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*Published in:*  
Diabetes Care

*DOI:*  
[10.2337/dci22-0003](https://doi.org/10.2337/dci22-0003)

*Publication date:*  
2022

*Document Version*  
Peer reviewed version

[Link to publication in Discovery Research Portal](#)

### *Citation for published version (APA):*

Siddiqui, M. K., Hall, C., Cunningham, S. G., McCrimmon, R., Morris, A., Leese, G. P., & Pearson, E. R. (2022). Using Data to Improve the Management of Diabetes: The Tayside Experience. *Diabetes Care*, 45(12), 2828-2837. <https://doi.org/10.2337/dci22-0003>

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## Using data to improve the management of diabetes – the Tayside experience

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Keywords: Data linkages; diabetes management; regional health systems; epidemiology

Word count 5456

Figures 4

This is an author-created, uncopyedited electronic version of an article accepted for publication in *Diabetes Care*. The American Diabetes Association (ADA), publisher of *Diabetes Care*, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of *Diabetes Care* in print and online at <http://care.diabetesjournals.org>.

## **Introduction**

Tayside is a region in the East of Scotland and forms one of nine local government regions in the country. It is home to approximately 416,000 individuals who fall under the National Health Service Tayside (NHS Tayside) health board who provide healthcare services to the population. In Tayside, Scotland a comprehensive informatics network for diabetes care and research has been established for over 25 years, expanding more recently to a comprehensive Scotland-wide clinical care system, Scottish Care Information-Diabetes or SCI-Diabetes. This has enabled improved diabetes screening, integrated management of diabetic retinopathy, neuropathy, nephropathy, cardiovascular health, and other comorbidities. The regional health informatics network links all these specialized services with comprehensive laboratory testing, prescribing records, general practitioner records, and hospitalization records. Not only do patients benefit from the seamless interconnectedness of these data, the Tayside bioresource has enabled considerable research opportunities and the creation of biobanks. This review describes how health informatics has been used to improve care of people diabetes in Tayside and Scotland and, through anonymized data linkage, our understanding of the phenotypic and genotypic etiology of diabetes and associated complications and co-morbidities.

### **The origins of diabetes health data linkage in Tayside**

The St Vincent Declaration in October 1988 was a prescient development in diabetes care (1). The global diabetes community from government health departments and patients' organizations in Europe, the World Health Organization in Europe and the International Diabetes Federation Europe came together to agree to programmatic targets for diabetes care in relation to diabetes outcomes and complications.

It was clear however, that identification of all individuals with diabetes in the population was essential if diabetes care was to be effective and measurable and the targets of St Vincent met. In the late 1980s, registries of patients with type 1 diabetes were relatively common, but there were few if any comprehensive registries of patients with type 2 diabetes in the United Kingdom. At that time the impact of type 2 diabetes had been grossly underestimated.

To address this challenge, an interdisciplinary collaboration of general practitioners, diabetologists and senior health service managers convened in 1994 to establish a region wide population-based diabetes monitoring control system. The aim was to develop state-of-the-art information technology to achieve quality assurance of the provision of health care for diabetes patients in Tayside, Scotland (current population 416,000)(2) . The secondary purpose was to create a trustworthy approach to population-wide diabetes research – supporting clinical trials, epidemiology, health

service research and the molecular understanding of diabetes care and its complications.

In 1996 the Diabetes Audit and Research in Tayside, Scotland (DARTS) was launched (3). It was a collaboration between 278 practitioners, 78 practices and 3 health trusts or hospitals (Ninewells Hospital in Dundee, Perth Royal Infirmary in Perth, and Stracathro Hospital in Brechin) all in Tayside. Arguably, it was the first time in the United Kingdom that an entire population subscribed to a joint single strategy for diabetes care and research that spanned primary, secondary, and tertiary care, and a care community that worked with patients to agree to comprehensive data sharing for care and research.

In the first phase, eight independent data sources were used to maximize complete ascertainment of cases of diabetes. This was enabled by the fact that in Scotland every person registered with a general practitioner is given a unique identifier called the community health index (CHI) number. This enabled linkage of diabetes prescriptions, hospital diabetes clinics, data from a mobile diabetes retinopathy screening unit, biochemistry data base and the Scottish Morbidity Record (SMR01 - which is a list of discharges from hospital according coded using the ICD 9 and 10 ontologies)).

