (%)	People without diabetes, n (%)	Total	People with diabetes, n (%)	People without diabetes, n (%)
Total	30 187	17 390 (57.6)	12 797 (42.4)	29 299	19 331 (66.0)	9968 (34.0)
Men, total	17 971	11 545 (64.2)	6426 (35.8)	19 485	14 163 (72.7)	5322 (27.3)
Men, age groups, years						
0–44	515	218 (42.3)	297 (57.7)	736	468 (63.6)	268 (36.4)
45–64	3376	2699 (79.9)	677 (20.1)	4989	4173 (83.6)	816 (16.4)
65–74	5077	3748 (73.8)	1329 (26.2)	5934	4621 (77.9)	1313 (22.1)
75–84	5710	3568 (62.5)	2142 (37.5)	5404	3761 (69.6)	1643 (30.4)
≥85	3293	1312 (39.8)	1981 (60.2)	2422	1140 (47.1)	1282 (52.9)
Women, total	12 216	5845 (47.8)	6371 (52.2)	9814	5168 (52.7)	4646 (47.3)
Women, age groups, years						
0–44	183	44 (24.0)	139 (76.0)	177	72 (40.7)	105 (59.3)
45–64	1011	747 (73.9)	264 (26.1)	1243	946 (76.1)	297 (23.9)
65–74	1900	1335 (70.3)	565 (29.7)	1945	1361 (70.0)	584 (30.0)
75–84	3429	1894 (55.2)	1535 (44.8)	2854	1606 (56.3)	1248 (43.7)
≥85	5693	1825 (32.1)	3868 (67.9)	3595	1183 (32.9)	2412 (67.1)

LLA, lower limb amputation.

DISCUSSION

The NDB is a comprehensive database of health insurance claims that are covered by the Japanese National Health Insurance system. Japan has universal health coverage, with local governments providing healthcare payments for approximately 2% of the population who are on welfare, with the exception of accidents (which is covered by automobile liability insurance or worker's accident compensation in a previous health insurance plan); thus, the NDB is considered to be the representative of almost all health claims in Japan.[8 9] Using information from the Japanese NDB dataset, we conducted cohort studies that comprised almost all LLAs in Japan during the study period. This is the first report of LLAs across Japan.

Although several studies have analysed amputation risk in people with diabetes, population-based and nationwide studies analysing amputation risk in populations with and without diabetes are still limited. Additionally, study design such as definition and counting LLA (counting all, counting only the first of the observation period, counting only the first of each year), sex-adjustment and age-adjustment method (all ages or only specific ages) were different significantly, so accurately comparing them is difficult. Considering this, compared with the few previous studies that evaluated only the first amputation in the observation period or each year to calculate the LLA incidence, LLA rates in the general population of this study were much lower (eg, 7.4–41.4 and 8.0–46.7 per 100 000 person-years in Europe and Australasia in

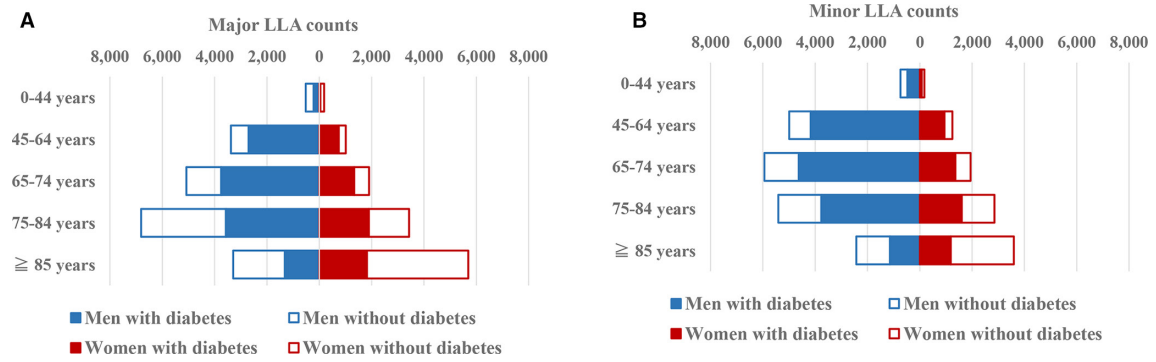

Figure 1 Results of sex-stratified and age-stratified analyses: (A) number of major lower limb amputation (LLA); (B) number of minor LLA.

Table 3 Age-adjusted incidence rate (per 100 000 person-year) of LLA in people with and without diabetes

Groups	Total	95% CI	With diabetes	95% CI	Without diabetes	95% CI	Relative risk (With/without)
	Incidence of major LLA						
Men	6.2	5.9 to 6.5	26.4	23.4 to 29.5	2.6	2.3 to 2.8	10.2
Women	3.5	3.3 to 3.7	17.3	14.5 to 20.1	2.0	1.8 to 2.2	8.7
Total	4.8	4.5 to 5.1	21.8	18.9 to 24.7	2.3	2.1 to 2.5	9.5
	Incidence of Minor LLA						
Groups	**Total**	**95% CI**	**With diabetes**	**95% CI**	**Without diabetes**	**95% CI**	**Relative risk (With/without)**
Men	7.1	6.7 to 7.5	39.3	35.7 to 43.0	2.2	2.0 to 2.5	17.9
Women	3.0	2.7 to 3.2	18.0	15.4 to 20.5	1.5	1.3 to 1.7	12.0
Total	5.0	4.7 to 5.3	28.4	25.3 to 31.4	1.9	1.7 to 2.1	14.9

LLA, lower limb amputation.

2010–2014, major and minor amputation, respectively[10]; 7.8–13.2 per 100 000 person-years in OECD in 2000–2011, major amputation[11]; in our study 4.8 and 5.0 per 100 000 person-years, major and minor amputation, respectively). Herein, the LLA rates among people with diabetes were much lower than those of previous studies (eg, 78–704 per 100 000 person-years in a systematic review in 1990–2010, major amputation[5]; 7.8–13.2 per 100 000 person-years in OECD in 2000–2011, major amputation[11]; in our study 21.8 and 28.4 per 100 000 person-years, major and minor amputation, respectively). There are several explanations for the observed lower incidence of LLA in Japanese patients. First, the Japanese population has a lower obesity rate than the Western population.[12 13] Second, the incidence of cardiovascular disease is much lower in Japan[14]; this contributes to lower risk for the progression of atherosclerosis, which is the most prevalent aetiology of LLA.

