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ORIGINAL ARTICLE

How to diagnose and classify diabetes in primary health care: Lessons learned from the Diabetes Register in Northern Sweden (DiabNorth)

OLOV ROLANDSSON[1], MARGARETA NORBERG[2], LENNARTH NYSTRÖM[2], STEFAN SÖDERBERG[3], MARIA SVENSSON[4], BERNT LINDAHL[5] & LARS WEINEHALL[2]

[1]*Department of Public Health and Clinical Medicine, Family Medicine, Umeå University,* [2]*Department of Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå University,* [3]*Department of Public Health and Clinical Medicine, Medicine, Umeå University,* [4]*Department of Molecular and Clinical Medicine-Nephrology, Institution of Medicine, Sahlgrenska Academy at University of Gothenburg, and* [5]*Department of Public Health and Clinical Medicine, Behavioural Medicine, Umeå University, Sweden*

Abstract

Objective. The objective was to create a diabetes register and to evaluate the validity of the clinical diabetes diagnosis and its classification. *Design.* The diabetes register was created by linkage of databases in primary and secondary care, the pharmaceutical database, and ongoing population-based health surveys in the county. Diagnosis and classification were validated by specialists in diabetology or general practitioners with special competence in diabetology. Analysis of autoantibodies associated with type 1 diabetes was used for classification. *Setting.* Primary and secondary health care in the county of Västerbotten, Sweden. *Patients.* Patients with diabetes (median age at diagnosis 56 years, inter quartile range 50–60 years) who had participated in the Västerbotten Intervention Programme (VIP) and accepted participation in a diabetes register. *Results.* Of all individuals with diabetes in VIP, 70% accepted to participate in the register. The register included 3256 (M/F 1894/1362) diabetes patients. The vast majority (95%) had data confirming the diabetes diagnoses according to WHO recommendations. Unspecified diabetes was the most common (54.6%) classification by the general practitioners. After assessment by specialists and analysis of autoantibodies the majority were classified as type 2 diabetes (76.8%). Type 1 diabetes was the second largest group (7.2%), including a sub-group of patients with latent autoimmune diabetes (4.8%). *Conclusion.* It was concluded that it is feasible to create a diabetes register based on information in medical records in general practice. However, special attention should be paid to the validity of the diabetes diagnosis and its classification.

Key Words: *Diabetes, classification, register, primary health care*

Background

The prevalence of diabetes mellitus in Sweden has been estimated at 2–4%, with an annual incidence of 0.2–0.4% and the majority of patients have type 2 diabetes [1–4].

Both type 1 and type 2 diabetes are associated with complications affecting various organs. This is due to damage in small vessels resulting in retinopathy, nephropathy and neuropathy, and macroangiopathy, i.e. an accelerated arteriosclerosis, resulting in cardiovascular morbidity and death [5,6]. Chronic diabetic complications affect quality of life and/or life expectancy and increase the burden not only for the individual patient but also for society at large, through increased costs for health care and loss of productivity [7].

The county of Västerbotten in Northern Sweden has one of the world's largest (n ~125 000) and most comprehensive datasets based on continuous population-based health surveys, the Västerbotten Intervention Programme (VIP) [8]. In addition, more than 90% of the participants in VIP have donated a blood sample to the medical biobank in Umeå, Sweden [9], which makes it one of the largest biobanks in the world. Together, the database and the biobank represent an opportunity for diabetes

Correspondence: Olov Rolandsson, Department of Public Health and Clinical Medicine, Family Medicine, Umeå University, 901 85 Umeå, Sweden. E-mail: olov.rolandsson@fammed.umu.se

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There is a trend for automated data retrieval from electronic patient records aiming to create high-quality registries.

- A diabetes register was created within the Västerbotten intervention programme; the basis for the diabetes diagnosis was studied and the diabetes classification between the general practitioners (GP) and specialists compared, and the diabetes was re-classified after analysis of autoantibodies associated with type 1 diabetes.
- This study shows that the vast majority of the diabetes diagnoses were in accordance with the WHO criteria but a large percentage of diabetes was classified as unspecified diabetes by the GPs; thus special attention should be paid to validation of data before automated retrieval of data from medical records in general practice.

research with the possibility to study the impact of a range of topics from the effect of gene–environment interactions on diabetes development to the effect of psychosocial stress on the incidence of diabetes and its complications. Therefore, we have created a diabetes register, "the Diabetes register in Northern Sweden" (DiabNorth), based on the VIP study cohort. The overall aim of DiabNorth is to establish a database to facilitate studies of risk factors for the development of diabetes per se and diabetes-related acute and long-term complications.

