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Comparison of the demographics, insulin use and clinical outcomes of insulin users with Type 2 diabetes in the Erewash (Integrated) Diabetes Service with the UK population

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Abstract:

Background: Insulin treated patients with Type 2 Diabetes require specialist multidisciplinary input to achieve treatment targets. We compared the demographics; achievement of combined NICE targets for HbA1c (<7.5%), blood pressure (<140/80) and total cholesterol (<4mmol/L); and insulin use between patients from a local Integrated Diabetes Service with a representative UK population

Methods: Cross-sectional evaluation of individual patient data from six randomly selected primary Care practices in Erewash Integrated Diabetes service was compared with The Health Improvement Network (THIN), UK primary care database.

Results: Baseline age (61.5years vs 65.8 years; $p < 0.0001$ and duration of insulin (4.3 vs 6.3 years, $P < 0.0001$) use was lower in the THIN population. Mean HbA1c was similar between the two cohorts but weight, blood pressure, total and LDL cholesterol was significant lower in the Erewash population compared with THIN. The combined achievement of HbA1c, total cholesterol and blood pressure was 17.5% in the Erewash cohort compared with 9.6% in the UK THIN cohort ($p < 0.0001$). There was a higher proportion of insulin users on basal-bolus than premix in the Erewash cohort (89.3% vs 10.7%) compared with THIN (59.0% vs 41.1%). Proportion of patients who received concurrent oral glucose lowering therapies in the Erewash integrated service was lower, except for SGLT2-inhibitor, (2.5% in the Erewash vs 0.5% in the THIN; $p < 0.0001$).

Conclusion: This model of integrated diabetes service appears to confer better clinical outcomes compared with the UK population. Further studies are required to investigate impact of this service model on health economic, patients' pathway and patient experience.

Introduction:

In view of the significant vascular benefits of tight glucose control in patients with type 2 diabetes (T2D) [1], consensus guidelines have recommended aggressive treatment escalations, including the earlier use of insulin therapy in patients with T2D in order to achieve optimal HbA1c target [2], an important Quality and Outcomes Framework (QOF) target for general practitioners [3]. The management of insulin treatment however is complex. Local preferences of healthcare providers and guidelines of Clinical Commissioning Groups (CCGs) plays an important role in determining patients' care package which includes advice on lifestyle modification, compliance, choice of insulin therapies and regimens, as well as education on self-titration of insulin dose.

Due to the rising cost and prevalence of diabetes [4], the responsibility for providing care for most patients with diabetes has fallen to primary care. However in many areas, the infrastructure to deliver an effective care is inadequate due to a variety of factors, including the lack of coordination between primary and secondary care. The Erewash Diabetes Service (EDS) in Derbyshire provides a novel set up of diabetes care which integrates delivery of its services across both primary and secondary care derived from experiences from two Southern Derbyshire Integrated service models - First Diabetes and Intercare Health [5] -and built on a strong consensus among policy-makers and patient groups on the importance of improving integrated care in the NHS [6,7]. This service model brings primary and secondary care together in a clinical, financial, and legal not-for-profit company, using programme budgeting, shared electronic clinical records, and integrated clinical governance to deliver clinical care to patients throughout their clinical journey and has received local and national recognition [8-10]. Clinical demographic data and clinical outcome among insulin treated patients with T2D within this model however is not available.

We therefore aimed to identify individual information of insulin users with T2D, who received medical care in Erewash, with a view of characterising their demographic profile, insulin regimen, and cross sectional clinical outcomes parameters (as HbA1c, weight and lipid profile), compared with the UK national data, with a view of identifying local differences for audit and improved clinical practice in our area.

Methods

Study Population and Design:

Based on the latest National Cardiovascular intelligence Network figures, the 2015 prevalence of diabetes in the Erewash region is 8.4%, which is higher than the national prevalence of 6.55%. According to the *2015 Director of Public Health Annual Report for Derbyshire*, 68.8% of adults in Derbyshire are classed as overweight or obese. This is higher than the East Midlands regional figures at 66.7% and the national figures for England at 64.7%.