This enabled the DARTS Team to identify 7596 patients living with diabetes, with methodology validated by annual validation of case records of a random selection of general practices using linked prescription, laboratory testing and eye screening services (Figure 1). This initial record linkage study created a population-based diabetes registry that acted as the fulcrum of over 25 years of diabetes research. The clinical, audit and research utility of DARTS in Tayside, led to its adoption by the Scottish Government, with roll out across Scotland initially as Scottish Care Information – Diabetes Collaboration (SCI-DC) in 2002 and more latterly as [SCI-Diabetes](#) (4). SCI-Diabetes achieved full national coverage during 2006.

### **The status of diabetes health data linkage in Tayside**

The SCI-Diabetes clinical database now includes electronic healthcare records for all patients with diabetes in Scotland, except for <0.5% who have opted out of the system, allowing joined up care for patients with diabetes wherever they are in Scotland. This is the source of a comprehensive annual audit of diabetes care (see the 2020 Scottish Diabetes Survey (5)) and is utilized for research by the Scottish Diabetes Research Network Epidemiology ([SDRN-Epi](#)) Group (6).

However, in this review we focus specifically on Tayside – where we have the longest follow up for patients with diabetes and comprehensive data linkage to a large breadth of clinical data, and linkage to a large biorepository. Leveraging this data, the [Tayside Diabetes Managed Clinical Network](#) publish annual reports and internal clinical audit on

the status of diabetes and diabetes care for professionals and patients in this health board (7). For research purposes, the Tayside diabetes and associated linked data is managed by the Health Informatics Centre (HIC) based at the University of Dundee, which acts on behalf of NHS Tayside health board as a Scottish regional Safe Haven(8). HIC provide secure, managed access to health data for researchers (<https://www.dundee.ac.uk/hic/>). All data are available and analyzed in an ISO27001 accredited Safe Haven environment, and research projects undergo a strict governance approval process. The data are normally processed under GDPR lawful basis of public task.

Routinely collected clinical data are collected and presented in the SCI-Diabetes electronic medical record through automated linkages with a series of electronic systems. Using the Community Health Index master patient index as a unique identifier and a clearly defined clinical dataset, records are collected and linked from primary care systems , laboratory systems , retinopathy screening, the Scottish Ambulance Service, hospital inpatient systems , ward-based blood glucose systems and others (as seen in Figure 1). These data are updated at least once every twenty-four hours, with laboratory data updated every four hours. Hospital clinicians across Scotland use SCI-Diabetes as their sole electronic medical record for diabetes care, contributing routine data and screenings directly into the system front-end. Key features of the platform include specialist functionality for primary and secondary care, podiatry, dietetics, diabetes specialist nursing and inpatient management. A flowchart demonstrating the combination of diabetes care data from different sources is shown in Figure 1.

Patients are added to SCI-Diabetes directly through patient registration forms where diabetes type and date of diagnosis are collected. In parallel, as diagnoses are recorded in primary care systems, these records will also be collected and processed to ensure that no patients are missed. As soon as an individual is registered with a General Practitioner in Scotland and a diabetes diagnosis is recorded, their data will be passed to SCI-Diabetes. The active population is maintained through linkage to the National Community Health Index service, which provides notifications as people move around Scotland, leave the country completely, or pass away. Consequently, there is very limited missing data. As such if the data are collected, they will be available in the SCI-Diabetes system.

For research purposes, many other national and local datasets can be linked, including: records of births and deaths, prescribing records, primary care data, laboratory testing, hospitalizations, surgeries and procedures, echocardiography, vascular laboratory, renal , cancer , mental health registries, Scottish Ambulance Services, and Accidents and Emergencies (or Emergency Room) admissions. These are detailed in the Supplementary appendix 1. Additionally, a flow chart detailing important stages in the development of this resource is provided in supplementary Figure 6.

