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Temporal HbA1c patterns amongst patients with type 2 diabetes referred for specialist care: Data from the S4S-DINGO-Diabetes Informatics Group

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ABSTRACT

Aims: To evaluate the achievement of HbA1c targets in patients with type 2 diabetes mellitus in specialist practice.

Methods: This audit was undertaken by members of the S4S Diabetes Informatics Group (DINGO), a consortium of Australian endocrinologists in private practice who contribute de-identified data from their electronic medical record, *Audit* 4 (Software 4 Specialists, S4S, Australia & New Zealand) for audit purposes. Data from patients with type 2 diabetes was extracted. Inclusion criteria were: initial age < 70 years, baseline HbA1c > 7% (53 mmol/mol), with at least another HbA1c recorded in the next 2 years, and a minimum of 2 years follow-up. Data was analysed using a linear mixed effects model.

Results: Of the 4796 patients in the dataset with type 2 diabetes mellitus, 1379 patients fulfilled inclusion criteria. The median age at initial consultation was 57 (49–64) years. The median baseline HbA1c was 8.7 (7.8–9.8)% (72 mmol/mol). There was a 1.0% reduction in HbA1c to 7.7 (7.1–8.6)% (61 mmol/mol) ($p < 0.0001$) in the first 3–6 months following referral, after which there were no further changes. The initial reduction was maintained with minimal loss of control at 4 years. By 3–6 months, 24% of patients achieved the target HbA1c.

Conclusions: Referral of patients with type 2 diabetes to an endocrinologist reduces HbA1c, and the effect is sustained over the medium term; however only a minority of patients reach targets.

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1. Introduction

One of the foremost aims of endocrinologists treating diabetes is the amelioration of hyperglycaemia in an attempt to reduce complications. Currently, the Australian Diabetes Society recommends a target glycated haemoglobin (HbA1c) level of ⩽7.0% (53 mmol/mol) for most patients, with individualisation of glycaemic targets depending on patient-specific factors [1]. It is known from randomised clinical trials that tight glycaemic control can prevent the onset and progression of end-organ complications in both type 1 and 2 diabetes [2,3]. However, Australian data suggests that achieving these targets may be difficult in routine clinical practice. In the primary care setting, only 42% of patients were able to reach a glycaemic target of ⩽7% [4]. In this population, those with poor glycaemic control (defined as HbA1c ⩾ 8.0%) usually represent the most complex of patients, with a longer duration of diabetes, and more complications compared to those achieving adequate levels of glycaemic control [5]. It is this subset of patients who are commonly referred to endocrinologists. However, previous studies suggest that patients under specialist care in hospital-based diabetes clinics may also fail to achieve prescribed HbA1c targets [6]. Similarly, in a multicentre study that examined the degree of HbA1c reduction after commencement of insulin in routine clinical practice, only 32.1% of patients achieved an HbA1c < 7% (53 mmol/mol) over 12 months [7]. Currently, there is a lack of data assessing the achievement of glycaemic targets in private practice. Thus, this audit was designed to evaluate the achievement of HbA1c targets in patients with type 2 diabetes mellitus, and its changes over time following specialist referral.

2. Materials and method

This retrospective and longitudinal audit was undertaken by members of the S4S Diabetes Informatics Group (DINGO), a consortium of Australian endocrinologists in private practice who periodically contribute de-identified data from their point of care electronic medical record, *Audit* 4 (Software 4 Specialists, S4S, Australia & New Zealand) for the purpose of understanding patterns of care and outcomes in real world clinical practice. Patients seen in Australian private endocrine practice are referred at the discretion of general practitioners (primary care physicians); these patients are usually complex and referred because they are failing to achieve glycaemic targets or have diabetes related complications. The referred group encompass the full range of socioeconomic status and include both fee paying and non-fee paying (funded by the Medicare program) patients. The contributing clinicians maintain their own databases and include both single practitioner and multi-practitioner sites. Following agreement on a protocol addressing a clinically important research question, and with the permission of each DINGO member, a single data cut is made in which specific data is extracted at each site where it is de-identified and encrypted before being sent over the internet to a central server for data aggregation. A copy of the individual site's exported data is maintained locally on their own Audit4 database. DINGO studies are necessarily retrospective and observational, but with the flexibility of extracting repeated observations from the entire historic electronic medical record they may be cross-sectional or longitudinal.

