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Exploring novel diabetes surveillance methods: a comparison of administrative, laboratory and pharmacy data case definitions using THIN

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ABSTRACT

Background The objective of this study was to identify patients with diabetes in a comprehensive primary care electronic medical records database using a number of different case definitions (clinical, pharmacy, laboratory definitions and a combination thereof) and understand the differences in patient populations being captured by each definition.

Methods Data for this population-based retrospective cohort study was obtained from The Health Information Network (THIN). THIN is a longitudinal, primary care medical records database of over 9 million patients in UK. Primary outcome was a diagnosis of diabetes, defined by the presence of a diabetes read code, or an abnormal laboratory result, or a prescription for an Oral Anti-diabetic drug or insulin. A 2-year washout period was applied prior to the index of diabetes to avoid inclusion of prevalent cases for each case definition.

Results This study demonstrated that different case definitions of diabetes identify different sub-populations of patients. When the cohorts were observed based on any measure of central tendency, each of the cohorts were reasonably comparable to each other. However, the distribution of each of the cohorts when grouped by age categories and sex, reveal differences. For example, using pharmacy case definition results in a bimodal distribution among women, one between 1–19 year and 35–39 age categories, and then again between 60–64 and 85 years—however, the histogram becomes more normally distributed when metformin was removed from the case definition.

Conclusion Our results suggest that clinical, pharmacy, laboratory case definitions identify different sub-populations and using multiple case definitions is likely required to optimally identify the entire diabetes population within THIN. Our study also suggests that age and sex of patients may affect the indexing of diabetes in THIN and is critical to better understand these variations.

Keywords diabetes, electronic medical records, surveillance

Introduction

Diabetes is one of the most costly and burdensome chronic disease of our time and is a condition that is increasing in epidemic proportions throughout the world.[1,2] Examination of the epidemiology of diagnosed diabetes is crucial to identify determinants of disease progression and plan preventative care practices that may reduce the risk of diabetes and it is complications. Surveillance of diabetes is a necessary first step toward its prevention and control.[2,3]

Using electronic medical record (EMR) databases can reshape the practice of diabetes surveillance,[4,5] streamline reporting diabetes outcomes, improve quality[6,7] and efficiency of diabetes care delivery.[8] Primary areas of benefit are reduction in drug expenditures, improved utilization of diagnostic testing and decreased billing errors.[6] EMRs create

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and store electronic patient record that includes information from the medical history, physical examinations, laboratory results, diagnoses and drug therapies.

Thus far, a majority of case definitions being used to identify the disease cohort rely solely on read codes and drug codes, however, these algorithms vary.[9–16] A standardized case definition for identifying patients with diabetes from detailed clinical information available in EMRs, applied across multiple health systems, would be a powerful tool for conducting comparative research, monitoring trends, analyzing geographic variation and conducting surveillance of diabetes. The objective of this study is to identify those patients with diabetes in a comprehensive primary care EMR database using a number of different case definitions (clinical, pharmacy, laboratory definitions and a combination thereof) to identify and understand the differences in patient populations being captured by each definition. The clinical case definition will extract all patients with a diabetes diagnosis code in their health records, the pharmacy case definition will label all patients as having diabetes if they have a prescription for an Oral Anti-diabetic drug (OAD) or insulin in their health record, and lastly the laboratory case definition will identify all patients as having diabetes if they have abnormal Hemoglobin A1C (HbA1c) or blood glucose or oral glucose tolerance test result in their health record.

Methods

Data source and design

A cohort study was performed using The Health Improvement Network (THIN). THIN (version 2012-05) is an electronic database consisting of prospectively collected medical records from over 12 million patients in UK.[17] Patients registered in THIN are nationally representative and have a similar age, sex and mortality distribution to that of the general UK population.[18,19] Approximately 6% of the UK population is registered in THIN. Vision software (London, UK), which provides a standardized system for data collection, was adopted by over 560 THIN practices starting in the mid-1990s.[20] It is used to capture demographic data, medical diagnoses (in the form of read codes), prescriptions and laboratory data.[21] The accuracy and completeness of THIN is well documented, and has been used for epidemiological studies of several chronic diseases,[22–28] including diabetes.[9–16] Due to its large and representative nature as well as the availability of outpatient data, THIN is an ideal data set to use for exploring novel diabetes surveillance methodologies.