A comparative cross-sectional study was conducted among people with T2D on insulin therapy, using local data obtained of patient population from 6 randomly selected Primary Care practices in Erewash, Derbyshire CCGs. This was compared with a cross-section of the UK national UK Primary Care data via The Health Improvement Network (THIN) database, a UK computerised anonymised longitudinal Primary Care records with details of over 10.5 million patients of which 4.8 million are currently active. These were derived in a non-interventional manner from 532 General Practices within the UK and contains information on important variables as demography, lifestyle factors, disease diagnoses, hospital admissions, laboratory results, drug prescriptions, and socio-economic status. THIN has been validated to be demographically representative of the UK population and has been invaluable in evaluating clinical outcomes [11]. We selected only patients with Insulin treated T2D as this is the most challenging group of patients with T2D, many of which require specialist multidisciplinary input and would best highlight the clinical effectiveness of a given model of a specialised diabetes service.

Six Primary Care centres were randomly from the 12 centres in the Erewash CCGs. Data from the centres were extracted via PRIMIS audit tool [12]. In both this and the THIN dataset population groups, we obtained data on all adult T2D insulin users, aged 18 and above, who initiated insulin therapy between January 2007 and 2014 in spite of previous or concurrent use of other glucose-lowering therapies (GLTs). Where similar patient identifiers were discovered in both populations, such patients were excluded.

Exposure and Outcome:

The main exposure was the use of insulin while the outcome was to compare demographic and clinical parameters among insulin-users, between the local Erewash Integrated service data and the UK national (THIN data).

Covariates:

Baseline demographic parameters as age, sex; clinical measures as body weight, body mass index (BMI) and blood pressure (systolic and diastolic); biochemical parameters as baseline HbA1c, creatinine level, total cholesterol levels, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides; as well as diabetes profile as the duration of diabetes, duration of insulin use; insulin regimen and the duration of treatment of diabetes were extracted and compared between these population groups.

Statistical Analyses:

Descriptive statistical analysis was done to obtain the mean and frequency distribution of the baseline demographics in both population groups.

Pearson's Chi-squared tests and independent student t-test were used to summarise and compare the categorical and continuous baseline variables respectively between the population groups. In the THIN dataset, missing data were generally accounted for using multiple imputations with the chained equation (MICE) model.

All analyses were conducted using Stata Software, version 14 with statistical significance put at a p-level ≤ 0.05 .

Results:

Patients Characteristics:

There were a total of 18,533 insulin-users of which 18,227 were derived from the UK national data, and 326 from the Erewash data. The mean age was 61.6 ± 13.6 years, while a little above half of the population (53.2%) were males. The mean HbA1c level was $8.7 \pm 1.8\%$; weight: $91.2 \pm 18.7\text{kg}$; with a greater proportion (62.5%) obese. Also, in both populations, Metformin (84.9%) was the commonest glucose lowering therapy (GLT) in use, followed by sulphonylurea (74.6%); thiazolidinedione (31.1%) and DPP4i (Dipeptidyl peptidase-4 inhibitor) (13.9%); while the least used GLT is Sodium-glucose Cotransporter-2 inhibitors (SGLT2) (0.5%). Finally, the premix insulin regimen was the commonest regimen in use. Table 1 is a summary of the baseline characteristics of the study population.

Insulin-users with T2DM: Erewash Integrated Diabetes service vs UK

i. Demographic Characteristics:

An independent t-test and chi-square test was run on both population samples to determine differences in the demographics of insulin-users with T2DM in both population groups (Table 2). The baseline age was 4.6 years significantly lower in the UK general population (61.5 years vs 65.8 years; $p < 0.0001$). There were similarities in gender distribution between both population groups (Males: 53.2% vs 54.0%, $\chi^2 = 0.0818$; $p = 0.775$).

ii. Clinical Parameters:

We explored the differences in important clinical parameters which predict treatment outcomes in the management of T2D. It was observed that HbA1c was similar in both populations (8.7% vs 8.5%; mean diff: 0.46; [95%CI: -0.16, 0.25]; $p = 0.6551$), but the duration of insulin use (6.3 years vs 4.3 years; mean diff; 2.61; [95%CI: 2.10, 3.10], $p < 0.0001$) were significantly higher in the Erewash integrated service compared to the UK national data.