The data cut for this audit was made in February 2013 from eight sites comprising 15 endocrinologists covering the states of New South Wales and Victoria. Inclusion criteria included: men and women with type 2 diabetes mellitus, initial age at presentation <70 years, baseline HbA1c > 7% (53 mmol/mol), with at least another HbA1c recorded in the next 2 years, and a minimum of 2 years follow-up. The age cut-off of 70 years was included as there is a higher likelihood of accepting higher individualised HbA1c targets for older patients. Data extracted from the software included age, gender, initial HbA1c and subsequent values up to 4 years from initial consultation, initial weight and body-mass index (BMI), blood pressure, lipids, blood glucose levels (BGLs), smoking status (ever smoked), microalbuminuria, and diabetic medications at first and last visit in the period of data extraction. If entry criteria regarding insulin use at baseline was absent, these patients were assumed not to be on insulin treatment at baseline. Ethics approval was obtained through the Western Sydney Local Health District Human Research Ethics Committee.

2.1. Statistical analysis

Analysis was conducted with SPSS version 22.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were employed to describe baseline characteristics. A linear mixed-effects model was utilised to analyse changes in HbA1c over time, due to a significant number of patients lost to follow-up after 3–6 months. Univariate logistic regression was used to determine predictors of achieving an HbA1c ⩽ 7% (53 mmol/mol) at 6–12 months. These included age, gender, duration of diabetes, baseline HbA1c, BMI, systolic blood pressure, total cholesterol, fasting BGL, smoking status, frequency of review, and baseline insulin use. Predictor variables found to have a p-value < 0.1 were then entered into a multivariate logistic regression model.

3. Results

3.1. Patient characteristics

Of the 4796 patients in the dataset with type 2 diabetes mellitus, 1379 patients fulfilled inclusion criteria. Baseline characteristics are described in Table 1. The median (interquartile) age at initial consultation was 57 (49–64) years. Fifty-eight percent were male and 42% were female. The median (interquartile) duration of diagnosed diabetes was 9 (4–15) years. The median (interquartile) baseline HbA1c was 8.7 (7.8–9.8)% (72 mmol/mol) and BMI was 31.7 (27.4–36.3) kg/m^2. According to BMI criteria, 84% of patients were overweight or obese (Table 1). The median (interquartile) albumin to creatinine ratio was 1.4 (0.7–5.2) mg/mmol and 9% of patients had macroalbuminuria, defined as an albumin to creatinine ratio (ACR) greater than 25 mg/mmol for males and greater than 35 mg/mmol for females.

Table 1 – Baseline clinical characteristics of patients (n = 1379). Data expressed as median (interquartile range).

	Variable/Median (Interquartile Range)
Age (years)	57 (49–64)
Gender (% male)	58%
Diabetes duration (years)	9 (4–15)
HbA1c (%)	8.7 (7.8–9.8)
Weight (kg)	
Male (n = 764)	94.0 (80.9–108.1)
Female (n = 520)	80.4 (69.2–96.2)
BMI (kg/m^2)	
Male (n = 528)	31.6 (27.6–35.6)
Female (n = 357)	32.1 (26.9–37.2)
Systolic BP (mmHg) (n = 901)	149 (134–160)
Diastolic BP (mmHg) (n = 901)	80 (73–90)
Total cholesterol (mmol/L) (n = 1101)	4.0 (3.4–4.8)
LDL cholesterol (mmol/L) (n = 964)	2.0 (1.6–2.7)
HDL cholesterol (mmol/L) (n = 999)	1.1 (0.9–1.3)
Triglycerides (mmol/L) (n = 1097)	1.5 (1.1–2.2)
Ever smoked (%) (n = 733)	54%
Urine ACR (mg/mmol) (n = 689)	1.4 (0.7–5.2)
No diabetes pharmacotherapy (%)	11%
Single oral hypoglycaemic agent (%)	17%
Dual oral hypoglycaemic agents (%)	24%
Triple oral hypoglycaemic agents (%)	9%
Oral hypoglycaemic agents with insulin (%)	18%
Insulin alone (%)	21%
Statin therapy (%)	47%
ACE inhibitor or ARB (%)	47%
Thiazide diuretic (%)	14%
ACE inhibitor or ARB + Thiazide Diuretic (%)	14%
Calcium antagonist	15%
Beta blocker	12%

