Demographics, insulin use and clinical targets in type 2 diabetes insulin users: comparison of a local integrated diabetes service vs a UK-wide cohort

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Abstract
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 mmHg) and total cholesterol (<4 mmol/L) and insulin use between patients from a local integrated diabetes service with those from a representative UK population.

A 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.

Baseline age (61.5 years vs 65.8 years; p<0.0001) and duration of insulin use (4.3 vs 6.3 years; p<0.0001) use were lower in the THIN cohort. Mean HbA1c was similar between the two cohorts but weight, blood pressure, total and LDL cholesterol were significantly 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 THIN cohort (p<0.0001). There was a higher proportion of insulin users on basal-bolus than on premix in the Erewash cohort (89.3% vs 10.7%) compared with THIN (59.0% vs 41.1%).

The proportion of patients who received concurrent oral glucose-lowering therapies in the Erewash integrated service was lower, except for SGLT2 inhibitors (2.5% in the Erewash cohort vs 0.5% in THIN; p<0.0001).

This model of an integrated diabetes service appears to confer better achievement for the NICE defined clinical targets compared with the THIN cohort. Further studies are required to investigate the impact of this service model on health economics, patient pathway and patient experience. Copyright © 2017 John Wiley & Sons.

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Key words
insulin; type 2 diabetes; integrated diabetes service

Introduction
In view of the significant reduction in micro- and macrovascular complications due to tight glucose control in patients with type 2 diabetes (T2DM), international consensus guidelines have recommended intensive and individualised treatment escalations, including the increased use of insulin therapy in patients with T2DM in order to achieve optimal HbA1c target – an important Quality and Outcomes Framework target for general practitioners. The management of insulin treatment, however, is complex. Local preferences of health care providers and guidelines of clinical commissioning groups (CCGs) play 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-titratin of insulin dose.

Due to the rising cost and prevalence of diabetes, the responsibility for providing care for most patients with diabetes has fallen to primary care. However, in many areas, the infrastructure to deliver effective care is inadequate due to a variety of factors, including the lack of coordination between primary and secondary care.

The Erewash Diabetes Service in Derbyshire was set up in 2011, and 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 – where, on their inception, they were the only model of services which integrate at organisational, clinical, information technology and financial levels. To
achieve this, the service 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. Close working between primary and secondary care staff as well as regular educational meetings would aim to up-skill primary care staff in the long term. This model of service was developed on a strong consensus among policy makers and patient groups regarding the importance of improving integrated care in the NHS,\textsuperscript{6,7} and has received local and national recognition.\textsuperscript{8-10} Clinical demographic data and clinical outcome among insulin-treated patients with T2DM within this model, however, are not available.

We aimed to identify individual information on T2DM insulin users receiving medical care in Erewash, Derby, regarding their demographic profile, insulin regimen, cross-sectional clinical outcome parameters (HbA\textsubscript{c}, weight and lipid profile), plus the proportion achieving the NICE targets, and compare these data against those of the UK national data; this was with a view to 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 6.5\%. 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 T2DM on insulin therapy, using local data obtained regarding the patient population from six randomly-selected primary care practices in Erewash CCGs. This was compared with a cross-section of the UK national primary care data via The Health Improvement Network (THIN) database – a computerised, anonymised, longitudinal primary care record with details of over 10.5 million patients of which 4.8 million are currently active. These records were derived in a non-interventional manner from 532 general practices within the UK and contain information on important variables such as demographics, 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.\textsuperscript{11} We selected only patients with insulin-treated T2DM as this is the most challenging group of patients with T2DM, many of whom 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 selected from the 12 centres in the Erewash CCGs. Most recent data from the centres (2016) were extracted via a PRIMIS audit tool.\textsuperscript{12} In both this and the THIN dataset population groups, we obtained data on all adult T2DM 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 clinical parameters, and the proportion achieving the NICE targets among insulin users between the local Erewash integrated service data and the UK national (THIN) cohort.