A valid diagnosis and classification of type of diabetes is the foundation of all high-standard studies. There is an increasing interest in retrieving data from medical records automatically [10]. This can be achieved using different software e.g. Medrave (http://www.medrave.com/estartsida.htm). However, these automatic downloads generate cases that are seldom validated, which might bias the results. Thus, we aimed to study the classification of patients in the register made by clinicians, diabetologists, and validation/re-classification after analysis of autoantibodies associated with type 1 diabetes.

Material and methods

Design of DiabNorth

The VIP was initiated in 1985 with the aim of preventing cardiovascular disease (CVD) and diabetes [8]. The reason for starting the VIP was the high CVD mortality in the county as compared with the rest of Sweden [11]. In the VIP, participants were invited to their local primary health care centre at the age of 40, 50, and 60 for a health examination including measurements of blood pressure, plasma lipids, height and weight, and a standardized oral glucose tolerance test (OGTT) after fasting overnight. They also answered a questionnaire concerning lifestyle factors such as tobacco, alcohol, and food habits and physical activity, socio-demographic characteristics, heredity, quality of life, social and emotional support, social network, working conditions, and self-reported health. The participants were asked to donate blood samples for research that are stored at –80°C at the Medical Biobank, Umeå University Hospital, Umeå, Sweden [9].

Organization and availability of DiabNorth

The organization and availability of DiabNorth is described on our website: http://www.diabetesregister.se.

The diabetes register in the VIP – DiabNorth: First recruitment in 2002

Between 1985 and 2002 74 000 people participated in the VIP and the vast majority (90.5%) also gave written consent to participate in research and donate a blood sample. In 2002 the VIP register 1990–2002 was linked to the register for primary and secondary care in the county, which was computerized in 1994, to identify individuals with a diabetes diagnosis who had participated in the VIP (Figure 1). We found 1948 subjects with a diagnosis of diabetes who were sent a letter asking for their consent to participate in the register; after one letter of reminder 1446 (74%) consented to participate in DiabNorth (Figure 1). Based on the date of participation in VIP and date of diagnosis we can distinguish prevalent cases from incident cases.

DiabNorth: Update in 2007

In 2007 the record linkage was repeated (see Figure 1). In addition, the VIP database was linked to the pharmaceutical register at the National Board of Health and Welfare to identify diabetes patients in Västerbotten who had bought diabetes drugs in 2005–2007.

Data collection, validation, and classification

Two research nurses visited all health institutions in the county to collect data from the medical records, including the diabetes classification by the clinicians, and compiled these in a structured form (Table I). These forms were reviewed by a specialist in internal medicine (Dr Lars Widman) and/or diabetologist

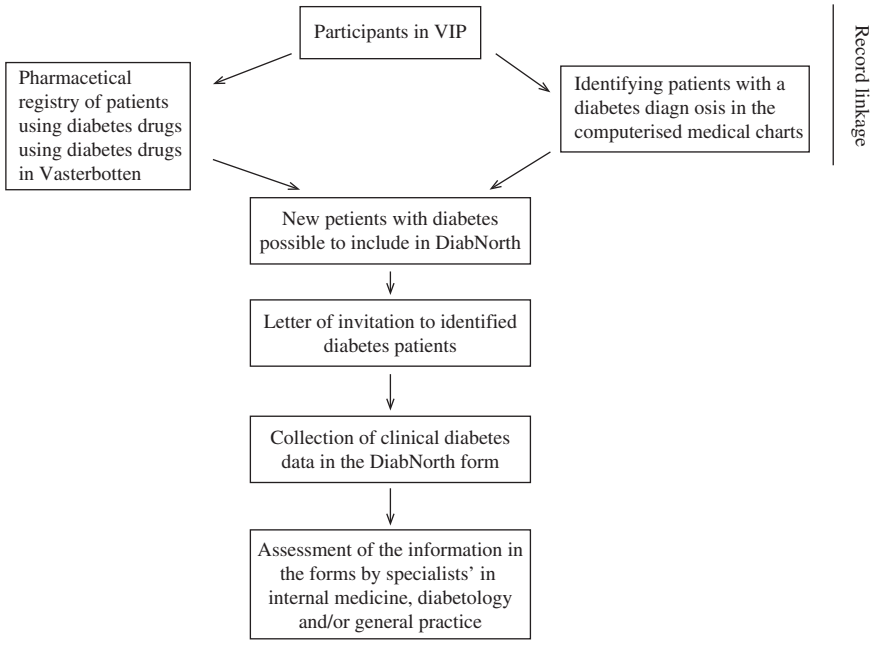

Figure 1. Data-generation process for including diabetes patients in DiabNorth.