In this study, the incidence of major and minor LLA was approximately 10 and 15 times higher, respectively, in people with diabetes compared with those without. Among people with diabetes, both peripheral arterial disease and peripheral neuropathy can cause foot ulceration and LLA. Strict chronic disease management (such as plasma glucose, blood pressure, lipids and renal failure control) is important to suppress arteriosclerosis. Peripheral vascular disease is often not diagnosed in patients with diabetes usually until the formation of a non-healing ulcer. Therefore, identification of patients with diabetes who are at high risk of ulceration is important and it can be achieved through annual foot screening.[2] There is an emerging focus on lifestyle interventions including weight loss and physical activity as well.[3] Further, in case of foot ulcer or foot infection, many experts (diabetologists, vascular surgeons, orthopaedics, interventional radiologists, infectious diseases specialists, specialised nurses, podiatrists and orthotic technicians) need to work together as a multidisciplinary team to prevent LLA.[15] In Japan, foot care performed by trained nurses has been approved for medical insurance coverage since 2008,[16 17] and bypass surgery and endovascular treatment have become significantly advanced.[18 19] Despite these efforts, our data indicate that the risk of LLA in people with diabetes remained significantly higher than in people without diabetes. This may be associated with the fact that despite the insurance coverage of nurse-provided foot care, only few patients actually availed foot care services. The medical expenses burden of LLA is large.[20] The LLA risk among people with diabetes is much higher and, therefore, more diligent screening and management of the people with diabetes are important to reduce the burden of quality-of-life reduction and the national healthcare expenditure associated with LLA.[21] The high risk of LLA in people with diabetes clarified in this study will help to develop national medical strategies such as more specialised diabetes treatments including insulin and foot care, expansion of team medical care

Table 4 Time trend of age-standarised and sex-standarised amputation rates (100 000 person-years, annual fiscal year)

	2013		2014		2015		2016	
Fiscal year	Rate	95% CI	Rate	95% CI	Rate	95% CI	Rate	95% CI
Major amputation								
Men and women with diabetes	22.8	17.3 to 28.3	20.9	15.6 to 26.1	20.0	13.9 to 26.1	20.0	14.7 to 25.4
Men with diabetes	26.8	22.2 to 31.4	25.0	19.0 to 31.0	22.9	17.7 to 28.2	25.7	19.1 to 32.3
Women with diabetes	19.1	12.8 to 25.4	17.0	12.4 to 21.6	17.2	10.4 to 24.1	14.7	10.6 to 18.8
Men and women without diabetes	2.6	2.0 to 3.1	2.2	1.7 to 2.6	2.1	1.7 to 2.5	2.1	1.7 to 2.6
Men without diabetes	3.1	2.4 to 3.7	2.5	2.0 to 3.0	2.3	1.8 to 2.8	2.4	1.8 to 2.9
Women without diabetes	2.1	1.7 to 2.5	1.9	1.5 to 2.3	1.9	1.5 to 2.2	1.9	1.5 to 2.3
Minor amputation								
Men and women with diabetes	29.0	21.7 to 36.4	25.5	19.4 to 31.6	25.7	19.7 to 31.7	28.9	22.0 to 35.8
Men with diabetes	39.6	30.9 to 48.4	35.9	28.1 to 43.6	34.9	27.8 to 42.0	39.8	31.7 to 47.9
Women with diabetes	19.0	13.1 to 25.0	15.6	11.1 to 20.2	17.0	12.0 to 22.0	18.6	12.8 to 24.4
Men and women without diabetes	2.1	1.6 to 2.6	1.7	1.3 to 2.1	1.9	1.2 to 2.7	1.7	1.3 to 2.1
Men without diabetes	2.7	2.1 to 3.3	2.1	1.6 to 2.6	2.1	1.6 to 2.5	1.9	1.5 to 2.4
Women without diabetes	1.6	1.2 to 2.0	1.4	1.0 to 1.7	1.8	0.7 to 2.8	1.4	1.1 to 1.8

and establishment of educational programmes and activities for patient empowerment.

In this study, a significant decline in the annual major amputation rate was observed in Japan and the annual minor amputation rate remained stable. Our finding concerning the time trend for major LLAs in people with and without diabetes is in line with results from other international studies, which mainly demonstrated decreased incidence of major LLAs. Major amputations decreased by 11.1% in 2005–2015 in the general population of Germany.[22] A progressive decrease was observed for major amputations among people with diabetes (−30.7%) and without diabetes (−12.5%) in 2001–2010 in Italy.[23] In detail, for major amputation, there was little change among men with diabetes and a decreasing trend in women with diabetes and men and women without diabetes in this study. These trends correspond to the findings of previous studies,[22] but biological factors might be contributing to sex differences in amputation rates.[24 25] However, the causes of the sex differences still need further research. Minor amputations in people with and without diabetes had different trends in each country. A significant but weaker decrease was observed for minor amputations in 2009–2013 in Belgium (5% and 3%, people with and without diabetes).[26] A relative increase of +12.8% was observed for minor amputations in 2005–2011 in Germany.[22] Minor amputations may indicate better quality of care as they maybe interventions to prevent major amputations and salvage the lower extremities. A stable number of the total amputations, or even an increase, may actually hide a higher number of minor vs major amputations, which in turn would indicate better performance.[11]

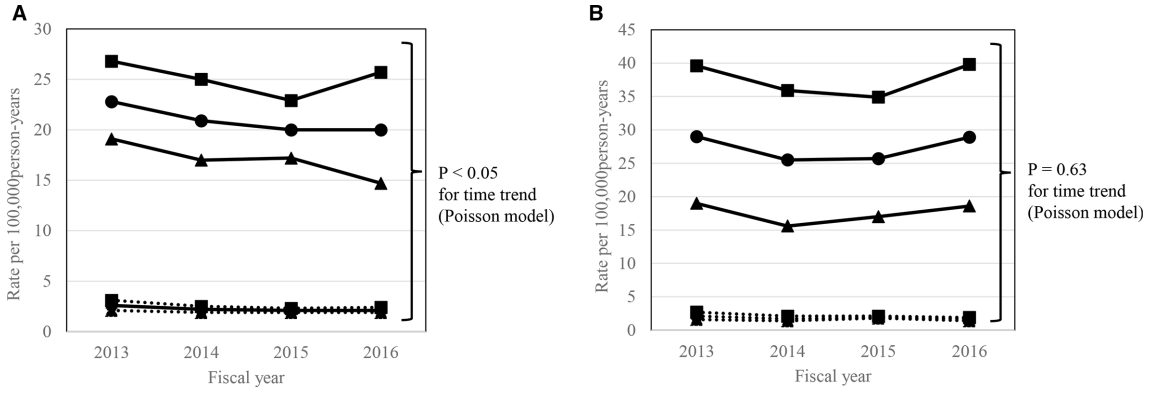

Figure 2 Time trend of age-standardised and sex-standardised amputation rate: (A) major amputation; time trend of age-standardised and sex-standardised major amputation rate. Solid lines, people with diabetes; dashed lines, people without diabetes; circles, men and women; squares, men; triangles, women. (B) Minor amputation. Time trend of age-standardised and sex-standardised minor amputation rate. Solid lines, people with diabetes; dashed lines, people without diabetes; circles, men and women; squares, men; triangles, women.