At presentation, 68% of patients were treated with oral hypoglycaemic agents, either as monotherapy (17%), in combination with one or more oral hypoglycaemic agents (33%) or dual therapy with insulin (18%). Twenty-one percent of patients were on insulin alone (Table 1). Of the patients receiving monotherapy, 82% were treated with metformin, 13% with sulfonylureas, 3% with dipeptidyl peptidase-4 inhibitors, and 2% with thiazolidinediones. Eleven percent of patients were not prescribed any form of glucose lowering agents at initial presentation. With regards to other medications, 47% of patients were treated with a statin, and 47% were on either an angiotensin converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) (Table 1).

3.2. *Temporal HbA1c patterns over years of follow-up*

The median (interquartile) baseline HbA1c was 8.7 (7.8–9.8)% (72 mmol/mol). Using a linear mixed-effects model to analyse changes in HbA1c within individual patients over time, the most significant reduction in mean HbA1c was in the first 3 months following referral to an endocrinologist ($p < 0.0001$) (Fig. 1). There was a significant 1.0% reduction in HbA1c to 7.7 (7.1–8.6)% (61 mmol/mol) at 3–6 months, following which there were no further changes. However, the initial reduction was maintained with minimal loss of control at 4 years, with a median HbA1c achieved of 7.7 (7.1–8.7)% (61 mmol/mol). At 3 to 6 months, only 1093 patients returned for follow-up, with patient numbers decreasing further to 355 at 4 years.

In terms of the proportion of patients reaching target HbA1c, 24% of patients achieved an HbA1c of ⩽7% (53 mmol/mol) at 3–6 months, with no significant changes following this (Fig. 2). Factors that predicted the attainment of an HbA1c ⩽ 7% (53 mmol/mol) at 6–12 months on univariate logistic regression included duration of diabetes, baseline HbA1c, frequency of review, and insulin use at baseline (Table 2). However, when variables were analysed using a multivariate model, only duration of diabetes (OR 0.941; 95% CI, 0.922–0.960), insulin use at baseline (OR 0.612; 95% CI, 0.462–0.812) and frequency of review (OR 1.02, 95% CI 1.001–1.04) were independent predictors of attaining an HbA1c ⩽ 7% at 6–12 months.

4. Discussion

Most society guidelines recommend an HbA1c target of ⩽7% (53 mmol/mol) to reduce the risk of diabetic complications in type 2 diabetes [1]. However, the results of this study have again emphasised the difficulties in achieving glycaemic targets in real-world clinical practice. In our cohort of patients who were referred to private endocrinologists, an HbA1c of 7.7 (7.1–8.6)% was achieved from a baseline of 8.7 (7.8–9.8)% (72 mmol/mol) after 3–6 months. Disappointingly, there were

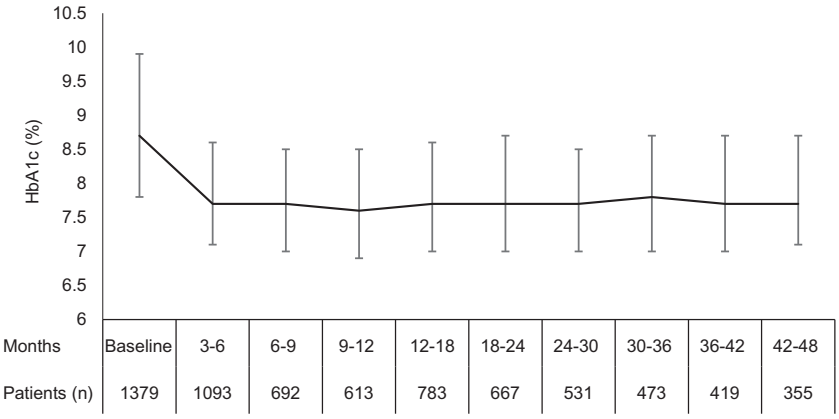

Fig. 1 – HbA1c (%) following referral to an endocrinologist. Data expressed as mean (interquartile range).