## **Diabetes in Tayside: Prevalence, prescribing and polypharmacy**

### *Individuals with diabetes*

In Figure 2 we show the number of individuals living with type 1 and type 2 diabetes in the Tayside area in each calendar year beginning in 1996 through to 2020. The data show an increase in the number of people with type 2 diabetes over the years until 2020. The stagnation observed in 2020, is most likely reflecting the impact of the COVID-19 pandemic on the detection and diagnosis of diabetes. For Type 1 diabetes the prevalence has been largely constant from 2006; the increase prior to this could reflect improved ascertainment and diagnosis.

### *Prescribing patterns and polypharmacy*

Prescribing history is available for all individuals residing in Tayside. Using this prescribing data, Figure 3 shows that the use of insulin has remained constant over the last 20 years, with a shift to increase in the use of triple therapy with less diet treated, mono and dual treated individuals. Figure 4 highlights the major polypharmacy experienced by patients – in 2019, over and above glucose lowering drugs, 70% of patients with type 2 diabetes were on 5 or more drugs, and 30% were on 10 or more drugs. The average number of medications used by this population of individuals is provided in Figure 4b. As observed, from 2005 to present, the average number of drugs individuals with type 2 diabetes was 5.

## **Use of health data to improve diabetes care in Tayside**

### *Clinical decision support*

The SCI-Diabetes system incorporates a guideline-driven clinical decision support, which was developed and trialed in Tayside prior to wider rollout across Scotland (9). This clinical decision support tool prompts for tests (lab or screening) to be requested if they have not been recorded in the last 15 months, and prompts regarding compliance with national guidelines. For example, if a patient has established microalbuminuria but is not treated with an ACE inhibitor (ACEi) or Angiotensin receptor blocker (ARB) a pop up will appear as the patient's records are accessed prompting the clinician to consider an ACEi or ARB. More simply, an alert will appear reminding the clinician that foot or eye screening is overdue. This simple support tool doubled the likelihood of a patient being screened for most complications and resulted in improved HbA1c.

### *My Diabetes My Way – a patient portal*

My Diabetes My Way ([MDMW](#)) is the NHS Scotland online portal supporting self-management for people living with diabetes across Scotland (10). Development began in Tayside in 2006 following funding received from the Scottish Diabetes Group, with subsequent launch of the service in October 2008. While initially launched as a web-based collection of interactive information resources, the service has evolved with the implementation of online records access for patients (December 2010), the introduction of a dedicated mobile app in August 2018 and online structured eLearning courses throughout 2019. Online records access has been a major eHealth objective for the Scottish Government, with MDMW offering patients access to a focused set of their SCI-Diabetes data alongside information to explain clinical measurements and links to information that is tailored to their condition (e.g. personalized information based on their current foot screening status). Patients can also contribute to their record by supplying home recorded results (6724 patients; 436379 records by the end of 2021), patient-reported outcome measures (2475 patients; 4828 forms) and personal goals (2956 patients; 11399 records). Many diabetes devices also connect to the platform, including blood glucose meters and continuous glucose monitors, while activity can be tracked through a collaboration with Fitbit (1216 users by end of 2021). The service reported 32,743 active users at the end of 2021, with evaluation showing improved patient satisfaction and a more recent health economic analysis demonstrating significant cost savings and improvements in quality of life associated with use of the service (11,12). An example screenshots from MDMW is provided in Supplementary Figure 1-5.

### *Better diagnosis of Type 1 diabetes*

Historically, diagnosis of Type 1 diabetes has largely been made on clinical grounds, which has led to some patients being misdiagnosed as Type 1 diabetes. In the UNITED(13) study, patients with diabetes diagnosed under the age of 30, still currently under the age of 50, from Tayside and the Exeter region, were systematically screened using a pipeline that included urinary c-peptide:creatinine ratio, pancreatic autoantibodies and a monogenic next generation sequencing panel. We showed that of 1365 patients, 386 had measurable insulin secretion; of these 216 were pancreatic autoantibody negative; of these 17 had monogenic diabetes (13). The remaining 199 included patients with type 1 diabetes, type 2 diabetes and other forms of diabetes. Some patients with monogenic diabetes and type 2 diabetes were able to stop insulin – some of whom had been on insulin for many years. The clinical utility and importance of c-peptide testing was highlighted by research from Mark Strachan and colleagues in Lothian, Scotland, who tested a random serum c-peptide in 859 individuals with a clinical diagnosis of type 1 diabetes. They showed that 114 (13.2%) had C-peptide  $\geq 200$  pmol/L and reclassified the diagnosis non-type 1 diabetes in 58 individuals (6.7%

of the tested cohort), with most of these being reclassified to type 2 diabetes. Overall, 1.5% successfully discontinued insulin, while a further 1.9% had improved glycaemic control following the addition of co-therapies (14).