A key strength of our study is that, by analysing data from the nationwide NDB that encompasses almost the entire Japanese population, this study is the first to evaluate the nationwide incidence of LLA in Japan. Nonetheless, this study has some limitations. First, many similar studies investigated only the amputations related to peripheral arterial disease or diabetes by excluding amputations due to trauma or malignancy using diagnosis codes attached to the amputation episodes; it was technically impossible to exclude amputations due to trauma or malignancy in this study. Second, in minor amputation, we could not distinguish between finger and toe amputations because of the coding system of the NDB. This means that the minor amputation rate reported in this study is overestimated, although toe amputations are more than finger amputations. Third, the total observable population of this study was approximately 150 million, although Japan has a population of approximately 127 million. Even considering new births, marriages, divorces, and changes in family names due to social circumstances, there could be slight deficits in the linking of the NDB. In the design of this study, at risk period was set from the first insurance use date to the last insurance use date; therefore, even if one person does have two IDs, it is not possible to count the same person more than once in the same period. Since the LLA rate is also calculated by the person-year method, it is considered that having two IDs does not affect the LLA rate. However, strictly speaking, in very rare cases, it is possible to overestimate the incidence if two LLAs are performed before and after the insurance change. Finally, the detailed medical information and parameters of each patient, including glycated haemoglobin, body weight, smoking history and family history, could not be reviewed because of the nature of the database. However, regarding smoking rate, which can be an important confounding factor, a previous study in Japan reported no difference between the diabetes group and the general population in terms of smoking status in sex-stratified and age-stratified analyses.[27] Furthermore, NDB is a comprehensive survey and the likelihood of selection bias is relatively small; additionally, we adjusted for sex and age while comparing LLA rates of people with and without diabetes. Therefore, it is unlikely that the study results will be significantly affected even if detailed medical information and parameters are considered.[28]

In conclusion, this is the first report of nationwide LLAs in Japan, and we found that the incidence of major and minor LLAs was 10 and 15 times higher, respectively, in people with diabetes compared with those without diabetes. A significant decline in the major amputation rate was observed and the annual minor amputation rate remained stable during the observation period. This information can help to create an effective national healthcare strategy for preventing limb amputations, which affect the quality of life of patients with diabetes and add to the national healthcare expenditure.

Author affiliations
[1]Department of Diabetes and Endocrinology, Nara Medical University, Kashihara, Nara, Japan
[2]Department of Public Health, Health Management and Policy, Nara Medical University, Kashihara, Nara, Japan
[3]Healthcare and Wellness Division, Mitsubishi Research Institute, Inc, Tokyo, Japan
[4]Center for Postgraduate Training, Nara Medical University, Kashihara, Nara, Japan
[5]Department of Nephrology, Nara Medical University, Kashihara, Nara, Japan
[6]Department of Doctor-Patient Relationships, Nara Medical University, Kashihara, Nara, Japan

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Contributors All authors contributed significantly. FK designed the study and wrote the manuscript. YN contributed to the study design, data analysis and discussion. TN provided advice on the study design and discussed the findings from an epidemiological perspective. TM, SK and TH performed the initial NDB analysis and provided technical advice. SO, YA, HI and YT evaluated the results from a clinical perspective. TI provided advice on the study design and discussed the findings from the public health viewpoint.

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ORCID iD
Tatsuya Noda http://orcid.org/0000-0002-3652-7547

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Supplementary Table S1 Diagnostic codes of diabetes.

Diagnosis in Japanese	Diagnosis in English	ICD-10 code	diagnosis code
１型糖尿病	Type 1 diabetes mellitus	E10	2500014
不安定型糖尿病	Brittle diabetes	E10	2500027
緩徐進行１型糖尿病	SPIDDM - [Slowly progressive insulin-dependent diabetes mellitus]	E10	8844022
１型糖尿病性昏睡	Type 1 diabetic coma	E100	8830030
１型糖尿病・昏睡合併あり	Type 1 diabetes mellitus with coma	E100	8841679
緩徐進行１型糖尿病・昏睡合併あり	SPIDDM with coma - [Slowly progressive insulin-dependent diabetes mellitus]	E100	8844026
１型糖尿病性低血糖性昏睡	Hypoglycemia in the context of type 1 diabetes mellitus	E100	8845065
１型糖尿病性ケトアシドーシス	Diabetic ketoacidosis in type 1 diabetes mellitus	E101	8830028
１型糖尿病・ケトアシドーシス合併あり	Type 1 diabetes mellitus with ketoacidosis	E101	8841680
緩徐進行１型糖尿病・ケトアシドーシス合併あり	SPIDDM with ketoacidosis - [Slowly progressive insulin-dependent diabetes mellitus]	E101	8844025
劇症１型糖尿病	Fulminant type 1 diabetes mellitus	E101	8844045
１型糖尿病性アシドーシス	Diabetic ketoacidosis in type 1 diabetes mellitus	E101	8845044
１型糖尿病性アセトン血症	Type 1 diabetic acetone hyperlipoproteinemia	E101	8845045
１型糖尿病性腎症	Type 1 diabetic nephropathy	E102	8830031
１型糖尿病・腎合併症あり	Type 1 diabetes mellitus with diabetic nephropathy	E102	8841681
１型糖尿病性腎症第１期	Type 1 diabetic nephropathy phase 1	E102	8843983
１型糖尿病性腎症第２期	Type 1 diabetic nephropathy phase 2	E102	8843984
１型糖尿病性腎症第３期	Type 1 diabetic nephropathy phase 3	E102	8843985
１型糖尿病性腎症第３期Ａ	Type 1 diabetic nephropathy phase 3A	E102	8843986
１型糖尿病性腎症第３期Ｂ	Type 1 diabetic nephropathy phase 3B	E102	8843987
１型糖尿病性腎症第４期	Type 1 diabetic nephropathy phase 4	E102	8843988
１型糖尿病性腎症第５期	Type 1 diabetic nephropathy phase 5	E102	8843989