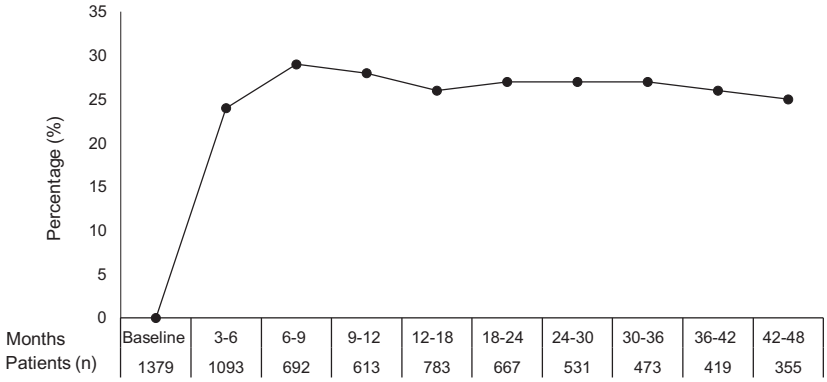

Fig. 2 – Percentage of patients at target HbA1c of ⩽7% (53 mmol/mol).

no further improvements following this, and only 24% of patients were able to reach a target HbA1c of ⩽7% (53 mmol/mol) at 3–6 months. On the other hand, it was reassuring to see that the initial drop in HbA1c was maintained for up to 4 years under specialist care.

The present audit is unique in that longitudinal changes in HbA1c and achievement of glycaemic targets has not previously been reported in such a cohort of specialist treated patients in private practice. In the 2013 Australian National Diabetes Audit – Australian Quality Clinical Audit (ANDA-AQCA), data was obtained from 29 hospital-based diabetes centres and only one specialist endocrinologist in private practice – in this audit, 33% of patients achieved an HbA1c ⩽ 7% (53 mmol/mol) [6]. Similarly, Bryant et al. [8] conducted an audit of the extent of glycaemic control in a cohort of patients with type 2 diabetes attending a tertiary hospital outpatient diabetes clinic, and found that only 30% of patients achieved an HbA1c level ⩽ 7% (53 mmol/mol). It appears that

Table 2 – Factors predicting the attainment of an HbA1c ⩽ 7% at 6–12 months on univariate logistic regression analysis.

	Odds ratio	95% Confidence interval	*p*-Value
Age	0.999	0.989–1.010	0.922
Male sex	0.945	0.732–1.221	0.666
Duration of diabetes	0.933	0.915–0.952	<0.001
Baseline HbA1c	0.931	0.861–1.008	0.077
Frequency of review	1.02	1.002–1.039	0.028
BMI	0.997	0.974–1.020	0.779
Systolic blood pressure	0.998	0.990–1.005	0.545
Total cholesterol	1.039	0.907–1.189	0.583
Fasting BGL	1.016	0.956–1.079	0.616
Smoking status	1.052	0.738–1.500	0.781
Baseline insulin use	0.592	0.449–0.780	<0.001

there are multiple barriers to the achievement of glycaemic targets across all levels of clinical care, from primary care to both public and private specialist diabetes centres. In the primary care setting, those with poor glycaemic control were identified to have a longer duration of diabetes, with more microvascular and macrovascular complications [5]. Barriers to achieving glycaemic targets in this population were thought to be multifactorial, and included both patient and physician factors. Patient factors included poor compliance, fear of side effects including hypoglycaemia and weight gain, as well as the natural progression of type 2 diabetes. Physician factors that have previously been identified include therapeutic inertia- a delay in commencing or addition of new therapy when glycaemic goals were not reached [5].