Covariates

Baseline demographic covariates were extracted for comparison between the two population groups. Covariates included: age and gender; clinical measures, e.g. body weight, body mass index (BMI) and systolic and diastolic blood pressure (BP); biochemical parameters, e.g. baseline HbA\textsubscript{c}, creatinine level, total cholesterol levels, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides; as well as diabetes profile regarding the duration of diabetes and duration of insulin use; insulin regimen; and the duration of diabetes treatment.

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 of ≤0.05.

Results

Patients’ characteristics

There were a total of 18 553 insulin users of whom 18 227 were derived from the THIN cohort, and 326 from the Erewash data. Overall, the mean age was 61.6±13.6 years, while a little above half of the population (55.2\%) were males.

The mean HbA\textsubscript{c} level was 8.7±1.8\% (72±20mmol/mol); mean weight was 91.2±18.7kg, with a greater proportion (62.5\%) obese.

Also, in both populations, metformin (84.9\%) was the most common GLT in use, followed by sulphonylureas (74.6\%), thiazolidinediones (31.1\%) and dipeptidyl peptidase-4 (DPP-4) inhibitors (13.9\%); while the least used GLTs were sodium-glucose cotransporter-2 (SGLT2) inhibitors (0.5\%).

Finally, the premix insulin regimen was the most common regimen in use.

Table 1 provides a summary of the baseline characteristics of the study population.
## Table 1. Baseline characteristics by population groups and differences between The Health Improvement Network and Erewash (Integrated) Diabetes Service cohorts

