Updated algorithms are required to differentiate type 1 from type 2 diabetes using the Virtual Diabetes Register

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The Virtual Diabetes Register (VDR) is an annually updated national register of all patients with diabetes mellitus. The VDR was designed to monitor the prevalence of diabetes in New Zealand and support quality improvement initiatives.[1,2] The register is compiled from publicly available health data based on patients' use of health services, including hospitalisation records, laboratory test results and pharmaceutical dispensing information. As of 2018, the VDR estimates that there are 253,480 patients with diabetes in New Zealand.[1] However, this is lower than the number forecast prior to 2017, due to a change in the algorithm used to define the VDR population.[3]

Although the VDR is a valuable tool in that it allows for the description of diabetes prevalence by geography, age, ethnicity and gender,[3,4] it does also have limitations. Currently, the VDR does not contain diagnosis information, and thus it is unable to discriminate between the different types of diabetes, namely type 1 diabetes (T1D) and the more common type 2 diabetes (T2D). This poses a problem if VDR data is to be used for research purposes, as often times a clinically defined population (eg, patients with T1D) is required for analysis. In some cases, this can be circumvented via the use of clinically confirmed patient registers, though these are generally restricted to a few individual district health board (DHB) databases that contain limited current up to date data rather than a national dataset. Hence algorithms using additional clinical data to differentiate between T1D and T2D are being developed to define these subset populations from the VDR. However, differentiating between T1D and T2D can be difficult, as T2D is becoming more common in youth and young adults and the onset of T1D in adulthood is becoming increasingly recognised.[5] Further, approximately 10% of patients with T1D will have negative islet cell antibody titres, and a similar proportion of patients with T2D will have mildly elevated autoantibody titres.[5] Consequently, misclassification of the type of diabetes is common in the community. Approximately one third of patients with T2D are misclassified as T1D,[6] and approximately 40% of adults with T1D are misdiagnosed with T2D.[7]

One algorithm designed to identify patients with T1D was published by McKergow et al in 2017,[8] and it has been used to define the T1D patient population in further work with VDR data.[9] However, the diagnostic accuracy of the McKergow algorithm has not been validated against a confirmed T1D clinical register. Hence, the aim of this study was to determine the accuracy of the McKergow algorithm by using it to predict which patients in the 2017 VDR dataset had T1D as compared to a known population of patients with confirmed T1D at the Waikato Regional Diabetes Services at Waikato District Health Board (WDHB) for the same time period. Ethics approval was granted for this study by the Health and the Disability Ethics Committee (ref: 17/NTB/222).

The Waikato VDR dataset used in this study included all patients registered in the national dataset and domiciled in the Waikato DHB region during 2017. As per the McKergow algorithm,[8] this included patients who died during 2017 and those not enrolled in a primary health organisation (PHO) (n=23,211). As such, this population is larger than the 21,767 reported on the VDR website,[1] as the latter excludes patients who are not alive or not enrolled in a PHO as of 31 December 2017.

The WDHB diabetes clinical register included 1,303 patients who have all had T1D diagnosed by an endocrinologist.[9] Patients in the initial WDHB dataset who were not part of the VDR extract were excluded (n=85), such that 1,218 patients were included in this study.

The McKergow algorithm was applied to the VDR data as described previously[8] but with the inclusion of additional data for 2014–2017 to account for the time period of study. This included diabetes medication dispensing data (1 January 2006–31 December 2017), hospital diagnosis and discharge data (1 January 1988–31 December 2017) and death records (2017) to determine the number of patients with T1D (Figure 1). Although not defined in the McKergow study, dispensed insulin in our study included insulin glargine, insulin isophane with insulin neutral, insulin aspart with insulin aspart protamine, insulin neutral, insulin zinc suspension, insulin neutral, insulin lispro, insulin glulisine, insulin aspart, insulin isophane and insulin lispro with insulin lispro protamine. Similarly, oral hypoglycaemics and alpha glucosidase inhibitors included metformin hydrochloride, vildagliptin with metformin hydrochloride, glibenclamide, gliclazide, glipizide, vildagliptin, pioglitazone and acarbose. Linkage between the datasets was undertaken using master National Health Index (NHI) numbers.