This work, among others, has established the clinical utility of c-peptide testing in patients with type 1 diabetes and has led to a national diagnostic pipeline for type 1 diabetes – we believe a first in the world. Importantly, the testing pipeline has been embedded within the SCI-Diabetes system to prompt c-peptide testing in those diagnosed more than 3 years previously, antibody testing in those who have retained c-peptide secretion, and the use of monogenic diabetes gene sequencing and derivation of a type 1 diabetes genetic risk score. In this way we hope that all patients with diabetes in Scotland will be accurately diagnosed and appropriately treated.

### *Type 1 diabetes, use of technology and glycaemic control*

Glycemic trends have improved over the last decade in Scotland based on an analysis of 30,717 people with type 1 diabetes, registered anytime between 2004 and 2016 in the national diabetes database. Overall, we reported that median (IQR) HbA1c decreased from 72 (SD: 21) mmol/mol in 2004 to 68(SD:21) mmol/mol in 2016. The largest reductions in HbA1c in this period were seen in children, from 69 (SD:16) mmol/mol to 63 (SD:14) mmol/mol, and adolescents, from 75 (SD:25) mmol/mol to 70 (SD:23) mmol/mol (15). In this population improvement in HbA1c appears to be the result of greater use of technology. Of the 4684 individuals with type 1 diabetes who commenced CSII between 2004 and 2019, HbA1c was shown to decrease after CSII initiation, with a median within-person change of -5.5 mmol/mol (IQR -12.0, 0.0), while the crude DKA event-rate was also significantly lower in post-CSII person-time compared with pre-CSII person-time: 49.6 events (95% CI 46.3, 53.1) per 1000 person-years vs 67.9 (64.1, 71.9) (16).

More recently, we have also documented population level improvements in glycemic control following the widespread introduction of flash glucose monitoring (FGM) (17). At the time of analysis, the prevalence of ever-FGM use had increased to 45.9% of the type 1 population. Use varied between 64.3% among children aged <13 years vs 32.7% among those aged ≥65 years; and 54.4% vs 36.2% in the least-deprived vs most-deprived quintile. Overall, the median (IQR) within-person change in HbA1c in the year following FGM initiation was -2.5 (-9.0, 2.5) mmol/mol, with this change varying markedly by pre-usage HbA1c: -15.5 (-31.0, -4.0) mmol/mol in those with HbA1c > 84 mmol/mol [9.8%]. Interestingly, benefit of FGM was found in all age bands, sexes and socioeconomic strata, and there were major reductions in rates of DKA and severe hypoglycemia (17). Taken together these findings show population benefit in real-world clinical practice of technologies in Type 1 diabetes and that, if their use was more



widespread it might be possible to address some of the health inequalities that have emerged in health care delivery.

### *Digital retinal imaging*

The ability to collect and link data on large numbers of patients from different sources permitted the evaluation of retinal photography when it was introduced as an alternative to direct ophthalmoscopy. In an early study on community based retinal screening in 2112 patients, non-mydratic photography identified around 5% of people with diabetes as having previously unrecognized retinopathy compared to previous checks using direct ophthalmoscopy (18), especially in rural areas (19). The 'new' process also seemed acceptable to people with diabetes (18). This data helped accelerate the adoption of retinal photography which in turn accelerated the development diabetes clinical registers due to the need for accurate patient information at a practical patient interfacing level. This helped patient research such as DARTS and SCI-Diabetes, and their use for more general diabetes care.

