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ORIGINAL RESEARCH

The Danish Centre for Strategic Research in Type 2 Diabetes (DD2) study: Collection of baseline data from the first 580 patients

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Abstract: This paper provides an overview of the baseline data collected in the nationwide Danish Centre for Strategic Research in Type 2 Diabetes (DD2) project. The paper presents descriptive data from the first 580 patients enrolled in the DD2. The DD2 database will contain detailed interview data, clinical examination data, and urine and blood samples from up to 10,000 patients newly diagnosed with type 2 diabetes each year, collected from general practitioners and hospital outpatient clinics in all of Denmark. Of the first DD2 patients enrolled, blood and urine samples have been obtained from 97%. The median age of the first 580 patients was 59 years and 322 (56%) were men. Median weight gain from age 20 to maximum lifetime weight was 29 kg for men and 31 kg for women, and 364 patients (63%) did not currently participate in regular sports activities. Two hundred and ninety two patients (50%) had a known family history of diabetes. Two hundred fifty (43%) of the 580 DD2 patients have also been enrolled in the Danish Diabetes Database for Adults from which additional clinical data can be obtained. Among these 250 patients (154 of whom were men, 96 women), 75 (49%) men were currently obese, and 63 (41%) were overweight, whereas 62 (65%) women were obese, and another 21 (22%) were overweight. Twenty-nine patients (12%) received insulin, 164 patients (66%) received oral antidiabetics only, and 57 (23%) received no antidiabetic treatment. Glycemic regulation was modest (the glycosylated hemoglobin A of 46% was ≥7.5%). Two thirds of the patients received antihypertensive and hypolipidemic treatment. Self-reported daily tobacco smoking (23%) and alcohol overuse (6%) seemed comparable to occurrence in the general Danish population. One quarter of the patients with newly diagnosed diabetes had a history of hospital-diagnosed comorbidity at baseline as included in the Charlson comorbidity index, in particular prior myocardial infarction (5%), cerebrovascular disease (5%), peripheral vascular disease (4%), chronic pulmonary disease (6%), and previous solid cancer (6%). In the future, the DD2 database represents a valuable source for outcome studies in type 2 diabetes.

Keywords: type 2 diabetes, epidemiological methods, registries, prognosis

Introduction

Denmark has 5.6 million mixed rural and urban inhabitants and is a welfare state, with tax-financed universal access to health services.[1] The Danish National Health Service guarantees unfettered access to primary care and public hospitals, which are free at point of delivery, and provides partial reimbursement for prescribed medications. Except for emergencies, patients' initial contact with the health care system is through their general practitioners (GPs), who provide referrals to hospitals and privately practicing specialists as necessary.[2]

In this setting, the nationwide Danish Centre for Strategic Research in Type 2 Diabetes (DD2) project started testing patient enrollment in late 2010. DD2 will be

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one of the world's largest prospectively designed diabetes research projects, and this is the first time a nationwide comprehensive type 2 diabetes research project of this kind has been conducted in Denmark. DD2 aims to enroll 10,000 patients per year when fully implemented nationwide, corresponding to approximately half of all patients with newly diagnosed type 2 diabetes in Denmark. The project will continue until at least 50,000 patients with type 2 diabetes have been enrolled. The DD2 database will contain detailed interview and clinical examination data from these patients, including background and lifestyle factors, tobacco and alcohol intake, physical activity, family history of diabetes, anthropometric and other clinical measurements, blood pressure and lipids, glycemic regulation, and treatment of diabetes. Many of these variables will be obtained by linking with current databases. All patients are registered by their unique personal identifier, the civil personal registration number (CPR number). This enables the DD2 cohort to be linked to a wide range of Danish medical and administrative registries, with detailed historical and prospective data on use of medications, hospital contacts and diagnoses, surgical procedures, dialysis, socioeconomic prognosis, and total and cause-specific mortality, as described in more detail elsewhere.[3]

The aim of the current paper is to present a short overview of the baseline data collected in the DD2 database. The paper includes a presentation of interview and clinical examination data from the first 580 patients enrolled in the DD2.

Baseline data: what is recorded in the DD2 database?