Some clinical measures as weight ($p = 0.0019$); BMI ($p < 0.0001$); systolic BP ($p = 0.0015$); diastolic BP ($p < 0.0001$); total cholesterol ($p < 0.0001$); low-density lipoprotein ($p < 0.0001$) and the proportion of the obese sub-population group (51.2% vs 62.7%; $p < 0.0001$) were significantly lower in the Erewash Integrated service population group, compared to the UK national data. Conversely, high-density lipoprotein ($p < 0.0001$); and glomerular filtration rate

($p=0.013$) were significantly higher in the local population, while triglycerides ($p=0.9859$) was similar in both.

iii. Use of Insulin and other GLTs:

Although in both populations, there was a higher proportion of insulin users on basal-bolus than premix (UK: 59.0% vs 41.1% and Integrated service: 89.3% vs 10.7%; $p < 0.0001$), the use of basal bolus was found to be very high (approximately 9:10) compared to premix in the Erewash local data (Table 2).

Similarly, there were significant differences in the proportion of users of other GLTs between the two population groups, and in all GLTs of interest, we reported a lesser proportion of users in the local data of Erewash integrated service, compared to the national except in Sodium-glucose Cotransporter-2 inhibitors (SGLT2i) in which 2.5% of the local integrated service population were taking, compared to 0.5% in the national data ($p < 0.0001$). Also, the proportion of metformin users was highest in both populations (85.6% vs 50.0%) compared to other GLTs, followed by sulphonylureas (75.7% vs 14.4%); while glinides were the least used GLT in the local population (0.3%), against SGLT2i (0.5%) in the national data.

iv. Achievement of NICE targets.

No significant difference was noted in the percentage of patients achieving NICE HbA1c target of 7.5% between the two population cohorts. However significantly higher number of patients within the Erewash cohort achieved NICE targets for total cholesterol, systolic and diastolic blood pressure, compared with the UK THIN population. Thus for the achievement of combined HbA1c, total cholesterol and blood pressure, 17.5% in the Erewash cohort achieved the combined target compared with 9.6% in the UL THIN cohort ($p < 0.0001$). (Table 3)

Discussion:

This observational study reports the demographic, metabolic and cardiovascular risk parameters, use of insulin therapy/ regimens and choices of concurrent oral glucose lowering therapies among patients with T2D undergoing routine care at a local Integrated Diabetes service compared with a representative UK cohort. While simple conclusions cannot be made from this cross-sectional data analysis, some discussion and speculation can be derived.

Firstly, the mean percentage of patients achieving the three NICE treatment targets of HbA1c <58mmol/mol, blood pressure of <140/80mmHg and total cholesterol <4mmol/L was significantly higher in the Erewash integrated service cohort compared with the UK (THIN) population. The mean HbA1c level and the % patients achieving HbA1c target of <7.5% within the Integrated care cohort was however comparable to the UK cohort. This was despite significantly longer duration of diabetes and of insulin therapy in the integrated care cohort. This is relevant because increased diabetes duration is known to be associated with progressive decline of HbA1c level [1], continual decline of C-peptide level [13,14] and reduced responsiveness to intensive insulin therapy [13], which is partly augmented by increased age. [15]. The latter is also relevant because our cohort is significantly older than the UK cohort. Importantly, cardiovascular risk profile such as systolic BP, diastolic BP, total cholesterol and low-density lipoprotein levels were significantly lower in the integrated care cohort compared to the UK population. The reason for this is not known but we would speculate that the implementation of cardiovascular risk reduction strategies among patients who receive their routine care in an integrated service is likely to be more robust than that in the general population. Unfortunately the extracted data did not provide us with information regarding the use antihypertensive statins and aspirin therapy in both patient cohorts. This study supports observation from a previous trial which randomised intermediate care clinics for diabetes versus usual care and reported greater achievement of achievement of all three of the NICE targets [16] in the intermediate care cohort.