緩徐進行１型糖尿病・腎合併症あり	SPIDDM with nephropathy - [Slowly progressive insulin-dependent diabetes mellitus]	E102	8844028
１型糖尿病性腎硬化症	Type 1 diabetic nephrosclerosis	E102	8845058
１型糖尿病性腎不全	Type 1 diabetic kidney failure	E102	8845059
１型糖尿病性網膜症	Type 1 diabetic retinopathy	E103	8830033
１型糖尿病・眼合併症あり	Type 1 diabetes mellitus with eye complication	E103	8841682
１型糖尿病性黄斑浮腫	Type 1 diabetic macular edema	E103	8843982
緩徐進行１型糖尿病・眼合併症あり	SPIDDM with eye complication - [Slowly progressive insulin-dependent diabetes mellitus]	E103	8844024
１型糖尿病性白内障	Type 1 diabetic cataracts	E103	8844346
増殖性糖尿病性網膜症・１型糖尿病	Proliferative diabetic retinopathy, type 1 diabetes	E103	8844536
１型糖尿病黄斑症	Type 1 diabetic macular disease	E103	8845043
１型糖尿病性眼筋麻痺	Type 1 diabetic eye muscle paralysis	E103	8845049
１型糖尿病性虹彩炎	Type 1 diabetic iritis	E103	8845053
１型糖尿病性中心性網膜症	Type 1 diabetic central retinopathy	E103	8845064
１型糖尿病性ニューロパチー	Type 1 diabetic neuropathy	E104	8830032
１型糖尿病・神経学的合併症あり	Type 1 diabetes mellitus with neurological complications	E104	8841683
緩徐進行１型糖尿病・神経学的合併症あり	SPIDDM with neurological complications - [Slowly progressive insulin-dependent diabetes mellitus]	E104	8844027
１型糖尿病性筋萎縮症	Type 1 diabetic muscular atrophy	E104	8845050
１型糖尿病性神経因性膀胱	Type 1 diabetic neuropathic bladder	E104	8845055
１型糖尿病性神経痛	Type 1 diabetic neuralgia	E104	8845056

1型糖尿病性自律神経ニューロパチー	Type 1 diabetic autonomic neuropathy	E104	8845057
1型糖尿病性多発ニューロパチー	Type 1 diabetic polyneuropathy	E104	8845062
1型糖尿病性単ニューロパチー	Type 1 diabetic mononeuropathy	E104	8845063
1型糖尿病性末梢神経障害	Type 1 diabetic peripheral neuropathy	E104	8845071
1型糖尿病・末梢循環合併症あり	Type 1 diabetes mellitus with peripheral circulation complications	E105	8841684
1型糖尿病性壊疽	Type 1 diabetic gangrene	E105	8843105
緩徐進行1型糖尿病・末梢循環合併症あり	SPIDDM with peripheral circulation complications - [Slowly progressive insulin-dependent diabetes mellitus]	E105	8844031
1型糖尿病性潰瘍	Type 1 diabetic ulcer	E105	8845046
1型糖尿病性血管障害	Type 1 diabetic vascular disease	E105	8845051
1型糖尿病性動脈硬化症	Type 1 diabetic atherosclerosis	E105	8845066
1型糖尿病性動脈閉塞症	Type 1 diabetic arterial occlusion	E105	8845067
1型糖尿病性末梢血管症	Type 1 diabetic peripheral vascular disease	E105	8845069
1型糖尿病性末梢血管障害	Type 1 diabetic peripheral vascular disease	E105	8845070
1型糖尿病・関節合併症あり	Type 1 diabetes mellitus with joint complications	E106	8841685
1型糖尿病・糖尿病性合併症あり	Type 1 diabetes mellitus with diabetic complications	E106	8841686
緩徐進行1型糖尿病・関節合併症あり	SPIDDM with joint complications - [Slowly progressive insulin-dependent diabetes mellitus]	E106	8844023
1型糖尿病性水疱	Type 1 diabetic blister	E106	8844626
1型糖尿病性浮腫性硬化症	Type 1 diabetic edematous sclerosis	E106	8844627
1型糖尿病性肝障害	Type 1 diabetic liver injury	E106	8845047

１型糖尿病性関節症	Type 1 diabetic arthropathy	E106	8845048
１型糖尿病性高コレステロール血症	Type 1 diabetic hypercholesterolemia	E106	8845052
１型糖尿病性骨症	Type 1 diabetic osteopathy	E106	8845054
１型糖尿病性精神障害	Type 1 diabetic mental disorder	E106	8845060
１型糖尿病性そう痒症	Type 1 diabetic pruritus	E106	8845061
１型糖尿病性皮膚障害	Type 1 diabetic skin disorder	E106	8845068
１型糖尿病性胃腸症	Type 1 diabetic gastroenteritis	E106	8845842
１型糖尿病・多発糖尿病性合併症あり	Type 1 diabetes mellitus with multiple diabetic complications	E107	8841687
緩徐進行１型糖尿病・多発糖尿病性合併症あり	SPIDDM with multiple diabetic complications - [Slowly progressive insulin-dependent diabetes mellitus]	E107	8844029
１型糖尿病・糖尿病性合併症なし	Type 1 diabetes mellitus without diabetic complecations	E109	8841688
緩徐進行１型糖尿病・糖尿病性合併症なし	SPIDDM without diabetic complications - [Slowly progressive insulin-dependent diabetes mellitus]	E109	8844030
インスリン抵抗性糖尿病	Insulin resistant diabetes mellitus	E11	2500001
２型糖尿病	Type 2 diabetes mellitus	E11	2500015
安定型糖尿病	Stable diabetes mellitus	E11	8830405
若年２型糖尿病	Juvenile type 2 diabetes	E11	8835244
２型糖尿病性昏睡	Type 2 diabetic coma	E110	8830041
２型糖尿病・昏睡合併あり	Type 2 diabetes mellitus with coma	E110	8841689

