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ORIGINAL RESEARCH

Resource use and outcomes associated with initiation of injectable therapies for patients with type 2 diabetes mellitus

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Abbreviations

AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; AfC, Agenda for Change; BMI, body mass index; DM, diabetes mellitus; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; HbA_{1c}, haemoglobin type A_{1c}; HCPs, healthcare professionals; LVF, left ventricular failure; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; T2DM, type 2 diabetes mellitus

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Abstract

Introduction: Management of type 2 diabetes mellitus (T2DM) often requires intervention with oral and injectable therapies. Across National Health Service (NHS) England, injectable therapies may be initiated in secondary, intermediate or primary care. We wished to understand resource utilization, pathways of care, clinical outcomes, and experience of patients with T2DM initiated on injectable therapies.

Method: We conducted three service evaluations of initiation of injectable therapies (glucagon-like peptide-1 receptor agonists (GLP-1 RAs) or basal insulin) for T2DM in primary, secondary and intermediate care. Evaluations included retrospective review of medical records and service administration; prospective evaluation of NHS staff time on each episode of patient contact during a 3-month initiation period; patient-experience survey for those attending for initiation. Data from each evaluation were analysed separately and results stratified by therapy type.

Results: A total of 133 patients were included across all settings; 54 were basal-insulin initiations. After initiation, the mean HbA_{1c} level fell for both types of therapies, and weight increased for patients on basal insulin yet fell for patients on GLP-1 RA. The mean cost of staff time per patient per initiation was: £43.81 for GLP-1 RA in primary care; £243.49 for GLP-1 RA and £473.63 for basal insulin in intermediate care; £518.99 for GLP-1 RA and £571.11 for basal insulin in secondary care. Patient-reported questionnaires were completed by 20 patients, suggesting that patients found it easy to speak to the diabetes team, had opportunities to discuss concerns, and felt that these concerns were addressed adequately.

Conclusion: All three services achieved a reduction in HbA_{1c} level after initiation. Patterns of weight gain with basal insulin and weight loss with GLP-1 RA were as expected. Primary care was less resource-intensive and costly, and was driven by lower staff costs and fewer clinic visits.

Keywords: diabetes, injectable therapies, outcomes, patient pathway, resource use, primary care, intermediate care, secondary care, service evaluation.

Introduction

Since 2011, the number of people diagnosed with diabetes mellitus (DM) in the UK has increased from 2.9 million to 3.2 million [1]. Management of type 2 diabetes mellitus (T2DM) often requires pharmacologic intervention with therapies given via the oral route. However, due to the progressive nature of the condition, patients may also require initiation of injectable therapies to improve glycaemic control. Current injectable therapies include use of insulin (basal, fast acting or pre-mixed) or glucagon-like peptide-1 receptor agonists (GLP-1 RAs).

Unlike oral therapies, injectable therapies often require additional time and resources during the initiation period. Depending on local protocols, initiation of injectable therapies may be undertaken in primary, intermediate or secondary care. In the UK, real-world evidence on best practice in initiation of injectable therapies, the associated healthcare costs and its impact on patient experience is lacking.

The rationale for using injectable therapies in T2DM management has been described at a national level. In 2009, the National Institute for Health and Care Excellence (NICE) issued guidance on the management of T2DM in England [2]. Guidance around T2DM management recommends initial therapy with metformin in obese or overweight patients. Metformin should be continued if control of blood glucose remains or becomes inadequate, with addition of another oral glucose-lowering

medication (e.g., sulfonylurea, dipeptidyl peptidase-4 inhibitors, thiazolidinediones) added to the treatment. Guidance also highlights the importance of achieving and maintaining a target level of HbA_{1c}. It recommends use of a GLP-1 RA if control of blood glucose remains or becomes inadequate and the person has a high body mass index (BMI) of ≥35 kg/m^2 [1] and problems associated with high body weight, or if the BMI is <35 kg/m^2 and losing weight would help other weight-related health problems, or if taking insulin would greatly affect his/her ability to work. GLP-1 RAs act in a glucose-dependent manner to improve glycaemic control and reduce weight, with a low risk of hypoglycaemia [3]. Use of insulin therapy is recommended if control of blood glucose remains or becomes inadequate with other measures, albeit with a known risk of hypoglycaemia and weight gain [4].