The DD2 project enrolls patients newly diagnosed with type 2 diabetes from GPs and hospital outpatient clinics throughout Denmark. The implementation and logistics of the DD2 project are described in detail elsewhere.[4] In brief, an online questionnaire is filled out by GPs or hospital physicians for each DD2 patient at the time of enrollment, and blood and urine samples are collected. Data are electronically transferred to the DD2 database managed by the Department of Clinical Epidemiology at Aarhus University Hospital. To make enrolling a large number of patients in the DD2 fast and simple, relatively few interview and clinical data are collected, and additional data are extracted from Danish population-based databases. Thus, the DD2 database is regularly updated through links with additional clinical data from the Danish Diabetes Database for Adults (DDDA), as described in detail elsewhere.[2]

Hospital outpatient clinics and GPs started enrolling DD2 patients and transferring data to the DD2 database in November 2010. Registration of patients and sample collection in the DD2 database were approved by the National Committee on Health Research Ehitics (Denmark) (record number S-20100082) and the Danish Data Protection Agency (record number 2008-58-0035). Patients volunteer to participate in the DD2 project and have to sign a written informed consent document, after first receiving detailed oral and written information approved by the National Committee on Health Research Ethics. (Denmark).

Data recorded in the DD2 database include each patient's identification number (CPR number), interview date, and detailed interview and clinical examination data. Blood and urine samples are obtained from each patient, either on the day of the interview or a later occasion, as described in detail by Nielsen et al.[4] The DD2 online registration form is also described by Nielsen et al.[4] Collected variables inputted directly in the DD2 database include hip–waist ratio, body weight at 20 years and maximum weight, alcohol intake, physical activity, family history of diabetes, and resting heart rate. Variables merged from the DDDA include date of first type 2 diabetes diagnosis, tobacco smoking, body mass index (BMI), blood pressure, glycosylated hemoglobin A (HbA_{1c}), albuminuria, plasma lipids, antidiabetic treatment, antihypertensive treatment including angiotensin-converting enzyme (ACE) inhibitors, hypolipidemic treatment, and examination of presence of diabetic foot and eye disease. Thus, up to 90 administrative and clinical variables are registered for each patient with type 2 diabetes.

Linking with the Danish National Registry of Patients[5] at baseline makes it possible to obtain a complete hospital contact history since 1977 for each participant before the date of enrollment. We obtained information on participants' major chronic diseases, defined as those included in the Charlson comorbidity index:[6] myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, liver disease, diabetes, hemiplegia, renal disease, cancer, and acquired immune deficiency syndrome. Based on hospital diagnosis codes for these conditions,[7] we computed a Charlson comorbidity index score for each person,[8] defining three comorbidity levels as low (score of 0), medium (1–2), and high (3+).

Data on the first 580 patients enrolled

Table 1 shows characteristics of the first 580 patients who have been enrolled and had interview and clinical

examination data transferred directly to the DD2 database by October 31, 2011. The median age of the study cohort was 59 years (interquartile range 51–64 years), and 322 (56%) were men (Table 1). Eighty-two percent of the patients were fasting when they arrived for the interview and enrollment. Blood and urine samples have been obtained from 97% of the patients and are stored at the DD2 biobank (data not shown; see Christensen et al[9]). The maximum lifetime weight reached among study participants was a median of 100 kg (interquartile range 86–116 kg, maximum 250 kg), while weight at 20 years of age was 70 kg median (interquartile range 60–80 kg, maximum 170 kg), corresponding to a median weight gain from age 20 to maximum lifetime weight of 29 kg for men and 31 kg for women (Table 1). A number of 364 patients (63%) did no regular sports activities, and 292 (50%) had a known family history of diabetes. Thirty-six patients (6%) reported having a total weekly alcohol intake in excess of the maximum safe amount recommended in Denmark at the time of DD2 study start (>14 drinks/week for women, >21 drinks/week for men) (Table 1).

Table 2 shows the history of hospital-diagnosed comorbidity at baseline among the 580 DD2 participants with newly diagnosed type 2 diabetes, ascertained by linking with the Danish National Registry of Patients. One quarter of the patients had comorbidities included in the Charlson comorbidity index before the date of enrollment. Prevalent comorbidities were prior myocardial infarction (5%), cerebrovascular disease (5%), peripheral vascular disease (4%), chronic pulmonary disease (6%), and previous solid cancer (6%) (Table 2).