２型糖尿病性低血糖性昏睡	Hypoglycemic coma in the context of type 2 diabetes mellitus	E110	8845094
２型糖尿病性ケトアシドーシス	Type 2 diabetic ketoacidosis	E111	8830040
２型糖尿病・ケトアシドーシス合併あり	Type 2 diabetes mellitus with ketoacidosis	E111	8841690
２型糖尿病性アシドーシス	Type 2 diabetic acidosis	E111	8845073
２型糖尿病性アセトン血症	Type 2 diabetic acetone hyperlipoproteinemia	E111	8845074
２型糖尿病性腎症	Type 2 diabetic nephropathy	E112	8830042
２型糖尿病・腎合併症あり	Type 2 diabetes mellitus with diabetic nephropathy	E112	8841691
２型糖尿病性腎症第１期	Type 2 diabetic nephropathy phase 1	E112	8843991
２型糖尿病性腎症第２期	Type 2 diabetic nephropathy phase 2	E112	8843992
２型糖尿病性腎症第３期	Type 2 diabetic nephropathy phase 3	E112	8843993
２型糖尿病性腎症第３期Ａ	Type 2 diabetic nephropathy phase 3A	E112	8843994
２型糖尿病性腎症第３期Ｂ	Type 2 diabetic nephropathy phase 3B	E112	8843995
２型糖尿病性腎症第４期	Type 2 diabetic nephropathy phase 4	E112	8843996
２型糖尿病性腎症第５期	Type 2 diabetic nephropathy phase 5	E112	8843997
２型糖尿病性腎硬化症	Type 2 diabetic nephrosclerosis	E112	8845087
２型糖尿病性腎不全	Type 2 diabetic kidney failure	E112	8845088
２型糖尿病性網膜症	Type 2 diabetic retinopathy	E113	8830045
２型糖尿病・眼合併症あり	Type 2 diabetes mellitus with eye complications	E113	8841692
２型糖尿病性黄斑浮腫	Type 2 diabetic macular edema	E113	8843990
２型糖尿病性白内障	Type 2 diabetic cataracts	E113	8844347
増殖性糖尿病性網膜症・２型糖尿病	Proliferative diabetic retinopathy, type 2 diabetes	E113	8844537

２型糖尿病黄斑症	Type 2 diabetic macular disease	E113	8845072
２型糖尿病性眼筋麻痺	Type 2 diabetic eye muscle paralysis	E113	8845078
２型糖尿病性虹彩炎	Type 2 diabetic iritis	E113	8845082
２型糖尿病性中心性網膜症	Type 2 diabetic central retinopathy	E113	8845093
２型糖尿病性ニューロパチー	Type 2 diabetic neuropathy	E114	8830043
２型糖尿病性ミオパチー	Type 2 diabetic myopathy	E114	8830044
２型糖尿病・神経学的合併症あり	Type 2 diabetes mellitus with neurological complications	E114	8841693
２型糖尿病性筋萎縮症	Type 2 diabetic muscular atrophy	E114	8845079
２型糖尿病性神経因性膀胱	Type 2 diabetic neuropathic bladder	E114	8845084
２型糖尿病性神経痛	Type 2 diabetic neuralgia	E114	8845085
２型糖尿病性自律神経ニューロパチー	Type 2 diabetic autonomic neuropathy	E114	8845086
２型糖尿病性多発ニューロパチー	Type 2 diabetic polyneuropathy	E114	8845091
２型糖尿病性単ニューロパチー	Type 2 diabetic mononeuropathy	E114	8845092
２型糖尿病性末梢神経障害	Type 2 diabetic peripheral neuropathy	E114	8845100
２型糖尿病・末梢循環合併症あり	Type 2 diabetes mellitus with peripheral circulation complications	E115	8841694
２型糖尿病性壊疽	Type 2 diabetic gangrene	E115	8843106
２型糖尿病性潰瘍	Type 2 diabetic ulcer	E115	8845075
２型糖尿病性血管障害	Type 2 diabetic vascular disease	E115	8845080
２型糖尿病性動脈硬化症	Type 2 diabetic atherosclerosis	E115	8845095
２型糖尿病性動脈閉塞症	Type 2 diabetic arterial occlusion	E115	8845096
２型糖尿病性末梢血管症	Type 2 diabetic peripheral vascular disease	E115	8845098

２型糖尿病性末梢血管障害	Type 2 diabetic peripheral vascular disease	E115	8845099
２型糖尿病・関節合併症あり	Type 2 diabetes mellitus with joint complications	E116	8841695
２型糖尿病・糖尿病性合併症あり	Type 2 diabetes mellitus with diabetic complications	E116	8841696
２型糖尿病性水疱	Type 2 diabetic blister	E116	8844628
２型糖尿病性浮腫性硬化症	Type 2 diabetic edematous sclerosis	E116	8844629
２型糖尿病性肝障害	Type 2 diabetic liver injury	E116	8845076
２型糖尿病性関節症	Type 2 diabetic arthropathy	E116	8845077
２型糖尿病性高コレステロール血症	Type 2 diabetic hypercholesterolemia	E116	8845081
２型糖尿病性骨症	Type 2 diabetic osteopathy	E116	8845083
２型糖尿病性精神障害	Type 2 diabetic mental disorder	E116	8845089
２型糖尿病性そう痒症	Type 2 diabetic pruritus	E116	8845090
２型糖尿病性皮膚障害	Type 2 diabetic skin disorder	E116	8845097
２型糖尿病性胃腸症	Type 2 diabetic gastroenteritis	E116	8848108
２型糖尿病・多発糖尿病性合併症あり	Type 2 diabetes mellitus with multiple diabetic complications	E117	8841697
２型糖尿病・糖尿病性合併症なし	Type 2 diabetes mellitus without diabetic complecations	E119	8841698
栄養不良関連糖尿病	Malnutrition-related diabetes mellitus	E12	2500037
膵性糖尿病	Pancreatic diabetes mellitus	E13	2500024
ステロイド糖尿病	Steroid diabetes mellitus	E13	2509003
二次性糖尿病	Secondary diabetes mellitus	E13	2509004
ウイルス性糖尿病	Viral diabetes mellitus	E13	8830756
薬剤性糖尿病	Drug-induced diabetes mellitus	E13	8840710