Similar guidelines to those provided by NICE include those presented by the American Diabetes Association (ADA) [5] and American Association of Clinical Endocrinologists (AACE) [6]. ADA guidelines recommend the following pharmacologic therapies for hyperglycaemia in T2DM: metformin as the initial pharmacologic agent; insulin therapy with or without additional agents in newly diagnosed T2DM patients with markedly symptomatic and/or elevated blood glucose levels or HbA_{1c}; addition of a second oral agent (GLP-1 RA or insulin) if non-insulin monotherapy at the maximum tolerated dose does not achieve or maintain the HbA_{1c} target over 3 months. Guidance also suggests that a patient-centred approach should be used to guide choice of pharmacologic agents and that, due to the progressive nature of T2DM, insulin therapy is eventually indicated for many patients.

Similarly, AACE guidelines for glycaemic control recommend that, to start, the baseline level of HbA_{1c} is selected. If it is: <7.5%, then monotherapy should be given; ≥7.5%, then dual therapy should be given; >9.0% with no symptoms, then triple therapy should be considered; >9.0% with symptoms, then insulin with other agents should be given.

DM management has a considerable impact on use of healthcare resources and is a high priority for the National Health Service (NHS) [7]. In 2012, it was estimated that ≈10% of the NHS budget was spent on DM management alone, which equates to £9.8 billion in direct costs in 2010/11 with £8.8 billion of the cost derived from T2DM patients [8]. Around 80% of this budget was spent on complications related to disease, including cardiovascular disease and hypoglycaemia [8]. A few studies have explored the cost of T2DM [8,9] and the healthcare resource use associated with basal insulin [10,11]. However, none have evaluated the time and costs of NHS staff associated with initiating and supporting therapy using basal insulin and GLP-1 RAs in a UK setting.

Across NHS England, the setting for initiating injectable therapies may occur in secondary, intermediate or primary care. The cost and resource use associated with this service may vary due to the complexity of the initiation (particularly for basal insulin in terms of dose titration) and the level of staff involvement (e.g. for the education and support of patients) which (at least in part) may influence the cost of the service per patient. Therefore, in accordance with the 2014/2015 NHS Mandate (between the government and NHS England) [12] to ensure good financial management and unprecedented improvements in value for money across the NHS (as specified in point 8), it is important to consider all relevant costs to gather complete understanding of the overall use of resources in each of these settings. Such information could be used to inform the delivery of diabetes care services.

Making better use of resources and addressing clinical goals are key to DM management. However, positive experiences by patients and involvement in decision-making have also been highlighted as important factors, particularly during initiation of injectable therapy [13,14]. The prominence of the patient experience has also been raised in commissioning standards [15] and the NHS Outcomes Framework (domain 4) [16]. The recent policy drive to bring care of long-term conditions closer to patients has led to diversification of service models for DM in the NHS so that injectable therapies may be initiated across different care settings. However, it is unclear how patients' experiences of injectable therapies for DM vary across these settings.

Therefore, using tariff cost and micro-costing analyses, the aim of this series of service evaluations was to understand: current resource utilisation and costs by NHS staff associated with initiating injectable therapies for T2DM; the pathways of care; clinical outcomes and patient experiences in primary, secondary and intermediate care and how this may differ for insulin and GLP-1 RA therapies.

Methods

We conducted three service evaluations of initiation of injectable therapies for T2DM (one each in primary, secondary and intermediate care) using three methods of evaluation for each service. These evaluations were: a retrospective cohort review of medical records and service administration systems; a prospectively self-reported evaluation of NHS staff time on each episode of patient contact during the initiation period; a survey of patients attending for initiation of injectable therapy for DM. There was no change to the care of patients for any part of these evaluations.

Centre description

Whitstable is a primary care medical practice with ≈1,600 patients with T2DM led by a clinician and two diabetes nurse specialists. Both nurses have training in DM management and one is an independent nurse prescriber. Patient data are captured electronically using the EMIS database from the Egton Medical Information Systems Group [17].

Craylands (South West Essex community trust) is an intermediate care nurse-led service (with consultant support

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from an Acute Trust) with ≈2,500 patients. The practice staff consists of three consultants, eight nurses and one dietician. All nurses are trained nurse prescribers apart from one. Patient data are captured electronically using the Systems 1 database.

Doncaster and Bassetlaw NHS Trust is a secondary care diabetes service run by a consultant together with the collaboration of diabetes nurse specialists, dieticians, podiatrists, and chiropodists. The nursing team provide support to the ward and medical staff to enable quick and safe discharge of patients back into primary care services. Patient data are captured in medical notes.