The 580 patients were linked to the DDDA at the beginning of December 2011 to collect additional diabetes data. Two hundred fifty (43%) DD2 patients were registered in the DDDA (Table 3). The reasons for delayed data patient entry in the DDDA have been described below and elsewhere.[2] As seen in Table 3, 58 (23%) were current daily smokers, and 93 (37%) were former smokers. Very few patients had a BMI within the normal range at enrollment in the DDDA: 75 (49%) out of 154 men were currently obese, and 63 (41%) were overweight; whereas 62 (65%) of 96 women were obese, and another 21 (22%) were overweight. One hundred sixteen (46%) patients had a median HbA_{1c} of 7.5% or more, and 36 (14%) of all patients had an albumin–creatinin ratio of 30 mg/g or more (the ratio was missing for 23% of patients). Patients received antidiabetic treatment in 77% of the cases: 29 patients (12%) received insulin, and 164 patients (66%) received oral antidiabetics only. Median systolic/diastolic blood pressure was 130/81 mmHg, and median total

Table 1 Characteristics of the first 580 patients with newly diagnosed type 2 diabetes enrolled in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) project

Variable	Patients with type 2 diabetes
Persons enrolled in DD2, n (%)	**N = 580 (100%)**
Age, median (quartiles), years	59 (51–64)
Age range, years	24–83
Gender, n (%)	
Male	322 (56)
Female	258 (44)
Patient fasting at time of enrollment,[a] n (%)	
Yes	477 (82)
No	89 (15)
Missing information	14 (2)
Resting heart rate, median (quartiles)	70 (62–76)
Waist-hip ratio in men, median (quartiles)	1.01 (0.97–1.05)
Waist-hip ratio in women, median (quartiles)	0.91 (0.88–0.96)
Weight gain in men	
Weight at age 20 years, median (quartiles), kg	76 (70–85)
Don't know weight at 20 years, n (%)	51 (16)
Maximum lifetime weight, median (quartiles), kg	106 (92–120)
Don't know maximum lifetime weight, n (%)	2 (1)
Weight gain since age 20, median (quartiles), kg	29 (18–41)
Weight gain in women	
Weight at age 20 years, median (quartiles), kg	59 (52–69)
Don't know weight at 20 years, n (%)	42 (16)
Maximum lifetime weight, median (quartiles), kg	94 (80–110)
Don't know maximum lifetime weight, n (%)	4 (2)
Weight gain since age 20, median (quartiles), kg	31 (20–41)
Alcohol use, n (%)	
Maximum 14/21 drinks/week[b] for women/men	544 (94)
More than 14/21 drinks/week for women/men	36 (6)
Days per week with 30+ minutes of physical activity	
0 days	95 (16)
1 day	40 (7)
2 days	78 (13)
3 days	76 (13)
4 days	52 (9)
5 days	57 (10)
6 days	27 (5)
7 days	155 (27)
Regular sports activities, n (%)	
Yes	216 (37)
No	364 (63)
Level of physical activity during the last year, n (%)	
Hard physical training and competitive sports several times a week	4 (1)
Leisure sports, heavy garden work or similar at least 4 hours per week	109 (19)
Walking, cycling or other light exercise at least 4 hours per week	364 (63)
I read, watch television, or have other sedentary activity	103 (18)
Family history of diabetes, n (%)	
Yes	292 (50)
No	227 (39)
Don't know	61 (11)

Notes: [a]Blood and urine samples are obtained either immediately at the interview or at a later occasion; [b]maximum safe amount recommended in Denmark at the time of DD2 study start.