(Professor Jan W. Eriksson) and/or general practitioners (Dr Olov Rolandsson and Dr Margareta Norberg) with a special interest and experience in diabetes. The diagnoses were thus validated and the type of diabetes was classified according to the WHO recommendations (Table II [12]). Subjects with incomplete data on, e.g., glucose values in their medical records precluded us from defining the subjects as having diagnosed diabetes according to the WHO criteria and they were therefore classified as "unclear diagnosis", and asymptomatic cases where a single diabetic glucose value was followed by repeated blood glucose values below the cut-off for diabetes were labelled as "not diabetes". Finally, a validation/re-classification was performed after analysis of autoantibodies associated with type 1 diabetes.

Analysis of autoantibodies

Autoantibodies associated with type 1 diabetes were analysed to identify patients with latent autoimmune diabetes (LADA), a subgroup of patients who develop phenotypic type 2 diabetes but have markers of autoimmunity [13,14]. LADA is classified as type 1 diabetes by the WHO [12]. The sub-classification might be of importance when choosing the optimal initial treatment. Thus, autoantibodies against glutamic acid decarboxylase, isoform 65 (GAD65Ab), i.e. autoantibodies associated with autoimmune diabetes [15] were analysed. The assay procedure is described in detail elsewhere [16–18]. The analysis was performed at the Lund University Clinical Research Centre, University Hospital MAS, Malmö, Sweden. GAD65Ab analysis was performed in plasma samples from 3018 patients, thus 238 (7.3%) patients lacked available samples. Two levels of GAD65Ab are presented: one intermediate level (> 31.0–59.0 U/mL) and one high level (> 59.0 U/mL) of GAD65Ab representing the 99th percentile among 400 healthy blood donors. In this study we used the higher cut-off to define GAD65Ab positivity.

Results

The register includes 1362 women and 1894 men. As shown in Table III, there is a large proportion of patients with unspecified diabetes. It should be noted that one patient could have more than one diagnosis. After the re-classification by a diabetologist, the proportion of unspecified diabetes decreased dramatically (Figure 2), but still constituted a substantial proportion (10.4%). After assessment by a diabetologist, 50 (14.8%) of the 338 patients with unspecified diabetes were GAD65Ab positive and were re-classified as having LADA. A total of 257 (76.0%) were antibody negative and re-classified as having type 2 diabetes. Thirty-one (9.2%) patients with unspecified diabetes were antibody negative but had phenotypic features and a need for insulin early in their disease, which resembles type 1 diabetes; due to the mixed features they remained in the unspecified group.

The median age at diagnosis was 56 years (interquartile range 50–60 years), with no age difference

Table I. Information in DiabNorth.

Variable	At diagnosis	At data collection
Civic number		x
Date of participation in VIP		x
Sex		x
Family history of diabetes specified by type of diabetes and by family relationship		x
Diabetes diagnosis in medical record? (type of care provider, date and type of diabetes)	x	x
Fulfilment of WHO criteria for diabetes (assessed by specialist)	x	
Verified diabetes diagnosis (classified by specialist as: type 1, type 2, secondary, unspecified, uncertain diagnosis, incorrect diabetes diagnosis, impaired glucose tolerance)		x
Pregnancy	x	
Pancreatic disease	x	
Other specific diseases or treatments that might influence the incidence of diabetes	x	
Diabetes medication		x
Use of anti-thrombotic medication[1]		x
Height (cm)	x	x
Weight (hg)	x	x
Hypertension		x
Systolic/diastolic blood pressure (mm Hg)[1]		x
Blood lipids[1]		x
U-albumin (classified as micro or macro)[1]		x
Fasting glucose	x	
2-h glucose	x	
Random glucose	x	
HbA1c	x	x
Autoantibodies against GAD65 and IA-2	x	x
C-peptide	x	x
Diagnosis of nephropathy[1]		x
Diagnosis of retinopathy[1]		x
Diagnosis of neuropathy[1]		x
Diagnosis of cardiovascular disease[1]		x
Notification if ECG is collected[1]		x

Note: [1]Denotes that information was collected in the 2007 updated version of DiabNorth

between men and women. The population was overweight (mean BMI 29.7 ± 5.1 kg/m^2) with a mean HbA1c of 63 ($\pm$ 13.0) mmol/mol. The distribution of sex, BMI, and HbA1c at diagnosis by antibody-verified diagnosis is presented in Table IV. Of the 3018 patients, 51 (1.7%, M/F 31/20) had intermediate and 188 (6.2%, M/F 93/95) had high levels of GAD65Ab i.e. GAD65Ab positive, of whom 145 (4.8%, M/F 79/66) were classified as having LADA.