<table>
<thead>
<tr>
<th>Baseline variable</th>
<th>THIN cohort (n=18 227)</th>
<th>Erewash integrated service (n=326)</th>
<th>Total (n=18 553)</th>
<th>Differences* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age (years): mean (SD)</td>
<td>61.5 (13.6)</td>
<td>65.8 (12.7)</td>
<td>61.6 (13.6)</td>
<td>-4.6 (-6.1, -3.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender: no. (%)</td>
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<tr>
<td>– Male</td>
<td>9695 (53.2)</td>
<td>176 (54.0)</td>
<td>9871 (53.2)</td>
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<tr>
<td>– Female</td>
<td>8532 (46.8)</td>
<td>150 (46.0)</td>
<td>8682 (46.8)</td>
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<tr>
<td><strong>Clinical parameters: mean (SD)</strong></td>
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<tr>
<td>Glycated haemoglobin (HbA1c)</td>
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<tr>
<td>– HbA1c (%)</td>
<td>8.7 (1.8)</td>
<td>8.5 (1.8)</td>
<td>8.7 (1.8)</td>
<td>0.4 (-0.16, 0.25)</td>
<td>0.6551</td>
</tr>
<tr>
<td>– HbA1c (mmol/mol)</td>
<td>72 (20)</td>
<td>69 (20)</td>
<td>72 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>32.5 (6.9)</td>
<td>30.3 (6.9)</td>
<td>32.5 (6.9)</td>
<td>1.63 (0.88, 2.39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>91.3 (18.7)</td>
<td>86.1 (20.4)</td>
<td>91.2 (18.7)</td>
<td>4.54 (1.67, 7.42)</td>
<td>0.0019</td>
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<tr>
<td>Blood pressure</td>
<td></td>
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<tr>
<td>– Systolic blood pressure (mmHg)</td>
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<tr>
<td>– Diastolic blood pressure (mmHg)</td>
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<tr>
<td>Cholesterol and triglycerides</td>
<td></td>
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<tr>
<td>– Total cholesterol (mmol/L)</td>
<td>4.5 (1.3)</td>
<td>4.1 (1.1)</td>
<td>4.5 (1.3)</td>
<td>0.34 (0.20, 0.49)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>– High-density lipoprotein (mmol/L)</td>
<td>1.2 (0.4)</td>
<td>1.3 (0.4)</td>
<td>1.2 (0.4)</td>
<td>-0.03 (-0.08, -0.02)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>– Low-density lipoprotein (mmol/L)</td>
<td>2.4 (1.1)</td>
<td>2.1 (0.9)</td>
<td>2.4 (1.1)</td>
<td>0.36 (0.23, 0.48)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>– Triglycerides (mmol/L)</td>
<td>2.0 (1.2)</td>
<td>1.7 (0.8)</td>
<td>2.0 (1.2)</td>
<td>-0.001 (-0.14, 0.13)</td>
<td>0.9859</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate (ml/min/1.73m²)</td>
<td>62.3 (21.0)</td>
<td>63.8 (21.5)</td>
<td>63.1 (21.3)</td>
<td>-1.35 (-3.73, -1.04)</td>
<td>0.013</td>
</tr>
<tr>
<td>Diabetes duration (years)**</td>
<td>3.9 (6.4)</td>
<td>8.7 (8.0)</td>
<td>6.3 (6.2)</td>
<td>-3.08 (-3.81, -2.35)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration of insulin use (years)†</td>
<td>4.3 (4.9)</td>
<td>6.3 (5.1)</td>
<td>4.3 (4.9)</td>
<td>-2.61 (-3.1, -2.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index categories: no. (%)</td>
<td></td>
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<tr>
<td>– ≤24.9kg/m²²</td>
<td>2455 (13.5)</td>
<td>56 (17.2)</td>
<td>2511 (13.5)</td>
<td>-1.35 (-3.73, -1.04)</td>
<td>0.013</td>
</tr>
<tr>
<td>– 25–29.9kg/m²²</td>
<td>4343 (23.8)</td>
<td>103 (31.6)</td>
<td>4446 (24.0)</td>
<td>-1.00 (0.04, 2.08)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>– ≥30kg/m²²</td>
<td>11 429 (62.7)</td>
<td>167 (51.2)</td>
<td>11 596 (62.5)</td>
<td>-1.35 (-3.73, -1.04)</td>
<td>0.013</td>
</tr>
<tr>
<td><strong>Other glucose-lowering therapies: no. (%)</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>15 593 (85.6)</td>
<td>163 (50.0)</td>
<td>15 756 (84.9)</td>
<td>-2.61 (-3.1, -2.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td>13 794 (75.7)</td>
<td>47 (14.4)</td>
<td>13 841 (74.6)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>5754 (31.6)</td>
<td>9 (2.8)</td>
<td>5763 (31.1)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Glucagon-like peptide 1 receptor agonists</td>
<td>1943 (10.7)</td>
<td>13 (4.0)</td>
<td>1956 (10.5)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sodium-glucose cotransporter-2 inhibitors</td>
<td>85 (0.5)</td>
<td>8 (2.5)</td>
<td>93 (5.0)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>790 (4.3)</td>
<td>1 (0.3)</td>
<td>791 (4.3)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dipeptidyl peptidase-4 inhibitors</td>
<td>2569 (14.1)</td>
<td>11 (3.4)</td>
<td>2580 (13.9)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Insulin regimen: no (%)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Basal-bolus</td>
<td>10 744 (59.0)</td>
<td>291 (89.3)</td>
<td>7518 (40.5)</td>
<td>-2.61 (-3.1, -2.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Premix</td>
<td>7483 (41.1)</td>
<td>35 (10.7)</td>
<td>11 035 (59.5)</td>
<td>0.00 (0.00, 0.00)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Differences: this is a measure of the differences in the variables between the 2 populations (mean difference in continuous variables with 95% confidence interval; and chi-squared test in categorical variables).

**Diabetes duration is time from first diagnosis of diabetes to date of initiating insulin.

†Duration of insulin use is the time between initiation of insulin and the date of commencing the study.

Abbreviations: THIN = The Health Improvement Network (THIN) UK primary care database; SD = standard deviation.
Comparision of the demographics, insulin use and clinical targets for type 2 diabetes patients

**Insulin-users: integrated service vs THIN cohort**

**Demographic characteristics.** An independent t-test and chi-square test were run on both population groups to determine differences in the demographics of insulin users with T2DM. (Table 1.) The baseline age was 4.3 years significantly lower in the THIN cohort (61.5 years vs 65.8 years; p<0.0001) while there were similarities in gender distribution between both population groups (males 53.2\% vs 54.0\%, chi-square = 0.0818; p=0.775).