Secondly, we observed a significantly greater use of a basal bolus insulin regimen compared with the premixed insulin regimen, in the integrated service compared with the UK population. These two insulin regimen are the two most widely used insulin regimens but there remains no overall consensus regarding the most effective or optimal insulin regimen for patients with diabetes mellitus [17]. The basal bolus regimen, which consists of multiple daily injections of rapid-acting insulin pre-prandially, in addition to a long-acting basal insulin, most closely

mimics the pattern of insulin secretion in individuals without diabetes [18]. The flexibility of this regimen is, however, undermined by its complexity in the need to count daily carbohydrate intake and adjust the insulin dose accordingly, as well as the lifestyle restrictions implicated by the high number of injections [19]. The premixed insulin regimen accounts for the majority of insulin prescriptions worldwide and consists of a fixed ratio of rapid-acting insulin and intermediate insulin combined; thereby eliminating the need for patients to mix the insulin themselves whilst also reducing the number of required daily injections. We would speculate that the much higher preference for a basal bolus insulin regimen relative to premixed regimen within an integrated service compared to the UK population reflects the greater patients' access to clinicians and diabetes educators, required for the more complex basal bolus regimen, accorded by an integrated diabetes service. Similarly this may also influence the much lower use of concurrent oral glucose lowering therapy in the integrated cohort, except for the SGLT2 inhibitor, a novel therapy for type 2 diabetes, associated with weight loss. The latter may explain the lower mean weight in the integrated service population, compared to the UK population, despite the higher background prevalence of overweight and obesity in the Erewash region compared with the UK population.

In a previous Cochrane systematic review on 'Intervention to improve the management of diabetes mellitus in primary care and community settings'[20], 41 studies were included which involved more than 200 practices and 48,000 patients. Majority of these studies involved intervention study which focused on 'up-skilling' of primary care (non specialist clinicians) via postgraduate education, patient tracking systems or other systems for regular follow-up, provision of patient education and/or a link research nurse to liaise with patient and clinicians, the impact of nurses in replacing physicians and the effectiveness of a pharmaceutical care model in delivering advice on glucose lowering therapy. No studies were identified that dealt with trial or audit outcome of an integrated service as defined by the 'Best practice for commissioning diabetes services' [21] and the 'a joint position statement from the Primary Care diabetes society, Association of British Clinical Diabetologist, Diabetes UK and the Royal college of Nursing [22]. Due to the cross sectional nature of this study, we were not able to investigate the health economic outcome, patient pathway and the patient experience of the integrated service – three of the most important non-clinical determinant of the success of an integrated service. Further prospective randomised trial is required to address the research gap.

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Tables:

Table 1: Baseline characteristics by population groups and differences between

Baseline variable	Population			Differences* (95% CI)	p-value
	THIN cohort (N = 18,227)	Erewash Integrated Service (N = 326)	Total (N = 18,533)		
Demographics					
Age (yrs), Mean (SD)	61.5 (13.6)	65.8 (12.7)	61.6 (13.6)	-4.6 (-6.1, -3.1)	<0.0001
Gender, No. (%)				$\chi^2 = 0.0818$	0.775
Male	9695 (53.2)	176 (54.0)	9871 (53.2)		
Female	8532 (46.8)	150 (46.0)	8682 (46.8)		
Clinical Parameters, Mean (SD)					
HbA1c (%)	8.7 (1.8)	8.5 (1.8)	8.7 (1.8)	0.4 (-0.16, 0.25)	0.6551
(mmol/mol)	72 (20)	69 (20)	72 (20)	-	-
BMI (kg/m ²)	32.5 (6.9)	30.3 (6.9)	32.5 (6.9)	1.63 (0.88, 2.39)	<0.0001
Weight (Kg)	91.3 (18.7)	86.1 (20.4)	91.2 (18.7)	4.54 (1.67, 7.42)	0.0019
SBP (mmHg)	136.3 (23.0)	132.2 (14.2)	136.3 (23.0)	3.30 (0.64, 5.96)	0.015
DBP (mmHg)	76.0 (10.8)	72.5 (9.2)	76.0 (10.8)	3.21 (2.02, 0.41)	<0.0001
TC (mmol/l)	4.5 (1.3)	4.1 (1.1)	4.5 (1.3)	0.34 (0.20, 0.49)	<0.0001
HDL (mmol/l)	1.2 (0.4)	1.3 (0.4)	1.2 (0.4)	-0.03 (-0.08, -0.02)	<0.0001
LDL (mmol/l)	2.4 (1.1)	2.1 (0.9)	2.4 (1.1)	0.36 (0.23, 0.48)	<0.0001
Triglyceride (mmol/L)	2.0 (1.2)	1.7 (0.8)	2.0 (1.2)	-0.001 (-0.14, 0.13)	0.9859
eGFR (mls/min/1.73m ²)	62.3 (21.0)	63.8 (21.5)	63.1 (21.3)	-1.35 (-3.73, -1.04)	0.013
Diabetes duration (yrs)	3.9 (6.4)	8.7 (8.0)	6.3 (6.2)	-3.08 (-3.81, -2.35)	<0.0001
Duration of insulin use (yrs)	4.3 (4.9)	6.3 (5.1)	4.3 (4.9)	-2.61 (-3.1, -2.1)	<0.0001
BMI Categories, No. (%)					
≤ 24.9kg/m ²	2455 (13.5)	56 (13.4)	2511 (13.5)	$\chi^2 = 18.07$	<0.0001
25-29.9kg/m ²	4343 (23.8)	103 (31.6)	4446 (24.0)		
≥ 30kg/m ²	11429 (62.7)	167 (51.2)	11596 (62.5)		
Other GLTs, No. (%)					
Metformin	15593 (85.6)	163 (50.0)	15756 (84.9)	$\chi^2 = 316.13$	<0.0001
Sulphonylurea	13794 (75.7)	47 (14.4)	13841 (74.6)	$\chi^2 = 634.39$	<0.0001
Thiazolidinedione	5754 (31.6)	9 (2.8)	5763 (31.1)	$\chi^2 = 124.12$	<0.0001
GLP-1ar	1943 (10.7)	13 (4.0)	1956 (10.5)	$\chi^2 = 15.12$	<0.0001
SGLT2	85 (0.5)	8 (2.5)	31 (0.5)	$\chi^2 = 25.37$	<0.0001
Glinides	790 (4.3)	1 (0.3)	791 (4.3)	$\chi^2 = 12.72$	<0.0001