As techniques in retinal photography developed and became digitalized, regional retinal screening programs became established. Linked Tayside SCI-diabetes data demonstrated that rates of retinopathy declined with time from 28% to 24% and referral rates to ophthalmology decreased from 5.9% to 3.1% from 2002 to 2004 (20). **This was achieved** by screening previously unreached patients despite an increasing incidence of diabetes. The rates of retinopathy were similar to other parts of the UK such as Liverpool (21) and showed a lower incidence than seen in the landmark Wisconsin epidemiological study of diabetic retinopathy (WESDR) which was one of the earliest epidemiological studies on retinopathy from 20 years earlier (22). **During the interim** diabetes care had improved. From 2001 to 2006 there was a 2.5 fold reduction in the percentage of people with diabetes receiving either any laser, or incident laser treatment in Tayside (23) reflecting improved diabetes management and new retinal screening modalities. This data was some of the first in the world to show a reduction in the use of retinal laser in a real-world population setting, and was before anti-VEGF treatment became generally used in the UK. This was followed by reductions in blindness rates (24) resulting in diabetes no longer being the commonest cause of blindness in the working age group in the UK.

Demonstrating reductions in use of laser and blindness using the new digital retinal screening resulted in the program becoming a recognized national screening program in 2006. Population-based data helped identify novel risk factors such as social deprivation (25), and that one missed appointment was associated with a 3-fold increased risk of needing laser photocoagulation emphasizing the need for good population coverage (25). Ongoing work linking data across all Scotland, Wales, Northern Ireland and seven regions in England reviewed outcomes in 354,549 people

with diabetes which helped refine the screening program by showing that it was safe for patients with no retinopathy over two successive years of screening to have their screening interval increased to two yearly (26). This policy has now been introduced in Scotland to make the program more efficient at a time when the prevalence of diabetes continues to increase. This was particularly valuable in the recent covid pandemic when retinal screening capacity was greatly reduced.

Thus, the Tayside and Scottish population-based data has helped validate and implement non-mydratic retinal photography which is now a national screening program in many nations. Data has shown a decreasing rate of referral to the eye clinic and a decreasing need for laser photocoagulation as a result of screening. Data has also helped adapt the program to offer two-yearly screening for a select group of patients.

### *Foot screening, ulceration and amputations*

One of the earliest population-based studies on amputation estimated rates across Tayside to be around 2.4 per 1000 people with diabetes, which was 12-fold higher than the population without diabetes (27). As SCI-Diabetes became used across Scotland it became possible to monitor national amputation rates using linked data sets such as diabetes records, hospital admissions, primary care records and others as described before. Scotland was one of the first nations to report a falling amputation rate from a full national dataset, with a decrease from 3.04 to 2.13 per 1000 people with diabetes undergoing any amputation between 2004 and 2008 (28). This represented a 29.8% decrease in all diabetes-related amputations with a 40.7% decrease in major amputations. Similar data was reported from the US about the same time (29)

Collection of foot ulcer data is more challenging than amputation data, as foot ulcer care is delivered by so many diverse clinical groups across primary and secondary care. One of the best studies examining ulcer incidence in NW England involved telephone follow up of 9710 patients previously selected to be screened in the community (30). Of the two thirds of patients who could be contacted for follow up, 2.2% self-reported developing an ulcer each year. It is possible that patients with less severe diabetes, or shorter duration of diabetes may have been less likely to be recruited, and so it is possible this may have represented an overestimate. Recent Scotland wide data, using data linkage to identify all ulcers from multiple sources reported an annual foot ulcer incidence of 1.1%, with 0.7% being first time ulcers (31). Although this may be an underestimate it represents one of the first population-based national estimates of foot ulceration. These data also showed that patients with foot ulcers are at much greater risk of death than amputation (5.3-fold higher in T2 diabetes and 2.4-fold higher in T1DM (30)) indicating the essential nature to focus on treating cardiovascular risk factors for people with foot ulcers.