**Clinical parameters.** We explored the differences in important clinical parameters which predict treatment outcomes in the management of T2DM. It was observed that HbA1c was similar in both populations (8.7\% vs 8.3\%; mean difference 0.4; [95\% CI -0.16, 0.25]; p=0.6551), but the duration of insulin use (4.3 years vs 6.3 years; mean difference 2.61; [95\% CI -2.10, -3.10]; p<0.0001) was significantly higher in the Erewash integrated service compared to the THIN cohort.

Some clinical measures were significantly lower in the Erewash integrated service population group compared to the THIN cohort – such as weight (p=0.0019); BMI (p<0.0001); systolic BP (p=0.0015); diastolic BP (p<0.0001); total cholesterol (p<0.0001); LDL (p<0.0001); and the proportion of the obese sub-population group (51.2\% vs 62.7\%; p<0.0001). Conversely, HDL (p<0.0001) and glomerular filtration rate (p=0.013) were significantly higher in the local population, while triglycerides (p=0.9859) were similar in both.

**Use of insulin and other glucose-lowering therapies.** Although in both populations there was a higher proportion of insulin-users on basal-bolus than on premix (THIN 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 9:1) compared to premix in the Erewash local data. (Table 1.)

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 found a lesser proportion of users in the local data of Erewash integrated service, compared to the national data – except for SGLT2 inhibitors: 2.5\% in the local integrated service population, compared to 0.5\% in the THIN cohort (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 SGLT2 inhibitors (0.5\%) in the national data.

**Achievement of NICE targets.** No significant difference was noted in the percentage of patients achieving the NICE HbA1c target of ≤7.5\% between the two population cohorts. However, compared with the THIN cohort, a significantly higher number of patients within the Erewash cohort achieved NICE targets for total cholesterol, and for systolic and diastolic BP. Thus, for the achievement of combined HbA1c, total cholesterol and BP, 17.5\% in the Erewash cohort achieved the combined target compared with 9.6\% in the THIN cohort (p<0.0001). (Table 2.)

**Table 2. The proportion of patients achieving the NICE targets of HbA1c ≤7.5\% (58mmol/mol), blood pressure <140/80mmHg, and total cholesterol <4mmol/L. THIN = The Health Improvement Network (THIN) UK primary care database.**

Discussion

This observational study reports the demographic, metabolic and cardiovascular risk parameters, use of insulin therapy/ regimens and choices of concurrent oral GLTs among patients with T2DM 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 ≤7.5\%, BP <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 percentage of patients achieving the HbA1c target of ≤7.5\% within the integrated care cohort was, however, comparable to the THIN cohort. This was despite a 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, continual decline of C-peptide...
The flexibility of this 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. The latter is also more closely mimics the pattern of secretion in individuals with diabetes mellitus. The majority of these studies involved interventions 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 patients and clinicians; the impact of nurses in replacing physicians; and the effectiveness of a pharmacetical 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’ and the joint position statement from the Primary Care Diabetes Society, the Association of British Clinical Diabetologists, Diabetes UK, and the Royal College of Nursing.

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 determinants of the success of an integrated service. A further prospective randomised trial is required to address the research gap.

### Key points

- The management of insulin treatment in people with type 2 diabetes is complex and involves multidisciplinary input on lifestyle modification, choice of therapy and insulin regimen, and education on self-titration of insulin dose
- Evidence based on the effectiveness of an integrated service model in this group of patients remains unclear
- This study showed that this model of integrated diabetes service is associated with better achievement of the NICE defined targets compared with a representative UK cohort

### Acknowledgements

We would like to take this opportunity to thank our previous colleagues within this service – Dr Rustam Rea and Dr Garry Tan. They were crucial in pioneering this novel model of integrated diabetes service, initially across southern Derbyshire and Derby City, which has now extended to the Erewash region of Derbyshire.

### Declaration of interests

There are no conflicts of interest declared.

### References

Comparison of the demographics, insulin use and clinical targets for type 2 diabetes patients

6. www.diabetes.org.uk/Documents/Position