Ascertainment of the diabetes cohorts

The study period was 1 January 1994 to 31 December 2013. The primary outcome was a diagnosis of diabetes, defined by the presence of patient's first recorded diabetes read code, or a prescription for an OAD or insulin, or an abnormal laboratory result—the index date for a case was the date of the first diagnosis of diabetes. To minimize misclassification of diabetes, a 2-year washout was applied to exclude prevalent cases. Each of the cohorts was followed from index date until the earliest of migration out of practice, death or last data collection up to 31 December 2013. There were overlaps between each of these cohorts captured. In theory, for example, it would be expected that all individuals with a prescription of OADs or insulin would have a diabetes read code in their record, however, this was not always true as the analysis below reveal:

a. *Clinical/Diagnostic Case Definition of Diabetes*

Read classification was used to code distinct diagnoses in THIN. For the diagnostic definition, patients with diabetes were identified with a recorded read code for diabetes in the medical table. Diabetes read codes were divided into two categories, 'specific approach' [Supplementary data, Appendix A] and a 'sensitive approach' [Supplementary data, Appendix B]. The specific approach included all codes where the presence of diabetes is explicitly stated 'annual diabetes follow-up' for example. The sensitive approach was designed to capture cases where the read code implied the presence of diabetes but was not a primary code for diabetes care, for example 'education in self-management of diabetes'. Two reviewers [B.K. and D.R.] independently evaluated the inclusion and exclusion of each read code to attain a consensus for both the approaches. Read codes for gestational diabetes and drug-induced diabetes were excluded.

b. *Laboratory case definition of diabetes*

Patients meeting any of the following criteria were defined as having diabetes in the laboratory case defined cohort:

(i) HbA1c level of 6.5% or higher OR (In THIN HbA1c is measured in mmol/mol units—an HbA1c of 48 mmol/mol (6.5%) as per National Institute for Clinical Excellence (NICE)[29] and World Health Organization (WHO)[30] guidelines is used at the cutoff).
(ii) Fasting blood glucose of 7.0 mmol/l or higher OR.
(iii) Random blood glucose of ≥11.1 mmol/l OR.
(iv) Fasting Oral Glucose Tolerance Test (OGTT) of ≥7.0 mmol/l or a 2 h OGTT of ≥11.1 mmol/l.

c. *Pharmacological Case Definition of Diabetes*

Patients with at least one prescription for an OAD or insulin [Supplementary data, Appendix C] were included in the pharmacological case cohort. Metformin is used to treat Polycystic Ovary Syndrome[31] in addition to being an OAD,

hence a sensitivity analysis within the pharmacological case cohort was performed including and excluding metformin to understand it is effect on the demographics of the population being captured.

Analysis

Mean and median age at diagnosis is calculated for each cohort using the patient's year of birth. Body Mass Index (BMI) was calculated using the last collected height and weight of each patient.[32] In addition, percentage of women and smoking status is determined for each cohort. Histograms of the distribution of cases of diabetes by sex and age categories for all cohorts are graphed.

Combination

In order to obtain a more inclusive diabetes cohort all case definitions were combined using each patient's unique identification number and the operator 'OR'. The youngest age at diagnosis is used to look at the distribution of diabetes by age and sex.

For the purposes of this study, MySQL was used for database management and analyses were performed with Stata 13 (Stata Corp LP, College Station, TX, USA).

Results

Table 1 shows the demographics of the cohorts obtained using each of the five case definitions, specific read code approach, sensitive read code approach, pharmacy case definition with metformin, pharmacy case definition without metformin, and laboratory case definition. The largest cohort was extracted using the laboratory case definition. This definition also captured the highest percentage of females. The oldest cohort, with a mean age of 60, was captured using the sensitive read codes approach.