Foot risk stratification has become increasingly used in healthcare settings to help target the use of scarce resources such as podiatry to where it is needed the most. Early Tayside-based SCI-Diabetes database studies enabled foot risk stratification to be validated. In Tayside, 3526 patients were followed up, and patients deemed to be at high risk according to a simple clinical algorithm were 80-fold more likely to develop an ulcer during 1.7 years of follow up (32). Possibly more importantly, low risk patients had a 99.6% (95%CI: 99.5-99.7%) chance of remaining ulcer free, indicating that it should be safe to direct resources to patients at higher risk. A follow up study of 7184 patients confirmed the findings and showed the risk stratification tool also predicted healing in those who did develop an ulcer (33). These studies have been confirmed by others with more detailed (34) and less detailed clinical assessments (35). Like patients with ulcers, those with high risk feet are 9-fold more likely to die than undergo an amputation according to population-based Scottish data (36).

People with foot disease tend to be treated in many different locations, such as specialist diabetes, vascular and orthopedic clinics, as well as outpatient general and specialist podiatry services. This makes collecting reliable epidemiological data particularly challenging. SCI-Diabetes collates data from multiple sources such as linking diabetes clinic information, with outpatient podiatry and surgical procedure and outcome that overcomes many of these problems. Data linkage enables the SCI-Diabetes dataset to be supplemented and cross-validated

Thus, Tayside and Scottish population-based data has helped validate foot risk stratification systems that are now widely used in practice, helping patients with the greatest need to have priority for scarce resources such as skilled podiatrists. The data has also helped define ulceration and amputation rates and document declining amputation rates

### **Use of diabetes health data to improve our understanding of diabetes**

Tayside diabetes health data has been used extensively over the last 20 years to help provide insight into the causes and consequences of diabetes, the risks of micro and macrovascular complications and pharmacoepidemiology. Here we highlight just a few examples of published research that have used this population data, linked prescribing, electronic health records, and genetic studies from bioresources.

## *Retinopathy and nephropathy in type 2 diabetes*

*Capitalizing on the retinal screening efforts in Tayside, epidemiological studies have explored the role of blood pressure and glycemic exposure with the risk of progression of retinopathy(37), as well as novel biomarkers of retinopathy progression(38). Recently, retinal images from the screening program have been subjected to a semi-automated artificial intelligence platform – VAMPIRE (Vascular Assessment and Measurement Platform for Images of the Retina). This helps classify features of morphology such as vessel tortuosity and fractal dimensions. Researchers in Tayside have demonstrated that features of retinal morphology are able to predict cardiovascular risk independent of polygenic risk scores and traditional clinical risk factors (39). Additionally, biomarker studies for the diabetic nephropathy have also been carried out in Tayside (40). Recently, these data were used to establish the higher rate of acute kidney injury (AKI) in individuals with type 2 diabetes compared to those without diabetes. However, it was found that decline in renal function following an AKI was slower in those with diabetes (41). HbA1c trajectories in T2D*

The rate of glycemic deterioration from diagnosis of T2D in a real-world cohort was modelled using a linear mixed model adjusting for drug exposure over time. We showed the rate of glycemic deterioration was a 1.4 mmol/mol increase in HbA<sub>1c</sub> (95%CI:1.3,1.4) per year (42), but with little progression in the elderly (those >70 years old at diagnosis), and more rapid in those with younger age and low HDL-Cholesterol. These data have been used to demonstrate how a younger age of onset and a poor lipid profile are predictors of glycemic deterioration (42,43). More recently, these data have been used to demonstrate how >60% glycemic variability (HbA<sub>1c</sub> Variability Score -HVS- defined as visit-to-visit changes >5.5mmol/mol) is associated with increased risk of cardiovascular and microvascular complications in people living with type 2 diabetes (44).

## *Linkage to bioresources – insights into biology and pharmacogenetics*

As of January 2022, over 24,000 individuals (comprised of 9,000 individuals who do not have diabetes, and 15,000 individuals with T2D) have genome-wide array data available as part of the GoDARTS and SHARE biobanks (45,46). While GoDARTS (Genetics of DARTS) is limited to individuals living in the Tayside and Fife regions of Scotland, SHARE is a Scotland-wide resource. All individuals with diabetes in GoDARTS or SHARE are part of the SCI-Diabetes system, while those without diabetes are members of the local population. All participants have linked prescribing, electronic health data, and specialist registry data. Genetic data is available from genome-wide arrays with imputation performed against both 1000Genomes and the Haplotype Reference Consortium. With longitudinal linkage of >20 years of prescribing,

biochemistry and electronic health data this is an unparalleled resource for the study of the genetics of diabetes, heart disease, chronic kidney disease etc. GoDARTS has been the substrate of over 135 original research publications and has an h-index of 70. A comprehensive list of publications using GoDARTS as either the primary or contributory data source can be found at [[www.researcherid.com/rid/K-9448-2016](http://www.researcherid.com/rid/K-9448-2016)] (Researcher ID: K-9448-2016)(45).