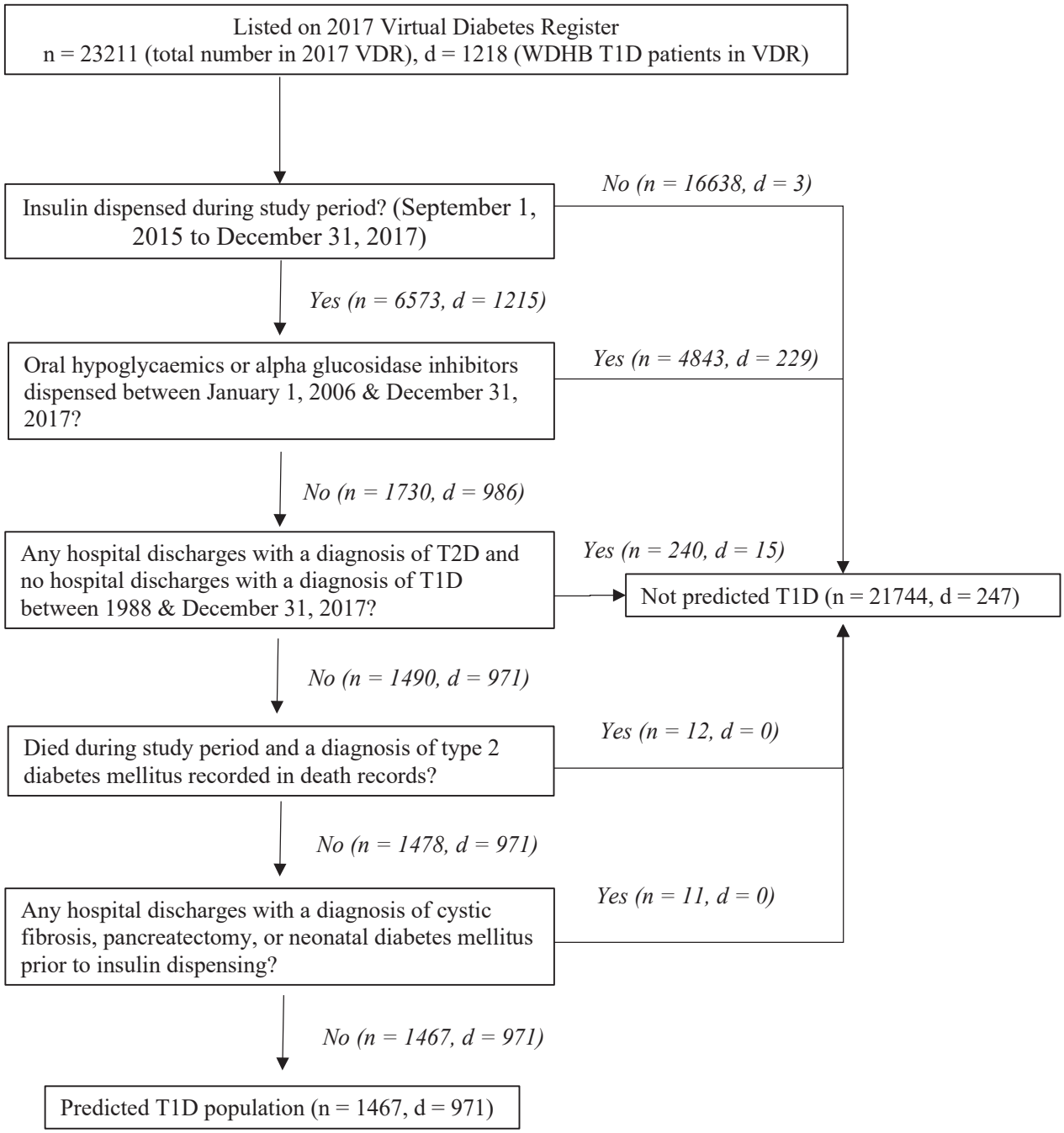
Upon running the McKergow algorithm, a total of 1,467 of 23,211 patients were predicted to have T1D. Of these, 971 had confirmed T1D as per the WDHB dataset (true positives), and 496 did not (false positives). Of the 21,744 patients who were predicted to not have T1D, 247 were recorded with confirmed T1D in the WDHB dataset (false negatives) whereas 21,497 were not (true negatives) (Figure 1). This gives the McKergow algorithm a sensitivity of 80%, a specificity of 98% and an overall accuracy of 97%—but a positive predictive value (PPV) of only 66%.

Although these values of specificity and accuracy look good, they are falsely representing the validity of this algorithm, as the overall accuracy would have still been >95% even if the algorithm had detected no cases of T1D, due to the fact that they comprise such a small proportion (~3.5%) of the VDR dataset. The currently low PPV of the McKergow algorithm is clinically significant, as shown by Wheeler et al, whose use of the algorithm underestimated insulin pump therapy by one third in Waikato patients with T1D.[9,10] Importantly, the algorithm excluded 229 of the 247 false negatives (patients with confirmed T1D) from the predicted T1D population because of their use of oral hypoglycaemic agents (Figure 1). This suggests that this may be the step in the algorithm that requires further fine tuning to improve the PPV.

However, it must be noted that, although we used the WDHB as a ground truth dataset, our study does have limitations. It is possible that a few of the false positives may have been true positives (eg, if they had never been to the WDHB regional diabetes clinic or hospital before and/or had been diagnosed in a different region before moving to the Waikato region). Further, there may be differences in the diabetes medications used in the algorithm in our study, as the medications used in the McKergow study were not defined,[8] and this may have influenced the results. Regardless, our results do suggest that the current algorithm does not appear to be accurate for differentiating T1D from T2D in the VDR.

In conclusion, due to the small proportion of patients with T1D in the VDR dataset and the large number of false positives and false negatives that were detected, the McKergow algorithm does not appear to be an overly effective or precise method for determining patients with T1D from the VDR. To ensure that ongoing T1D research in New Zealand is effective, further work is needed to define a suitable algorithm for defining subsets of patients from the VDR, including benchmarking against other known clinical datasets.

Figure 1: Predicted population of type 1 diabetes mellitus (T1D) from the 2017 VDR register (n=23,211) compared to a known WDHB clinical register of patients with confirmed T1D (d=1,218).



Competing interests:
Nil.

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