Retrospective review

Patients were included in the retrospective review if they were aged ≥18 years at the time of initiation of GLP-1 RA or basal insulin and had a diagnosis of T2DM initiated on GLP-1 RA or basal insulin between 1 January 2010 and 31 December 2012. Patients who had been initiated previously with GLP-1 RA or basal insulin before 1 January 2010 were excluded.

Patients were identified from relevant prescribing systems and their date of initiation of GLP-1 RA/basal insulin cross-referenced with their date of birth by a member of the clinical care team to check for eligibility. Consecutive eligible patients were included, working backwards from clinic attendance on 31 December 2012. It was intended that an equal number of patients initiated with GLP-1 RAs and basal insulin would be included.

Data were obtained from clinical records, including patient case notes and local administrative and clinical databases, as applicable for each of the three settings (primary, secondary and intermediate care). Data were collected by clinical staff (secondary care and primary care) or by the evaluation facilitators themselves (intermediate care).

Feasibility work suggested that commonly patients would attend a three-month follow-up visit after initiation of basal insulin or a GLP-1 RA which would be a readily identifiable event. It was anticipated that "post-initiation" data would be collected at that visit. Once data collection was underway, it was apparent that this was not necessarily the case. "End of initiation" review appointments were not necessarily identifiable from medical records. Hence, those records were reviewed for ≤5 months after the index date (the index date is considered to be the date that treatment was initiated) for HbA_{1c} and 6 months after the index date for weight and the BMI. Similarly, not all the required baseline data were available at the date of initiation (index date), so records were reviewed for ≤2 months before the index date for HbA_{1c} and ≤3 months before or 7 days after the index date for weight and the BMI.

No explicit consent was sought from patients to use their medical records for service evaluations. Under UK regulations, such consent was not required at the time evaluations were conducted because service evaluations were treated as a necessary part of good quality care and hence included in the implicit consent given upon acceptance of clinical care. Review from Research Ethics Committee was not sought because service evaluation falls outside the remit of NHS Research Ethics Committees [18].

Evaluation of NHS staff time

Health professionals were eligible to take part in evaluation of NHS staff time if they were involved in the initiation and/or follow-up of patients initiated on a GLP-1 RA or basal insulin during the 3 months after initiation and consented to complete the time-record form. Eligible staff were identified and approached by a senior member of staff who explained the study to them and sought their consent to participate. Data were collected by NHS staff who completed a self-reported time-record form immediately after each patient contact in clinics or by telephone during the period of initiation of injectable therapy. Patient contacts were taken from staff-time evaluations of the prospective phase of the evaluation.

Questionnaire on patient experiences

Patients were eligible to take part in completing questionnaires on patient experiences if they: were aged ≥18 years at the time of initiation of GLP-1 RA or basal insulin; had a diagnosis of T2DM initiated on GLP-1 RA or basal insulin; were attending clinic during a specified 2-month period (at any point during the 3-month initiation phase); consented to complete a patient questionnaire. Patients who had been initiated with a GLP-1 RA or basal insulin were excluded. Patients who attended clinics were identified and checked for eligibility by clinic staff by cross-referencing the date of initiation of a GLP-1 RA/basal insulin with their date of birth. Eligible patients were approached by clinic staff who explained the study to them, provided them with written information, and sought their consent to participate.

Data regarding patient experiences of the service were collected using a specifically designed questionnaire for patient self-reporting. Participating patients were provided with a questionnaire to complete during their attendance or at home according to their preference, and a pre-paid envelope was provided for return of the questionnaire. If returned patient questionnaires contained missing or obviously incorrect data, these data were treated as "missing" and the patient was not contacted to resolve queries.

Data analyses

Data from each service evaluation were analysed separately. There was no pooling of data because it was intended only for local use in each setting. Results were stratified by type of injectable therapy. Tabulations were conducted using Microsoft Excel. Outcomes were tested using the Student's *t*-test for comparison of two mean values and ANOVA for comparing the mean values of three groups.

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Microcosting analyses of the cost of initiation

Hourly rates for healthcare professionals (HCPs) were taken from the Personal Social Services Research Unit publication *Unit Costs of Health and Social Care* (2013 edition) [19]. These rates were applied to the mean time per episode as self-reported by NHS staff to calculate a mean cost per visit type. The 2013 edition of this publication did not include an hourly rate for consultant time, but instead an overall contracted hours rate (£139). However, the 2010 edition of this publication [20] provides an estimate of 69% of consultant time as direct patient contact. This weighting was applied to the contracted hours rate to give an hourly rate for direct patient contact time of £201.