Discussion

We found it feasible to create a diabetes register based on medical charts in primary health care since the vast majority (95%) of the diabetes diagnoses were in accordance with the WHO criteria even though a large percentage of diabetes was classified as unspecified diabetes by the GPs. The unspecific proportion was reduced through assessment by specialists and after analysis of autoantibodies.

Table II. The 1999 WHO criteria for diabetes diagnosis.

At least one of the following criteria:

1. One diabetic[1] fasting glucose in combination with another diabetic blood glucose test (fasting, 2-h or random)
2. Diabetic result in an oral glucose tolerance test (OGTT) in combination with an additional diabetic blood glucose value collected in a fasting state or at random. If there are two OGTTs, both must be above the cut-off for diabetes
3. A random blood glucose in combination with an additional diabetic blood glucose either collected in a fasting state, 2-h or at random
4. At least one typical clinical symptom of diabetes (e.g. excessive thirst, polyuria etc.) in combination with one diabetic blood glucose collected at random

Note: [1]Cut-off for diabetic blood glucose: fB-glucose $\geq$ 6.1 mmol/L, fP-glucose $\geq$ 7.0/L; 2-h post glucose load: B-glucose $\geq$ 10.0 mmol/L (venous), $\geq$ 11.1 (capillary), plasma $\geq$ 11.1 (venous), $\geq$ 12.2 mmol/L (capillary).

Table III. Distribution of diagnoses made by clinicians, diabetes specialists, and after analysis of GAD65A.

Type of diabetes	Clinical diagnosis n (%)	Specialist diagnosis n (%)	Final diagnosis[1] n (%)
Type 1 diabetes	125 (3.1)	100 (3.1)	235 (7.2)
Type 2 diabetes	1203 (29.6)	2329 (71.5)	2501 (76.8)
Secondary diabetes	71 (1.7)	105 (3.2)	105 (3.2)
Unspecified diabetes	2219 (54.6)	338 (10.4)	31 (1.0)
Unclear diagnosis	190 (4.7)	189 (5.8)	189 (5.8)
Gestational diabetes	37 (0.9)	24 (0.7)	24 (0.7)
Not diabetes	0	162 (5.0)	162 (5.0)
IGT	221 (5.4)	9 (0.3)	9 (0.3)
No. of diagnoses	4066	3256	3256

Note: [1]Final diagnosis: diagnosis after assessment by specialist and analysis of GAD65Ab.

The high proportion of patients classified with "unspecified diabetes" could partly be due to the fact that GPs at some health care centres routinely used "unspecified diabetes", even at centres that provided high-quality diabetes care. After a re-classification by a diabetologist this classification remained in only one out of every 10 patients with diabetes. However, the proportion was further reduced after analysis of GAD65Ab, indicating a clinical use of autoantibody analysis. The question of analysing GAD65Ab on all newly diagnosed adult diabetes patients has recently been evaluated by the National Board of Health and Welfare. They concluded that at the moment there is not enough scientific evidence for a general recommendation for autoantibody analysis; however, in Southern Sweden GAD65Ab is currently analysed in clinical practice.

The diagnosis in the medical record was correct for 95% of the patients. Some of the incorrect diagnosed patients were obese and had hypertension and hyperlipidemia; thus they were at high risk of diabetes, which may have affected the clinicians' decision to diagnose them as having diabetes, even after one single glucose value above the diagnostic cut-off. These individuals might develop diabetes later on but they did not fulfil the WHO criteria for the disease at the time of their clinical diagnosis. Another potential explanation might be that these patients had already begun lifestyle interventions between the first and second time point of blood sampling for diabetes diagnosis.