Index of diabetes by age in THIN

Diabetes in THIN by age using specific read codes

Histogram plotted of diabetes cases, using specific read codes, resulted in a slightly left-skewed histogram [Fig. 1]. More number of younger patients were picked up in this cohort compared to the sensitive approach. More number of women were captured up until 39 years of age and again those that are 75 years and older.

Diabetes in THIN by age using sensitive read codes

Using sensitive read codes resulted in a slightly left-skewed histogram. The number of males being coded with diabetes was higher compared to females except between ages 20–29 and again those older than 80 years of age.

Diabetes in THIN by age using pharmacy case definition

Histogram plotted, using pharmacy case definition, resulted in a bimodal distribution among women, similar to what was observed with the specific read codes and laboratory case definition. There were two peaks observed, one between 1–19 year and 35–39 age categories, and then again between 60–64 and 85 years; however, the histogram became more normally distributed when metformin was removed from the case definition.

Diabetes in THIN by age using laboratory case definition

A normal distribution of diabetes cases was observed when using laboratory case definition. There were more females with an abnormal laboratory test result in the early age groups, those ≤19 years and child bearing years ≤39 years,

Table 1 Diabetes in THIN by each Case Definition

	Specific approach (specific diabetes) read codes	*Sensitive approach (sensitive diabetes) read codes*	*Laboratory definition*	*Pharmacological definition*	*Pharmacological definition (w/o metformin)*
N	146 724	98 592	155 282	58 451	39 300
Female, *N* (%)	71 634 (48.82%)	44 002 (44.63%)	79 793 (51.39%)	28 854 (49.36%)	17 830 (45.37%)
Mean age at diabetes diagnosis (standard deviation)	56.82 (18.95)	60.18 (17.73)	56.21 (18.73)	55.26 (18.55)	56.50 (18.74%)
Median age at diabetes diagnosis	59	62	58	57	59
Mean BMI (kg/m^2)	26.57 (10.90)	28.30 (9.74)	26.41 (10.69)	28.48 (10.14)	27.88 (10.35)
Current smoker, *N* (%)	25 645 (17.48%)	16 859 (17.10%)	27 224 (17.53%)	10 425 (17.84%)	6 813 (17.34%)
Never smoker, *N* (%)	62 560 (42.64%)	40 558 (41.14%)	66 093 (42.56%)	23 762 (40.65%)	15 789 (40.18%)