DPP4i	2569 (14.1)	11 (3.4)	2580 (13.9)	$\chi^2 = 30.74$	<0.0001
Insulin Regimen					
Basal-bolus	10744 (59.0)	291 (89.3)	7518 (40.5)	$\chi^2 = 122.15$	<0.0001
Premix	7483 (41.1)	35 (10.7)	11035 (59.5)		

**Differences- This is a measure of the differences in the variables between the two populations (mean difference in continuous variables with 95% confidence interval; and chi-square test in categorical variables).*

SD (standard deviation); Diabetes duration is time from first diagnosis of diabetes to date of initiating insulin; Duration of insulin is the time between initiation of insulin and date of commencing study

MET (metformin); SU (sulphonylurea); GLP-1ar (Glucagon-like peptide 1); INS (insulin); SGLT2 (Sodium-glucose Cotransporter-2 inhibitors); Glinides (Meglitinides); DPP4i (Dipeptidyl peptidase-4 inhibitors)

BMI (body mass index); SBP (systolic blood pressure); DBP (diastolic blood pressure); HbA1c (haemoglobin A1c); HDL (high-density lipoprotein); LDL (low-density lipoprotein); TC (total cholesterol); eGFR (estimated glomerular filtration rate)

Table 2: The proportion of patients achieving the NICE targets of HbA1c $\leq 7.5\%$ (59 mmol/mol); Blood Pressure $<140/80$ mmHg and Cholesterol: 4 mmol/l.

	THIN cohort	Erewhash Integrated Service	Chi-square	p-value
HbA1c				
< 7.5%	4,195 (27.0)	91 (28.0)	0.1463	0.702
$\geq 7.5\%$	13,312 (73.0)	235 (72.0)		
Total Cholesterol				
< 5.0mmol/L	12,025 (66.0)	258 (79.1)	24.82	<0.0001
≥ 5.0 mmol/L	6,202 (34.0)	68 (20.9)		
Diastolic BP				
≤ 80 mmHg	12,069 (66.2)	267 (81.9)	35.37	<0.0001
> 80mmHg	6,158 (33.8)	59 (18.1)		
Systolic BP				
≤ 140 mmHg	10,651 (58.4)	247 (78.8)	36.69	<0.0001
> 140mmHg	7,576 (41.6)	79 (24.2)		
NICE Target*	1,750 (9.6)	57 (17.5)	22.64	<0.0001

**NICE target: Proportion of patients achieving the NICE targets of HbA1c $\leq 7.5\%$ (59 mmol/mol); Blood Pressure $<140/80$ mmHg and Total Cholesterol: 4 mmol/l.*