ウイルス性糖尿病・昏睡合併あり	Viral diabetes mellitus with coma	E130	8843122
膵性糖尿病・昏睡合併あり	Pancreatic diabetes mellitus with coma	E130	8843377
ステロイド糖尿病・昏睡合併あり	Steroid diabetes mellitus with coma	E130	8843390
二次性糖尿病・昏睡合併あり	Secondary diabetes mellitus with coma	E130	8843450
薬剤性糖尿病・昏睡合併あり	Drug-induced diabetes mellitus with coma	E130	8843621
ウイルス性糖尿病・ケトアシドーシス合併あり	Viral diabetes mellitus with ketoacidosis	E131	8843121
膵性糖尿病・ケトアシドーシス合併あり	Pancreatic diabetes mellitus with ketoacidosis	E131	8843376
ステロイド糖尿病・ケトアシドーシス合併あり	Steroid diabetes mellitus with ketoacidosis	E131	8843389
二次性糖尿病・ケトアシドーシス合併あり	Secondary diabetes mellitus with ketoacidosis	E131	8843449
薬剤性糖尿病・ケトアシドーシス合併あり	Drug-induced diabetes mellitus with ketoacidosis	E131	8843620
ウイルス性糖尿病・腎合併症あり	Viral diabetes mellitus with renal complications	E132	8843124
膵性糖尿病・腎合併症あり	Pancreatic diabetes mellitus with renal complications	E132	8843379
ステロイド糖尿病・腎合併症あり	Steroid diabetes mellitus with renal complications	E132	8843392
二次性糖尿病・腎合併症あり	Secondary diabetes mellitus with renal complications	E132	8843452
薬剤性糖尿病・腎合併症あり	Drug-induced diabetes mellitus with renal complications	E132	8843623
ウイルス性糖尿病・眼合併症あり	Viral diabetes mellitus with eye complications	E133	8843120
膵性糖尿病・眼合併症あり	Pancreatic diabetes mellitus with eye complications	E133	8843375
ステロイド糖尿病・眼合併症あり	Steroid diabetes mellitus with eye complications	E133	8843388

二次性糖尿病・眼合併症あり	Secondary diabetes mellitus with eye complications	E133	8843448
薬剤性糖尿病・眼合併症あり	Drug-induced diabetes mellitus with eye complications	E133	8843619
ウイルス性糖尿病・神経学的合併症あり	Viral diabetes mellitus with neurological complications	E134	8843123
膵性糖尿病・神経学的合併症あり	Pancreatic diabetes mellitus with neurological complications	E134	8843378
ステロイド糖尿病・神経学的合併症あり	Steroid diabetes mellitus with neurological complications	E134	8843391
二次性糖尿病・神経学的合併症あり	Secondary diabetes mellitus with neurological complications	E134	8843451
薬剤性糖尿病・神経学的合併症あり	Drug-induced diabetes mellitus with neurological complications	E134	8843622
ウイルス性糖尿病・末梢循環合併症あり	Viral diabetes mellitus with peripheral circulatory complications	E135	8843128
膵性糖尿病・末梢循環合併症あり	Pancreatic diabetes mellitus with peripheral circulatory complications	E135	8843383
ステロイド糖尿病・末梢循環合併症あり	Steroid diabetes mellitus with peripheral circulatory complications	E135	8843396
二次性糖尿病・末梢循環合併症あり	Secondary diabetes mellitus with peripheral circulatory complications	E135	8843456
薬剤性糖尿病・末梢循環合併症あり	Drug-induced diabetes mellitus with peripheral circulatory complications	E135	8843627
ウイルス性糖尿病・糖尿病性合併症あり	Viral diabetes mellitus with diabetic complications	E136	8843126

膵性糖尿病・糖尿病性合併症あり	Pancreatic diabetes mellitus with diabetic complications	E136	8843381
ステロイド糖尿病・糖尿病性合併症あり	Steroid diabetes mellitus with diabetic complications	E136	8843394
二次性糖尿病・糖尿病性合併症あり	Secondary diabetes mellitus with diabetic complications	E136	8843454
薬剤性糖尿病・糖尿病性合併症あり	Drug-induced diabetes mellitus with diabetic complications	E136	8843625
ウイルス性糖尿病・多発糖尿病性合併症あり	Viral diabetes mellitus with multiple diabetic complications	E137	8843125
膵性糖尿病・多発糖尿病性合併症あり	Pancreatic diabetes mellitus with multiple diabetic complications	E137	8843380
ステロイド糖尿病・多発糖尿病性合併症あり	Steroid diabetes mellitus with multiple diabetic complications	E137	8843393
二次性糖尿病・多発糖尿病性合併症あり	Secondary diabetes mellitus with multiple diabetic complications	E137	8843453
薬剤性糖尿病・多発糖尿病性合併症あり	Drug-induced diabetes mellitus with multiple diabetic complications	E137	8843624
ウイルス性糖尿病・糖尿病性合併症なし	Viral diabetes mellitus without diabetic complications	E139	8843127
膵性糖尿病・糖尿病性合併症なし	Pancreatic diabetes mellitus without diabetic complications	E139	8843382
ステロイド糖尿病・糖尿病性合併症なし	Steroid diabetes mellitus without diabetic complications	E139	8843395

二次性糖尿病・糖尿病性合併症なし	Secondary diabetes mellitus without diabetic complications	E139	8843455
薬剤性糖尿病・糖尿病性合併症なし	Drug-induced diabetes mellitus without diabetic complications	E139	8843626
糖尿病	Diabetes mellitus	E14	2500013
糖尿病合併症	Diabetic complications	E14	2507028
糖尿病性昏睡	Diabetic coma	E140	2502006
糖尿病性低血糖性昏睡	Hypoglycemic coma in the context of diabetes mellitus	E140	8838076
糖尿病性アシドーシス	Diabetic acidosis	E141	2501002
糖尿病性アセトン血症	Diabetic acetonemia	E141	2501003
糖尿病性ケトアシドーシス	Diabetic ketoacidosis	E141	2501005
糖尿病性腎症	Diabetic nephropathy	E142	2503005
糖尿病性腎不全	Diabetic renal failure	E142	2503007
糖尿病性腎硬化症	Diabetic nephrosclerosis	E142	8838071
糖尿病性虹彩炎	Diabetic iritis	E143	2504004
糖尿病性中心性網膜症	Diabetic central retinopathy	E143	2504005
糖尿病性白内障	Diabetic cataract	E143	2504006
増殖性糖尿病性網膜症	Proliferative diabetic retinopathy	E143	2504010
糖尿病黄斑症	Diabetic maculopathy	E143	2504012
糖尿病網膜症	Diabetic retinopathy	E143	2504013
糖尿病性眼筋麻痺	Diabetic ophthalmoplegia	E143	8838065
糖尿病黄斑浮腫	Diabetic macular edema	E143	8844089
糖尿病性神経痛	Diabetic neuralgia	E144	2505011
糖尿病性末梢神経障害	Diabetic peripheral neuropathy	E144	2505018