It is likely that patients referred to private endocrinologists represent those with more complex pathology, including poorer glycaemic control, longer duration of diabetes, and significant comorbidities. Compared to a cohort of patients with complex type 2 diabetes referred to hospital diabetes clinics [9], our population had a similar HbA1c and higher blood pressure at baseline. Nine percent of patients had macroalbuminuria, a substantially higher proportion than the 4% reported in the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial, which enrolled patients with type 2 diabetes and a history of major macrovascular and microvascular disease [10]. Furthermore, the majority of our patients (89%) were on one or more form of glucose-lowering agent, and 18% were on both insulin and oral hypoglycaemic agents. A high proportion of patients (47%) were also treated with statins and anti-hypertensive agents, reflecting significant cardiovascular risk factors. Factors predicting the achievement of HbA1c levels $\leqslant$ 7% (53 mmol/mol) reflected milder severity of diabetes, so no doubt the complexity of our patients contributed to the difficulties achieving adequate glycaemic control in this cohort of patients.

The complexity of the patients, including long-term diabetes mellitus and co-morbidities, may also have influenced HbA1c targets set by the treating endocrinologist. Results from clinical trials including ACCORD (Action to Control Cardiovascular Risk in Diabetes) have shown that tight glycaemic control was associated with increased mortality, particularly amongst subjects with known cardiovascular disease or HbA1c > 8.5% (69 mmol/mol) at baseline [11]. It is now recommended that HbA1c targets be individualised, taking into consideration the presence of cardiovascular disease, diabetes duration, comorbidities, and problems with severe hypoglycaemia [1]. We have attempted to limit this confounder by restricting our analysis to people under 70 years of age. Nonetheless, explicit or implicit individualised HbA1c target settings may have influenced the HbA1c levels achieved for the group as a whole.

A limitation of our study is the large number of patients who attended only one initial consultation, and the drop off in the ensuing years, which reflects real world clinical practice. It is likely that the more complex patients were required to return for follow-up, while those who achieved target HbA1c levels were discharged back into the care of their primary care physician. Hence the lack of improvement in HbA1c may in part be due to selection bias through retention of the most challenging patients. We cannot specifically conclude that the improvement in the initial 3–6 months is different to the reduction that would have been found following referral to another type of clinician. Another factor which may have contributed to the drop-off in follow-up rates is the practice of being a "consultant physician", whereby the specialist assesses the patient and then provides guidance to the general practitioner for the patient's ongoing management, rather than having the patient return regularly for review. Furthermore, it would be useful to understand inter-practice variations in patient socioeconomic status, health literacy, general practitioner support, and access to allied health, which we were unable to assess in this study, but may also impact on the achievement of glycaemic targets.

The results of this audit may suggest a need for an overall change in practice across all levels of care. We had previously found that there was better glycaemic control at hospitals where a shared care approach was instituted between primary care physicians and specialist diabetes clinics [12]. This model involves the primary care physician taking on most of the routine care of diabetes, supported by specialist diabetes clinics in a consultative and complications screening role. The percentage of patients achieving target HbA1c levels in the shared care model was 43.5% compared to 29% in a routine care model [12]. This is supported by a randomised controlled trial where a shared care approach achieved a greater improvement in patients achieving target HbA1c than a hospital diabetes outpatient clinic [9]. Across the literature, the benefits of a shared care model extends to widespread improvements in health outcomes, with reductions in cardiovascular morbidity, all-cause mortality, hospitalisations, healthcare spending, and higher quality of care [13–15]. Thus, improved collaboration between general practitioners and specialists may result in better glycaemic outcomes than those reflected in this audit. One important factor in a shared care model is the ability of the primary care physician to see the patient more regularly than the busy hospital clinic, and institute early changes in management, and also deal with crises in glucose control. In contrast to hospital clinics, however, private practice enables greater flexibility in the frequency of patient review, thus frequent or impromptu review is often possible. The finding that the frequency of specialist review is a predictor of successful attainment of HbA1c targets suggest that this is an important factor. Nonetheless, it remains a challenge to prioritise those who need frequent review whilst other patients are discharged back to general practice in the knowledge that than can be referred back if needed, in a similar manner to the hospital shared care model.

In conclusion, patients with type 2 diabetes referred to endocrinologists represent a complex cohort of patients, with a long duration of disease and high baseline HbA1c levels. Following initial consultation, a significant improvement in HbA1c is usually achieved, with a proportion of patients achieving target levels. This effect is sustained over the medium term. At the same time, the results of this study also reflect the difficulties in achieving glycaemic targets in real-world clinical practice.

Conflicts of interests

We declare no conflicts of interest.

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