Table 2 Hospital-diagnosed comorbidity at baseline among 580 patients with newly diagnosed type 2 diabetes, ascertained by linkage with the Danish National Registry of Patients

N (%) participants in DD2 who can currently be linked to the Danish National Registry of Patients	Patients with type 2 diabetes 580 (100%)
Comorbidities at baseline, n (%)[a]	
Prior myocardial infarction	28 (4.8)
Congestive heart failure	7 (1.2)
Peripheral vascular disease	22 (3.8)
Cerebrovascular disease	31 (5.3)
Dementia	0 (0.0)
Chronic pulmonary disease	36 (6.2)
Connective tissue disease	5 (0.9)
Peptic ulcer disease	8 (1.4)
Mild liver disease	7 (1.2)
Hemiplegia	1 (0.2)
Moderate to severe renal disease	7 (1.2)
Solid cancer	32 (5.5)
Leukemia	1 (0.2)
Lymphoma	1 (0.2)
Moderate to severe liver disease	1 (0.2)
Metastatic solid cancer	5 (0.9)
AIDS	2 (0.3)
Charlson comorbidity index score, n (%)[b]	
Low (0)	434 (74.8)
Medium (1–2)	119 (20.5)
High (≥3)	27 (4.7)

Notes: [a]Comorbidities included in the Charlson comorbidity index, except diabetes; [b]for the calculation of the Charlson index score levels, see text.
Abbreviations: AIDS, acquired immune deficiency syndrome; DD2, Danish Centre for Strategic Research in Type 2 Diabetes.

cholesterol was 4.4 (interquartile range 3.7–5.1) mmol/L. One hundred and fifty-six patients (62%) received antihypertensive treatment, and 160 (64%) received hypolipidemic agents.

Data quality

When evaluating the overall quality of data for the enrolled DD2 patients, it is important to consider whether all data are recorded (no missing data) and whether the information recorded in the database is correct. Information in the database is entered by physicians and transferred electronically from the participating centers[4] directly from the online questionnaire on the DD2 homepage (http://www.dd2.nu) with theoretically minimal risk of data loss. The data quality is confirmed with automatic validation at data entry, for example, invalid/"false" CPR numbers are not accepted. To improve data quality, all variables must be filled in the questionnaire; however, a few variables have a "don't know" category, as seen in Table 1. We found that data completeness was 100% for demographic variables and for most clinical characteristics (eg, anthropometric measurements, heart rate,

Table 3 Characteristics of 250 patients enrolled in the nationwide Danish Centre for Strategic Research in type 2 Diabetes (DD2) project who are currently registered in the Danish Diabetes Database for Adults

Variable	Patients with type 2 diabetes
N (%) participants in DD2 who currently are registered in the Danish Diabetes Database for Adults	250 (43)
Tobacco smoking, n (%)	
Never smoker	89 (36)
Former smoker	93 (37)
Current smoker, daily	58 (23)
Current smoker, occasionally	4 (2)
Smoking status listed unknown	6 (2)
Height and weight in men (n = 154)	
Height, median (quartiles), cm	178 (174–184)
Height missing, n (%)	5 (3)
Current weight, median (quartiles), kg	96 (86–109)
Weight missing, n (%)	2 (1)
Current BMI, n (%)	
<18.5 kg/m^2	0 (0)
18.5–24.9 kg/m^2	11 (7)
25–29.9 kg/m^2	63 (41)
30+ kg/m^2	75 (49)
BMI missing	7 (2.8)
Height and weight in women (n = 96)	
Height, median (quartiles), cm	165 (160–170)
Height missing, n (%)	2 (2)
Current weight, median (quartiles), kg	91 (78–102)
Weight missing, n (%)	0 (0)
Current BMI, n (%)	
<18.5 kg/m^2	1 (1)
18.5–24.9 kg/m^2	10 (10)
25–29.9 kg/m^2	21 (22)
30+ kg/m^2	62 (65)
BMI missing	2 (2)
HbA_{1c}, n (%)	
<7.5%	133 (53)
≥7.5%	116 (46)
HbA_{1c} missing	1 (0.4)
Albuminuria, n (%)	
Albumin–creatinin ratio < 30 mg/g	156 (62)
Albumin–creatinin ratio ≥ 30 mg/g	36 (14)
Albumin excretion ≥ 30 mg/day	1 (0.4)
Albuminuria listed "unknown"	57 (23)
Blood pressure, median (quartiles), mmHg	
Systolic	130 (122–144)
Diastolic	81 (75–90)
Lipids, median (quartiles), mmol/L	
Total-cholesterol	4.4 (3.7–5.1)
HDL-cholesterol	1.2 (1.0–1.4)
LDL-cholesterol	2,4 (1.9–3.1)
Triglycerides	1.7 (1.2–2.5)
Antidiabetic treatment, n (%)	
Insulin only	9 (4)
Insulin and oral	20 (8)
Oral	164 (66)