糖尿病性筋萎縮症	Diabetic muscular atrophy	E144	2505021
糖尿病性神経因性膀胱	Diabetic neuropathic bladder	E144	8838069
糖尿病性自律神経ニューロパチー	Diabetic autonomic neuropathy	E144	8838070
糖尿病性多発ニューロパチー	Diabetic polyneuropathy	E144	8838074
糖尿病性単ニューロパチー	Diabetic mononeuropathy	E144	8838075
糖尿病性ニューロパチー	Diabetic neuropathy	E144	8838078
糖尿病足病変	Diabetic foot lesion	E144	8848634
糖尿病性神経障害性疼痛	Diabetic neuropathic pain	E144	8848768
糖尿病性壊疽	Diabetic gangrene	E145	2506006
糖尿病性動脈閉塞症	Diabetic arterial occlusion	E145	2506011
糖尿病性潰瘍	Diabetic ulcer	E145	8838063
糖尿病性血管障害	Diabetic angiopathy	E145	8838066
糖尿病性動脈硬化症	Diabetic arteriosclerosis	E145	8838077
糖尿病性末梢血管症	Diabetic peripheral vascular disease	E145	8838079
糖尿病性末梢血管障害	Diabetic peripheral vascular disease	E145	8838080
糖尿病足壊疽	Diabetic foot gangrene	E145	8848632
糖尿病足潰瘍	Diabetic foot ulcer	E145	8848633
糖尿病性関節症	Diabetic arthropathy	E146	2507025
糖尿病性皮膚障害	Diabetic skin disorders	E146	2507029
糖尿病性肝障害	Diabetic liver injury	E146	8838064
糖尿病性高コレステロール血症	Diabetic hypercholesterolemia	E146	8838067
糖尿病性骨症	Diabetic osteopathy	E146	8838068
糖尿病性精神障害	Diabetic mental disorder	E146	8838072
糖尿病性そう痒症	Diabetic pruritus	E146	8838073

糖尿病性水疱	Diabetic blister	E146	8844652
糖尿病性浮腫性硬化症	Diabetic edematous sclerosis	E146	8844653
高血糖高浸透圧症候群	Hyperglycemia hyperosmolarity syndrome	E146	8845128
糖尿病・糖尿病性合併症なし	Diabetes mellitus without diabetic complications	E149	8843439
非糖尿病性低血糖性昏睡	Hypoglycemic coma not in the context of diabetes mellitus	E15	8839324
果糖尿症	Levulosuria	E741	8831401
本態性果糖尿症	Essential levulosuria	E741	8840104
良性果糖尿症	Benign levulosuria	E741	8841021
腎性糖尿	Renal glycosuria	E748	2714002
青銅性糖尿病	Bronze diabetes mellitus	E831	8835941
膵全摘後二次性糖尿病	Secondary diabetes after pancreatectomy	E891	8835685
１型糖尿病合併妊娠	Pregnancy with type 1 diabetes	O240	8830029
２型糖尿病合併妊娠	ıith type 2 diabetes	O241	8830039
妊娠糖尿病	Pregnancy diabetes mellitus	O244	6489003
妊娠中の糖尿病	Overt diabetes in pregnancy	O249	8838621
妊娠中の耐糖能低下	Impaired glucose tolerance in pregnancy	O998	8838619
妊娠糖尿病母体児症候群	Gestational diabetes maternal syndrome	P700	8838633
糖尿病母体児	Diabetes maternal infant	P701	8838081
新生児一過性糖尿病	Neonatal transient diabetes mellitus	P702	7751001
新生児糖尿病	Neonatal diabetes mellitus	P702	7751002
新生児一過性高血糖症	Neonatal transient hyperglycemia	P708	8844233
境界型糖尿病	Borderline type diabetes mellitus	R730	2500031
耐糖能異常	Impaired glucose tolerance	R730	2713009

化学的糖尿病	Chemical diabetes mellitus	R730	8831132
潜在性糖尿病	Latent diabetes mellitus	R730	8836104
前糖尿病	Pre-diabetes mellitus	R730	8836563
高血糖症	Hyperglycemia	R739	8833419
一過性糖尿	Transient diabetes mellitus	R81	7915002
五炭糖尿症	L-Xylulosuria	R81	7915003
高血糖性糖尿	Hypoglycemic glycosuria	R81	8833420
食事性糖尿	Dietary glycosuria	R81	8834843
情動性糖尿	Emotional glycosuria	R81	8835464
正常血糖性糖尿	Euglycemic glycosuria	R81	8835871
糖尿	Glycosuria	R81	8838062

Supplementary Table S2 Codes of antidiabetic medications

Types of antidiabetic medication	**Medicine codes**
Sulfonylureas	610412056, 610443002, 610443003, 613960002, 613960003, 613960008, 613960017, 613960026, 613960027, 613960028, 613960038, 613960039, 613960078, 620000048, 620002031, 620002032, 620003159, 620003160, 620003947, 620003948, 620006030, 620006890, 620009209, 620871601, 620872002, 620872003, 620872004, 620872009, 620872016, 620873202, 620873301, 620873402, 620873702, 621982701, 621997001, 621997101, 621998701, 621998801, 621998901, 621999001, 621999301, 621999401, 621999701, 621999801, 622000601, 622000701, 622001701, 622001801, 622004701, 622004801, 622005501, 622005601, 622005802, 622009802, 622009901, 622010001, 622011401, 622011501, 622011601, 622011701, 622013401, 622013501, 622013601, 622016001, 622016101, 622017301, 622017401, 622017501, 622017901, 622018001, 622018802, 622020903, 622021003, 622021801, 622021901, 622022001, 622022101, 622023501, 622023601, 622025201, 622025301, 622025801, 622025901, 622026501, 622026601, 622029901, 622030001, 622031401, 622031501, 622033001, 622033101, 622033201, 622033701, 622033801, 622035701, 622035801, 622036002, 622037901, 622038001, 622039901, 622048401, 622048501, 622058801, 622058901, 622059002, 622059102, 622075601, 622088301, 622088401, 622103201, 622114701, 622114801, 622118501, 622122201, 622122301, 622127301, 622127401, 622127501, 622128101, 622137701, 622141101, 622141302, 622143402, 622144001, 622159301, 622169102, 622169301, 622176301, 622177501, 622186201, 622187301, 622190001, 622190801,