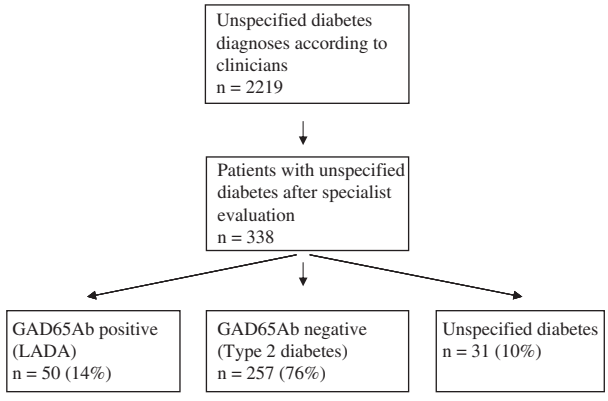

Figure 2. Flow chart of re-classification of patients with unspecified diabetes according to specialist evaluation and after measurement of GAD65Ab.

These findings of the overall validity of the clinicians' diabetes diagnoses is consistent with the observation made by Britt et al. [19], where the reliability of the morbidity defined by GPs was assessed by two observers. In line with Månsson et al. [20] we found it feasible to collect valid data, i.e. correct diabetes diagnosis, from the primary health care medical records. However, due to the misclassification, or in this study rather the absence of classification by the clinicians, solely an electronic data collection without any validation procedure would have diminished the accuracy and value of the diabetes register.

Our prevalence of LADA is consistent with the findings in the UKPDS [21], while there are studies that have reported higher prevalence of LADA in the same age group [14]. These differing results may be due to the use of different assays [18] and different cut-offs [22], as indicated by our higher prevalence when the lower cut-off for GAD65Ab positivity was used, but a difference between populations cannot be excluded.

Our register may have some weaknesses and flaws. First, not all GPs record a diagnosis for each and every visit. Second, we may have missed some patients with diabetes who were given diet and lifestyle recommendations and were not prescribed any oral hypoglycaemic agents (OHA) or insulin.

In conclusion, we have shown that it is possible to create a diabetes register based on the information in the primary health care medical records and on participation in one of the largest population-based health surveys in the world. However, the diabetes classification can be improved by expert assessment and additional laboratory analyses of autoantibodies associated with type 1 diabetes.

What is unique about DiabNorth?

DiabNorth will be the first Swedish diabetes register including more than 3500 patients with diabetes in this age-span with the possibility to perform both cross-sectional and longitudinal studies. The coverage of DiabNorth in 2007 was 3256 (28.7%) of Västerbotten County's 11 352 diabetes patients (official data from the County Council) in all ages.

Table IV. Distribution of sex, BMI, and HbA1c at diagnosis by antibody-defined diagnoses.

	T1D (n = 235)	T2D (n = 2501)	Secondary diabetes (n = 105)	Unspecified diabetes (n = 31)	Unclear diagnosis (n = 189)	GDM (n = 24)
Women (%)	46.4	39.9	47.6	29.0	47.6	100
BMI	26 (23–29)	30 (27–33)	29 (25–32)	28 (24–33)	29 (26–33)	28 (25–31)
HbA1c	8.1 (6.1–10.2)	6.3 (5.5–8.3)	7.1 (5.7–9.0)	8.0 (5.7–9.6)	5.3 (4.8–5.9)	6.7 (5.2–16.0)

Note: Data are presented as percentage and median (interquartile range). T1D = type 1 diabetes; T2D = type 2 diabetes; GDM = gestational diabetes mellitus.

In contrast with the National Diabetes Register (NDR), DiabNorth is a register designed for research while NDR is a national population-based register for assessment of quality in diabetes management. Since DiabNorth can be linked to the VIP with its repeated measurement and the medical biobank with stored blood samples, DiabNorth can be used to perform longitudinal studies regarding time trends of predictors for diabetes, as well as studying the role of different genes and biomarkers for the development of long-term complications associated with diabetes. In the NDR research is mostly done using epidemiological techniques. In this respect our register may have more similarities to the newly started research register in the county of Skåne, i.e. the "All New Diabetics in Skåne" (ANDIS, http://andis.ludc.med.lu.se/).

There are both local and national diabetes registries in Sweden developed for different purposes. DiabNorth is unique because it is based on diabetes patients in primary care, the register is run and managed by general practitioners, and many of the studies are conducted by PhD students in general practice. Thus, DiabNorth will contribute substantially to research of high international quality performed in general practice. Our observations on classification and the forthcoming results will be fed back to our clinical colleagues.

In our future plans to extend the register we have also started a process whereby we will expand our diabetes register to include patients with diabetes from the MONICA (Multinational MONItoring of Trends and Determinants of CArdiovascular Disease) Northern Sweden screening database, thus including patients from two of Sweden's largest population-based studies.

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Declaration of interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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