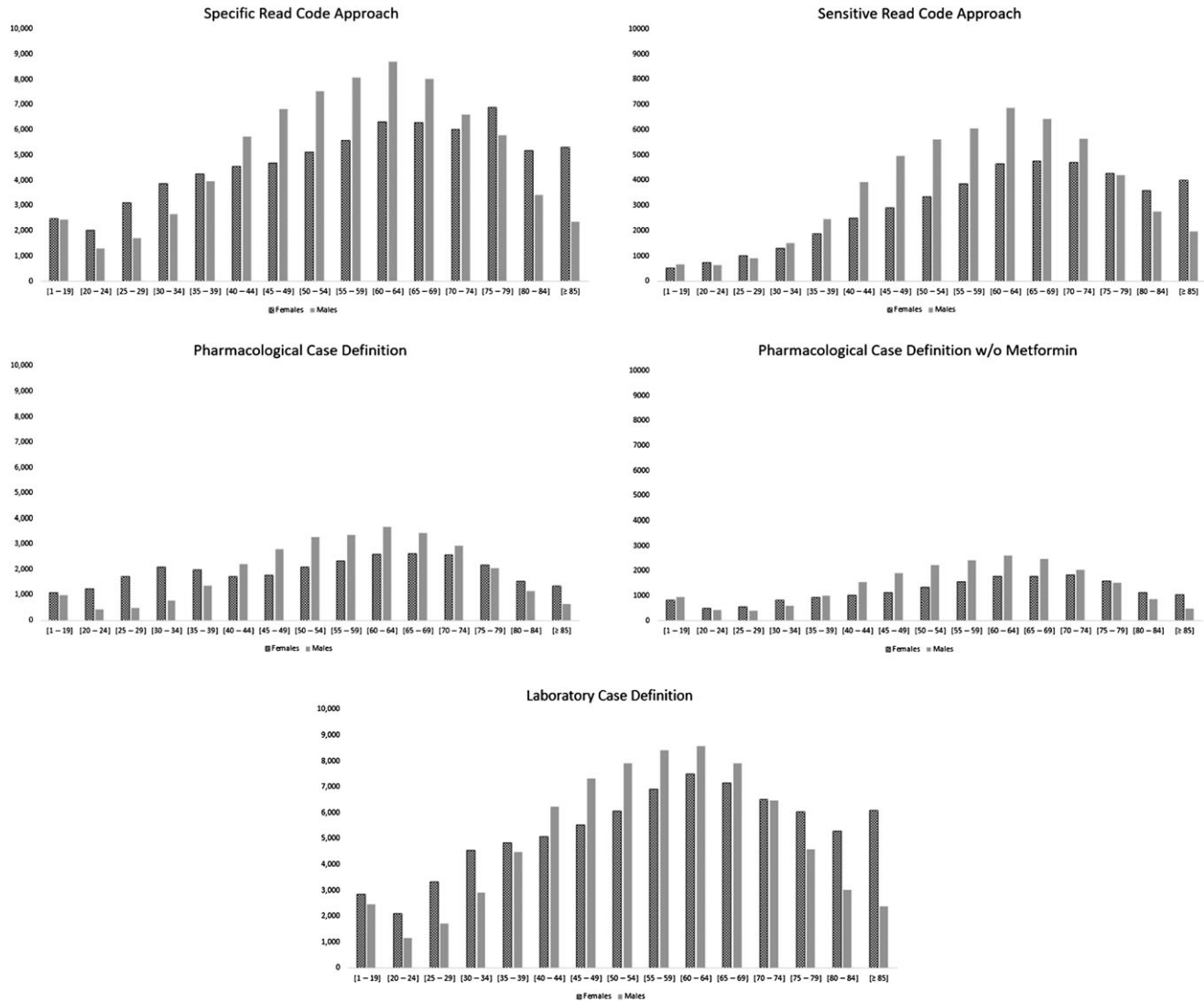

Fig. 1 Diabetes in THIN by Age Distribution for each case definition.

and again in the older age categories where age ≥75 years—this was very similar to the trend observed using specific read codes and pharmacological case definition.

Combination

Histogram plotted against age categories, using the 'OR' operator, was normally distributed [Fig. 2]. The total number of cases using this definition is 240 764 with 51% being females. The mean age at diagnosis was 56 years and the median age was 57 years. Fifty-six percentage of diabetes cases were indexed using laboratory case definition, followed by specific read codes approach comprising 31% of this cohort, 5% by pharmacy case definition, 4% by specific read codes approach, and remaining 4% by a combination of more than one case definition [Supplementary data, Appendix D].

Discussion

This study demonstrated that different case definitions of diabetes identify different sub-populations of patients in the THIN database. When observing the four different cohorts based on any measure of central tendency, each of the cohorts appeared reasonably comparable to each other. However, the size of the sub-populations varies widely, and the distribution of each of the cohorts when grouped by age categories and sex, reveal important differences. In this study, when specific read codes are used to extract the cohort of interest, it comprised of a younger patient population with a higher percentage of women compared to the sensitive read code approach.

More women being picked up by this definition maybe as a result of misclassification of those women with gestational

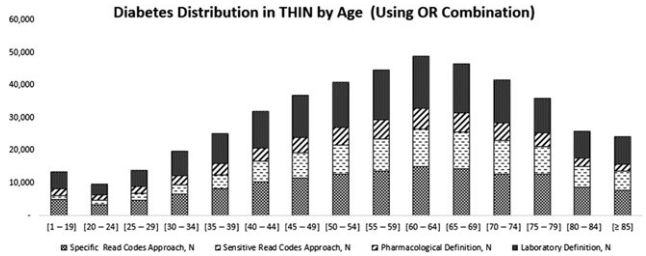

Fig. 2 Diabetes in THIN by Age using 'OR' Combination.