Mean costs per episode were applied to the mean number of each episode of care (initiation visits, follow-up visit, and follow-up telephone call) per 3-month period to calculate a mean per patient cost of resource use during the full 3-month initiation period. If data were missing for the staff time evaluation used, for example, for telephone follow-up call times for basal insulin initiations in all settings and GLP-1 RA initiations in primary care, no costs were applied to this resource use.

HCPs and Agenda for Change (AfC) banding

HCPs involved in initiation and follow-up visits included consultant physicians, practice nurses, and nurses with NHS banding 5, 6 and 7 as defined by the current AfC grading and pay system for all NHS staff [21]. The AfC job-evaluation system determines a point score that is used to match jobs to one of the nine pay bands. A fully qualified nurse would start at band 5.

NHS tariff cost analyses

For intermediate and secondary care, the relevant national cost for initiation was derived from the 2014/15 outpatient tariff for Diabetic Medicine [22]. This is a cost for an appointment in a consultant-led clinic in an outpatient setting (usually in an acute hospital). There may be locally agreed intermediate care tariffs, however, in the absence of published evidence on the tariff cost in intermediate care. The same cost was applied to an initiation in an intermediate care setting [23], which is likely to overestimate the true costs of this service.

For each patient, tariff costs were applied to initiations. The number of follow-up visits was recorded and a full 3-month initiation period cost was calculated. These data were used to calculate mean per patient costs. No costs were calculated for primary care because the NHS reference costs are not applicable in such a setting.

Results

Retrospective review

A total of 133 patients were included across all settings. Patients were included if they were considered to require initiation of injectable therapy. Fifty patients were included from each of the primary and intermediate care settings; 23 (46%) and 29 (58%), respectively, were initiations for basal insulin. Thirty-three patients were included from secondary care, of which 2 (6%) were initiations for basal insulin. There were fewer initiations for basal insulin assessed in secondary care due to the difficulty in identification of patients initiated on basal insulin, primarily due to local prescribing protocols and because patients may have been prescribed GLP-1 beforehand.

Demographics

Patient age ranged from 31 years to 85 years. The mean (SD) age for patients initiated on basal insulin was 51.0 (9.9) years for secondary care, 60.1 (14.7) years for intermediate care, and 67.7 (11.5) years for primary care. There was a similar percentage of male and female patients in each setting, with the proportion of males ranging from 12 (44%) for GLP-1 RA initiations in primary care to 15 (65%) basal-insulin initiations in primary care. Of 133 patients, 131 had received oral antidiabetic therapy previously. Demographics, reported co-morbidities, and prescribing of oral medicines are reported in Table 1.

Body weight, the BMI and HbA_{1c} outcomes at the end of initiation

After initiation of basal insulin, the mean weight (in kg) increased for patients in all three settings; in secondary care from 97.0 to 104.0, in intermediate care from 82.8 to 92.9, and in primary care from 89.2 to 94.6. However, the mean weight (in kg) fell in all three settings after initiation of GLP-1 RA; in secondary care from 112.5 to 108.3, in intermediate care from 113.8 to 107.2, and in primary care from 114.3 to 110.7 (Table 2).

After initiation of basal insulin, the mean (SD) BMI (in kg/m^2) increased for patients in all three settings; in secondary care from 30.0 (n=1) to 32.0 (n=1), in intermediate care from 29.9 (7.5) to 32.2 (8.8), and in primary care from 30.2 (7.9) to 31.6 (8.8). By contrast, after initiation of GLP-1 RA, the mean (SD) BMI (in kg/m^2) decreased for patients in all settings; in intermediate care from 37.2 (6.5) to 36.5 (4.0), in secondary care from 38.0 (7.2) to 36.3 (6.6), and in primary care from 39.9 (5.9) to 37.5 (3.5).

The mean (SD) HbA_{1c} fell after initiation of both types of injectable therapies in all three settings. For basal insulin initiations, HbA_{1c} fell in intermediate care from 9.9 (1.7)% (85 mmol/mol) to 8.0 (1.5)% (64 mmol/mol) ($P<0.001$) and in primary care from 10.1 (2.1)% (87 mmol/mol) to 8.0 (1.2)% (64 mmol/mol) ($P<0.001$). For GLP-1 RA initiations, HbA_{1c} did not

Table 1. Demographics and characteristics of patients at initiation.