	622193301, 622194901, 622198001, 622202201, 622202801, 622205101, 622205501, 622208901, 622211501, 622217701, 622219701, 622221001, 622222001, 622242001, 622246801, 622252501, 622254701, 622271101, 622271201, 622271301, 622313200, 622313300, 622338501, 622338601, 622338701
Meglitinides	622462501, 622462401, 620001908, 620001907, 622053601, 622040901, 622041001, 610432026, 610432027, 622196601, 622119301, 622230001, 622196701, 622119401, 622230101, 610432032, 610432033, 622518201, 622525401, 622515301, 622523401, 622521001, 622518101, 622525301, 622515201, 622523301, 622520901
α-glucosidase inhibitors	610406390, 620002841, 620002843, 620004045, 620004072, 620004071, 620008727, 620008726, 621665301, 621683401, 621673501, 621691201, 622090001, 621689303, 621689001, 621690402, 621690901, 621690203, 620002120, 620004069, 620005557, 620005558, 620005559, 620005560, 620005561, 620008071, 620008072, 620008073, 621953301, 621943301, 620009287, 621896502, 622008602, 620009286, 621896402, 622008502, 620009296, 620009294, 620009293, 622302301, 620009297, 621958801, 620005360, 621785002, 621942202, 620009295, 620009291, 620009289, 620009288, 622302201, 620009292, 621958701, 620005359, 621784902, 621942102, 620009290, 621937201, 621937101, 613960082, 613960081, 622053601, 622432501, 622426601, 622426701, 620003127, 620003128, 620003129, 620002121, 610406391, 621953401, 620004046, 620004070, 620005562, 620008074, 620005563, 620005564, 620005565, 620008075, 620005566, 621943401, 620008076, 620004073, 620002845, 621690303, 620008729, 620008728, 620004074, 621689403, 621689101, 621691001, 621691601, 621665401, 621683501, 620002847, 622090101, 621690502, 621673601
Biguanides	622517101, 622450401, 622450301, 620004480, 620004502, 620005979, 610463145, 621986401, 621986301, 610444147, 621974701, 622242501, 622070801, 621676001,

	620005570, 622427201, 622421901, 622424401, 622421101, 622412701, 622438401, 622417101, 622432601, 622436301, 622427301, 622422001, 622424501, 622421201, 622448601, 622438501, 622417201, 622432701, 622466601
Thiazolidinediones	621990901, 621991001, 610432040, 610432041, 622048501, 622048401, 622065301, 622061601, 622041402, 622155901, 622063201, 622156901, 622144601, 622167201, 622045401, 622159401, 622056001, 622147501, 622175601, 622071901, 622065401, 622061701, 622041502, 622156001, 622063301, 622157001, 622144701, 622167301, 622045501, 622159501, 622056101, 622147601, 622175701, 622072001, 622320800, 622320900, 622065101, 622042901, 622061401, 622166801, 622182401, 622041202, 622079101, 622155701, 622063001, 622066201, 622164301, 622062302, 622047701, 622049901, 622046801, 622163301, 622053101, 622081801, 622059201, 622045201, 622053801, 622055801, 622147301, 622078301, 622175401, 622071701, 622065201, 622043001, 622061501, 622166901, 622182501, 622041302, 622079201, 622155801, 622063101, 622066301, 622164401, 622062402, 622047801, 622050001, 622046901, 622163401, 622053201, 622081901, 622059301, 622045301, 622061001, 622055901, 622147401, 622078401, 622175501, 622071801, 621986401, 621986301, 622086101, 622086001
Dipeptidyl peptidase-4 inhibitors	621950901, 621951001, 621951101, 621970601, 621970701, 621970801, 621980701, 621986001, 621986101, 621986201, 622086001, 622086101, 622093501, 622182601, 622201701, 622245601, 622245701, 622277501, 622288401, 622415401, 622415501, 622448901, 622449001, 622450301, 622450401, 622517101
Sodium glucose cotransporter 2 inhibitor	622340101, 622360601, 622401201, 622401301, 622306601, 622306701, 622336801, 622342001, 622341901, 622335701, 622335801

Rapid-acting insulin	621911101, 621911301, 621911201, 620008895, 621926901, 622252701, 620008893, 620008894, 620008916, 640451027, 620007460
Short-acting insulin	620008897, 620000265, 620008909, 620008907, 622114401
Long-acting insulin	622440701, 620008945, 620008943, 620007536, 622198901, 622199001, 622410901, 622484801, 622411001, 621927001, 620008952, 620008953
Immediate-acting insulin	620000266, 620008912, 620008910, 622114501, 620002441, 620007459
Premixed insulin	620002439, 620007461, 620002440, 620007462, 620008915, 620008913, 622114601, 620000269, 620000448, 620008896, 621973201, 621973301, 640453023
Combination-acting insulin	622451001, 622450901
Glucagon-like peptide-1 receptor agonist	622038401, 622038301, 621974801, 622229001, 622406001, 622267001, 622442201

Supplementary Table S3 Amputation codes

	Medical procedure receipt codes (in Japan)
Major LLA	
above-knee/transfemoral amputation	150051610
below-knee/transtibial amputation	150051710
Hindquarter amputation/ Hip disarticulation	150052210
through-knee amputation	150052310
Minor LLA	
Foot amputation, trans-metatarsal amputation, Lisfranc disarticulation	150051810
Foot joint disarticulation	150052610
Finger and toe amputation	150051910
Finger and toe joint disarticulation	150052710

Supplementary Table S4 The population of Japanese national census (2015)

Age group, years	total	men	women	Age group, years	total	men	women	Age group, years	total	men	women
0–4	4,987,706	2,550,921	2,436,785	**35–39**	8,316,157	4,204,202	4,111,955	**70–74**	7,695,811	3,582,440	4,113,371
5–9	5,299,787	2,714,591	2,585,196	**40–44**	9,732,218	4,914,018	4,818,200	**75–79**	6,276,856	2,787,417	3,489,439
10–14	5,599,317	2,868,024	2,731,293	**45–49**	8,662,804	4,354,877	4,307,927	**80–84**	4,961,420	1,994,326	2,967,094
15–19	6,008,388	3,085,416	2,922,972	**50–54**	7,930,296	3,968,311	3,961,985	**≥85**	4,887,487	1,461,624	3,425,863
20–24	5,968,127	3,046,392	2,921,735	**55–59**	7,515,246	3,729,523	3,785,723	**Total**	127,094,745	61,841,738	65,253,007
25–29	6,409,612	3,255,717	3,153,895	**60–64**	8,455,010	4,151,119	4,303,891				
30-34	7,290,878	3,684,747		**60-65**	9,643,867	4,659,662	4,984,205				