GoDARTS is part of global consortia in the study of type 2 diabetes: including Wellcome Trust Case Control Consortium (WTCCC) and Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC). Through these consortia, GoDARTS has contributed to key studies including the discovery of risk loci for: type 2 diabetes (47–52) glucose homeostasis (53) and glycemic traits (54). GoDARTS is now part of the Accelerated Medicines Partnership Type 2 Diabetes Knowledge Portal which is an open-source repository for genome-wide data from all major type 2 diabetes studies (55). This resource allows researchers to look up phenotypes (e.g. fasting insulin) and find all genetic association results, and conversely, allows the investigation of all known phenotype associations for a given genetic variant or gene. Data from the Tayside bioresource has also contributed to the trans-ethnicity discovery of the greater genetic burden of beta-cell dysfunction in Asian Indians compared to white Europeans as part of the India-Scotland Partnership for Precision Medicine in Diabetes (INSPIRED) (56).

Due to linkage to prescription encashment (meaning the collection of a prescription from a pharmacy by the patient) data, GoDARTS has also enabled research into the genetics of drug response, i.e. pharmacogenomics. GoDARTS has been central to the genome-wide discovery of variants associated with response to metformin (*ATM* and *GLUT2*-encoded by *SLC2A2*) (57,58) Using GoDARTS data researchers observed that the heritability of metformin response was 34% (95CI:1-68). (58,59). Recently the study led a multi-centre GWAS of glycemic response to sulfonylureas identifying variants in *SLCO1B1* and *GXYLT1* (60–62). This study showed that heritability of response to sulfonylureas was between 26-48%. Interestingly, the study demonstrated a variant in *SLCO1B1* was the substrate of an interaction between statin use and response to sulfonylurea therapy, where variant carriers who were also on statin therapy had limited response to sulfonylureas. Such studies have played a key role in laying the groundwork for precision medicine in diabetes care. Additionally, GoDARTS has been used for candidate gene studies of response to metformin (*SLC29A4* and *SLC29A1*) (63) and thiazolidinediones (*CYP2C8* and *SLCO1B1*) (64). Genetic variants associated with statin response (e.g. *LPA*, *HMGCR*) and adverse drug reactions to statins have been discovered and validated in GoDARTS (*SLCO1B1* and *LILRB5*) (65–68), and the study is a key contributor to the Genomic Investigation of Statin Therapy (GIST) consortium (69). Exome sequencing of GoDARTS samples led to the discovery of common and rare variants in the gene *F5* being associated with increased risk of ACE-

inhibitor or ARB-induced ADRs. The recent availability of exome sequencing data allows for the investigation of the role of rare variants in pharmacogenomics and other disease areas.

### **The future use of diabetes health data to change clinical care**

As outlined, in Tayside we have a comprehensive electronic medical record system that is used for all diabetes healthcare encounters, and is accessible by patients. The available data is anonymized and used for research and linked to a large variety of other clinical and biobank data. However, the potential for this data to inform on and improve clinical care is huge and largely untapped. One such area is in clinical decision support, and the use of AI methods to develop powerful prediction models. For example, the extensive longitudinal record data for prescribed drugs, BMI, HbA1c can be used to develop prediction models for 'best drug' based upon predicted HbA1c reduction, weight gain/loss and side effects and these predictions can be used by the clinician and patient to inform on clinical care. Given the low cost of genotyping arrays (less than the cost of a chest x-ray), soon genetic data will be embedded in the medical records and support pharmacogenetic based prescribing in diabetes. This vision is about to become reality in Tayside where, with £2.8M of funding from the Scottish Government (Chief Scientists Office) precision diabetes care will soon be implemented. We are developing an intelligent Diabetes (iDiabetes) platform that will include enhanced patient phenotyping including the use of genetic risk scores and measurements of NTpro-BNP, hsTroponin, and liver fibrosis markers as well as potential drug response prediction tools to support more precise prescribing. We will also be using the existing clinical information intelligently – to flag to clinicians and patients about risks of hypoglycemia, poor adherence to medication and declining renal function. All precision recommendations and risks will be made available to people with diabetes via an iDiabetes page on the My Diabetes My Way patient portal.