			Secondary Care n=33		Intermediate Care n=50		Primary Care n=50	
			Insulin	**GLP-1 RA**	**Insulin**	**GLP-1 RA**	**Insulin**	**GLP-1 RA**
Number of patients	n, %		2 (6%)	31 (94%)	29 (58%)	21 (42%)	23 (46%)	27 (54%)
Age	Mean (SD)		51.0 (9.9)	57.3 (10.6)	60.1 (14.7)	57.0 (9.6)	67.7 (11.5)	59.0 (10.0)
Gender	% patients	Male	2 (100%)	20 (64.5%)	14 (48.3%)	11 (52.4%)	15 (65.2%)	12 (44.4%)
Weight (kg)	Mean (SD)		97.0 (n=1)	112.5 (18.2) (n=31)	82.8 (25.8) (n=23)	113.8 (19.7) (n=17)	89.2 (27.8) (n=19)	114.3 (21.5) (n=27)
BMI (kg/m^2)	Mean (SD)		30 (n=1)	38.0 (7.2) (n=31)	29.9 (7.5) (n=22)	37.2 (6.5) (n=16)	30.2 (7.9) (n=20)	39.9 (5.9) (n=27)
HbA$_{1c}$ % (mmol/mol)	Mean (SD)		- (n=0)	9.6% (1.4%) 81 mmol/mol (n=29)	9.9% (1.7%) 85 mmol/mol (n=22)	9.6% (1.6%) 81 mmol/mol (n=15)	10.1% (2.1%) 87 mmol/mol (n=17)	9.4% (1.4%) 79 mmol/mol (n=23)
Co-morbidities	n(%) patients	Hypertension	1 (50%)	26 (84%)	14 (48%)	5 (24%)	14 (61%)	18 (67%)
	n(%) patients	Hypercholesterolaemia	-	3 (10%)	9 (31%)	8 (38%)	1 (4%)	1 (4%)
	n(%) patients	Hyperlipidaemia	-	0 (0%)	0 (0%)	0 (0%)	1 (4%)	2 (7%)
	n(%) patients	Chronic kidney disease	-	0 (0%)	0 (0%)	0 (0%)	4 (17%)	3 (11%)
	n(%) patients	Other*	-	0 (0%)	0 (0%)	0 (0%)	5 (22%)	3 (11%)
	n(%) patients	None documented	1 (50%)	4 (13%)	12 (41%)	11 (52%)	6 (26%)	8 (30%)
Prescribing of oral medicines								
At east one oral medicine pre initiation	% patients		2 (100%)	30 (97%)	29 (100%)	21 (100%)	22 (96%)	27 (100%)
Sulphonylurea alone or in combination	% patients		1 (50%)	26 (84%)	22 (76%)	16 (76%)	18 (78%)	16 (59%)
Metformin alone or in combination	% patients		1 (50%)	28 (90%)	23 (79%)	20 (95%)	15 (65%)	24 (89%)

*Other; obesity (3), myocardial infarction (2), LVF (1), peripheral vascular disease (1), pancreatico-duodenectomy (1)
GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA$_{1c}$, haemoglobin type A$_{1c}$; LVF, left ventricular failure; SD, standard deviation.

change significantly in secondary care, going from 9.6 (1.4)% (81 mmol/mol) to 9.1 (2.1)% (76 mmol/mol) (P>0.1), but did fall significantly in intermediate care from 9.6 (1.6)% (81 mmol/mol) to 8.3 (1.3)% (70 mmol/mol) (P<0.01), and in primary care from 9.4 (1.4)% (79 mmol/mol) to 7.9 (1.8)% (62 mmol/mol) (P<0.005).

Adverse events

For patients initiated on basal insulin, none in secondary care, 5 in intermediate care, and 4 in primary care had hypoglycaemia documented in their medical records during their first 3 months of treatment. Only 1 patient in secondary care and 1 patient in intermediate care initiated on GLP-1 RAs had a record of a hypoglycaemic event. No primary-care patients initiated on a GLP-1 RA were reported as having a hypoglycaemic event. Other documented adverse events (not related to hypoglycaemia) during the initiation period for GLP-1 RA were reported by 11 (36%) patients in secondary care, 9 (43%) in intermediate care, and 10 (37%) in primary care.

Table 2. Clinical outcomes at 3-month follow-up post-initiation.