(*Continued*)

Table 3 (*Continued*)

Variable	Patients with type 2 diabetes
None	57 (23)
Insulin pump, n (% of insulin treated)	0 (0)
Antihypertensive treatment, n (%)	156 (62)
ACE-inhibitor or ATII-antagonist treatment, n (%)	121 (48)
Hypolipidemic treatment, n (%)	160 (64)
Eye screening completed, n (%)	147 (59)
Foot examination completed, n (%)	232 (93)

Abbreviations: ACE, angiotensin-converting enzyme; ATII, angiotensin II; BMI, body mass index; HbA_{1c}, glycosylated hemoglobin A; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

physical activity, or alcohol use). The largest proportion of "don't know" responses was encountered for weight at 20 years of age (16% reported "don't know") and family history of diabetes (11% reported "don't know"). Hospital comorbidity history in Denmark since 1977 is complete, since all Danish hospitals report diagnoses to the Danish National Registry of Patients.[5] We did not systematically validate the entered data in this report; this will be possible through future research projects, random spot checks, and linking to independent national registries using the CPR numbers, for example, to the Nationwide Prescription Database.[10] The impact of missing or incorrectly measured data in the DD2 depends on the research question and study design. Missing data (eg, on family history of diabetes or overweight at age 20) hamper studies on the prevalence of these conditions but do not necessarily hamper analytic epidemiological studies if the measurement errors are unrelated to other study variables.

We found that only 43% of the first 580 patients in the DD2 database were also enrolled in the DDDA database (Table 2) at present and could have their DD2 data enriched by linking to the DDDA. This is probably related to delayed DDDA enrollment. The DDDA focuses on clinical performance measures during the last year among persons with known (prevalent) type 2 diabetes.[2] Thus, it is possible but not mandatory for clinics and physicians to report newly diagnosed diabetes patients in the DDDA database at the time of first contact and it is therefore likely that while some clinics report their newly diagnosed diabetes patients immediately, others do not. This presumption is supported by the fact that the 250 DD2 patients who had available DDDA data were reported from relatively few hospital diabetes clinics, compared with the number of clinics that are known to regularly report diabetes patients to the DDDA (not shown). We therefore expect the proportion of DD2 patients who have supplementary data available in the DDDA to increase substantially in the future. Among patients registered in the DDDA, completeness of data is also very high – for example, more than 95% for smoking, BMI, HbA_{1c}, blood pressure, and all blood tests and medications, except for albuminuria (for which 23% is missing).

The current patient sample was predominantly reported from hospital diabetes clinics and may include patients with more severe than average newly diagnosed type 2 diabetes. Representativeness is likely to increase when more GPs begin to include diabetes patients in the DD2.[4]

Conclusion

We have presented data for the first 580 patients enrolled in the DD2. Up to 90 interview and clinical examination data variables are registered for each participant. The median age was 59 years, almost all patients were overweight or obese, and half of the participants had a family history of diabetes. Two thirds received oral antidiabetics only and 12% received insulin, with modest glycemic regulation. Two thirds of patients received antihypertensive and hypolipidemic treatment. One quarter had previous hospital-diagnosed comorbidity, cardiovascular disease in particular. We found that completeness of primary DD2 variables was very high, except for weight at age 20 and family history of diabetes, which must be improved. Another limitation was the fact that less than half of the DD2 participants were currently recorded in the DDDA database to have their clinical data enriched. We believe that future updated data links will substantially improve completeness.

The DD2 database will become a very valuable source for large clinical epidemiological research and outcome studies in type 2 diabetes. The database provides ongoing longitudinal registration of a wealth of data on patients with diabetes not routinely available in medical registries. Linking other unique Danish population-based registries with the DD2 database will make it possible to ascertain complete data on these patients' previous and future use of medications, hospital contacts and diagnoses, surgical procedures, dialysis, socioeconomic prognosis, and total and cause-specific mortality.

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of the project are listed on the project website at www.DD2.nu.

Disclosure

The authors report no conflicts of interest in this work.

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