### **Conclusion**

In this review we have described a 25-year journey, from a Diabetes Audit and Research database in Tayside, to a comprehensive clinical system covering all of Scotland and enabling joined up care, for patients (via My Diabetes My Way), and for primary and secondary care wherever someone with diabetes is cared for in Scotland. This has resulted in improved diabetes care and improved diabetes outcomes. This comprehensive clinical tool has also been the foundation for extensive contribution to our understanding of the causes and consequences of diabetes. Yet with the increasing availability of data and the exponential growth of computational performance and data science, it seems likely that we are just at the beginning of the journey.

## Acknowledgements

We would like to acknowledge Magalie Guignard-Duff and Dr. Louise Donnelly for providing data aggregates. The authors would like to acknowledge the residents of Tayside who have actively participated in diabetes research. We are grateful the general practitioners, the Scottish School of Primary Care for their help in recruiting participants, and to the whole team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. Data provision and linkage was carried out by the Health Informatics Centre, University of Dundee (HIC: <https://www.dundee.ac.uk/hic> ) with analysis of anonymized data performed in an International Organization for Standardization 27001 – and Scottish Government accredited, secure safe haven. HIC standard operating procedures have been reviewed and approved by the NHS East of Scotland Research Ethics Services, and consent for this study was obtained from the NHS Fife Caldicott Guardian. We would also like to acknowledge NHS Tayside the original data owner.

GoDARTS is funded and supported by the Wellcome Trust Type 2 Diabetes Case Control Collection (072960/Z/03/Z, 084726/Z/08/Z, 084727/Z/08/Z, 085475/Z/ 08/Z, 085475/B/08/Z) and as part of the EU IMI-SUMMIT programme). Tenovus Scotland and Diabetes UK grants. SHARE is NHS Scotland Research (NRS) infrastructure initiative and is funded by the Chief Scientists Office of the Scottish Government. Additional Funding and initiation of the spare blood retention at NHS Tayside was supported by the Wellcome Trust Biomedical Resource Award Number 099177/Z/12/Z. Additional genome-wide array data was funded by the National Institute for Health Research (NIHR) (INSPIRED 16/136/102) using UK aid from the UK Government to support global health research. These studies comply with the Declaration of Helsinki.

Restrictions apply to datasets. The data sets presented in this article are not readily available as they contain individual-level identifiable information. All analysis of anonymized data are performed in an International Organization for Standardization 27001 – and Scottish Government accredited, secure safe haven. Data requests can be initiated by contacting corresponding author.

## Figure legends

*Figure 1. The flow of data related to diabetes care in Scotland. This graph shows how the confluence of data from the National Health Service (NHS) and the Scottish Diabetes care network results in linkages across the spectrum of care.*

*Figure 2. Bar plots showing the total number of individuals in each calendar year who have type 1 diabetes and type 2 diabetes.*

*Figure 3. Scatter plot (with locally estimated scatterplot smoothing or LOESS) showing the proportion of individuals with type 2 diabetes receiving mono-therapy (in olive green triangles), dual-therapy (light green squares), triple-therapy (blue crosses), insulin (pink crossed squares), and finally those only advised non-pharmacological measures (orange circles). Individuals prescribed insulin in addition to other diabetes therapies are removed from dual- and triple-therapy groups and presented under the insulin therapy category.*

*Figure 4. Polypharmacy in type 2 diabetes. Figure 4a shows the proportion of individuals with diabetes on 5 or more or 10 or more concurrent therapies. Figure 4b shows the types of drugs prescribed in patients with type 2 diabetes mellitus in Tayside and Fife in 2019. This excludes glucose lowering treatments.*



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