diabetes since the list of specific diabetes read codes includes codes such as diabetic monitoring, diabetic on diet only even though definite codes for gestational diabetes were excluded. Compared to this cohort, sensitive diabetes read codes identifies the oldest population of all the case definitions. This approach likely identifies people with more complicated diabetes given this definition included read codes for diagnosis of 'retinal abnormality' and 'foot exams' for example. These types of codes maybe used by general practitioners who are providing treatment to patients with diabetes-related complications. Though a 2-year washout period is applied to this cohort, it is possible that older people are presenting with complications. As seen in the literature, women are less likely to have hospital stays and fewer physician visits compared to men in older population.[33] The same is observed in THIN using this case definition as males make up more than half of the cohort.

Pharmacy drug data is a valuable source for measuring population's burden of disease, when clinical data are missing. There is an underlying assumption that individuals with diabetes, Type 2 in particular, are treated with lifestyle interventions, however, in this study itself it can be seen that 17% of cases would have been missed if the pharmacy case definition was not included in the 'OR' combination. This work has distinctly shown demographic differences between cohort using all OADs and the cohort removing metformin from the drug definition—this is an important outcome to recognize when using only pharmacy definition to extract a diabetes cohort.

Laboratory data is a source of health information that has potential value in diabetes surveillance, in fact the case definition (mentioned above) is referred to as the 'gold standard'.[34] Using the laboratory case definition in THIN yielded the largest diabetes cohort. However, it is important to note that the isolated use of laboratory data is likely to be suboptimal because some individuals with diabetes will be managed by physicians using only occasional glucometer testing at home or in their doctors' offices, without laboratory testing. Others maybe so well controlled that they do not have abnormal laboratory test results.[34] The reason for such a large cohort included in the study could be a result of some patients being mislabeled. Those patients may have diabetes based on elevated blood glucose measurements taken during episodes of acute illness, stress or hyperglycemia, while subsequent measurements were normal. Abnormal laboratory results were more likely to be present than clinical because of subclinical disease conditions. Lastly, an additional reason for the large cohort could be the inclusion of a population with 'pre-diabetes' using this definition. This study included HbA1c cut offs which is less sensitive but more specific and has a higher positive predictive value to identify people at risk for later development of diabetes.[35] However, the greatest forte lies in the potential use of combined data sources to optimize case detection of diabetes.[34]

Limitations

There are significant limitations to surveillance using EMR data that need to be considered, including inconsistencies in coding practices between physicians and practices that may affect the performance of case identification algorithms; incomplete data on patients' diagnoses, laboratory test results and drug prescriptions.

Another drawback of using EMRs or any clinical data is that it captures data on only those individuals who utilize healthcare. There is a notable limitation that diabetes disproportionately affects individuals of lower socio-economic status and impairs access to the healthcare system.[36] In addition, relatively healthy individuals with fewer medical care encounters are missed, resulting in decreased sensitivity of such surveillance methodologies.[37] The frequency of preventive care received by individuals with diabetes maybe overestimated if it is based on only administrative health and clinical data. Despite the limitations of using these data for surveillance to understand trends in diabetes and targeting prevention efforts, most approaches provide valuable information. Understanding the limitations of each approach and the data source being used, can enhance the effectiveness of diabetes surveillance at a population level.

Conclusion

Defining a case definition for diabetes surveillance is fundamental and requires an assessment of the objectives and logistics of the EMR being used as data source. It is fundamental to understand that each case definition by itself or a combination will affect the population being identified. THIN is an EMR with diagnoses, laboratory tests and prescriptions data. Therefore, there are three distinct ways of defining diabetes in THIN—using read codes, laboratory

test results or prescription data. Our results suggest that different case definitions identify different sub-populations. Using multiple case definitions can optimally identify the entire diabetes population within THIN. Our study also suggests that there are age and sex-related coding practices and it is important to better understand these practices and how diabetes is indexed in THIN.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online.

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Conflict of interest

None declared.

Authors' contribution

BK carried out the analysis and wrote the manuscript. Dr HQ, Dr GGK, Dr SB and Dr DR provided final approval of the version to be published. All authors read and approved the final manuscript.

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