			Insulin	GLP-1 RA	Insulin	GLP-1 RA	Insulin	GLP-1 RA
HbA_{1c} % (mmol/mol)	Mean (SD)		9.6% (na) 81 (n=l)	9.1% (2.1%) 76 (n=12)	8.0% (1.5%) 64 (n=10)	8.3% (1.3%) 67 (n=8)	8.0% (1.2%) 64 (n=12)	7.9% (1.8%) 63 (n=7)
	% patients	≥1% reduction in HbA_{1c}	0/0	5/12	6/10	3/5	7/9	4/5
Weight (kg)	Mean (SD)		104.0 (na) (n=l)	108.3 (15.4) (n=19)	92.9 (34.3) (n=10)	107.2 (19.3) (n=5)	94.6 (29.1) (n=19)	110.7 (23.9) (n=11)
	% patients	≥3% reduction in weight	0/1	8/19	1/8	1/4	0/17	6/11
BMI (kg/m^2)	Mean (SD)		32.0 (na) (n=1)	36.3 (6.6) (n=20)	32.2 (8.8) (n=11)	36.5 (4.0) (n=4)	31.6 (8.8) (n=19)	37.5 (3.5) (n=12)
Reduction in BMI	% patients		0/1	80.0% (16/20)	33.0% (3/9)	66.7% (2/3)	33.3% (6/18)	75.0% (9/12)

Data were included on patients with a BMI/weight recorded within 3–6 months after the initiation date and 3–5 months after the date of initiation for HbA_{1c}.
GLP-1 RA, glucagon-like peptide-1 receptor agonist; SD, standard deviation.

For patients initiated on a GLP-1 RA, the most common side effect was nausea/vomiting/diarrhoea affecting 5 (16%) secondary-care patients, 7 (33%) intermediate-care patients, and 6 (22%) primary-care patients. In secondary care, 1 patient discontinued treatment due to nausea and 1 patient due to a swollen face. In intermediate care, 1 patient withdrew 13 days after experiencing nausea and vomiting. None of the patients who experienced hypoglycaemia withdrew from treatment during the period of data collection.

Evaluation of NHS staff time

More patients were analysed in the retrospective data analysis, but data from the prospective evaluation of NHS staff time was received on fewer initiations than expected. Due to local prescribing protocols in primary care, it was particularly difficult to identify eligible patients for injectable initiation to estimate the NHS staff time involved in this activity for this evaluation.

Time to referral

Patients had median (interquartile range (IQR)) waiting time from referral to initiation of basal insulin of 1.3 (1.1–2.2) weeks in primary care, and 4.5 (1.5–6.7) weeks in intermediate care. Median (IQR) waiting time from referral to GLP-1 RA initiation was 2.0 (0.9–2.9) weeks in primary care and 4.1 (3.1–6.4) weeks in intermediary care. Data regarding time from referral to initiation was not available for secondary care because referral was commonly conducted by telephone and not recorded in records for secondary care.

Number of clinic attendances and follow-up telephone calls

For patients initiated on basal insulin and GLP-1 RA, respectively, the mean (SD) number of clinic visits during the 3 months after initiation was 6.5 (0.7) and 4.3 (1.3) in secondary care, 3.8 (1.9) and 3.0 (1.3) in intermediate care, and 3.6 (1.5) and 2.4 (0.9) in primary care. The number of patients attending >5 times during the 3 months after basal insulin and GLP-1 RA initiation, respectively, were 2 (100%) and 10 (33%) in secondary care, 7 (24%) and 2 (10%) in intermediate care, and 6 (29%) and 0 (0%) in primary care.

The mean (SD) number of telephone follow-up calls during the 3 months after basal insulin and GLP-1 RA initiation, respectively, were 2.5 (1.6) and 1.0 (1.1) in primary care, 1.6 (1.7) and 0.6 (0.7) in intermediate care, and 0.1 (0.2) in secondary care (GLP-1 RA only). The number of patients having ≤2 follow-up calls during the period of basal insulin and GLP-1 RA initiation, respectively, were 21 (72%) and 21 (72%) in intermediate care, 14 (66%) and 24 (88%) in primary care, and 2 (100%) and 31 (100%) in secondary care.

NHS staff time during the initiation phase

In primary care, the initiation visit was reported as 30 min and the follow-up visit as 15 min. Two episodes of care were evaluated and a diabetes practice nurse managed the consultation (Table 3).

In intermediate care, the initiation visit was reported to range from 55 min to 60 min. Follow-up initiation visit was reported to be 60 min for basal insulin and 30 min for GLP-1

Table 3. NHS staff time to deliver care episodes.

				Secondary Care		Intermediate Care		Primary Care	
Variable				**Insulin**	**GLP-1 RA**	**Insulin**	**GLP-1 RA**	**Insulin**	**GLP-1 RA**
Healthcare professional time									
Initiation visits	Overall	Minutes	Mean (SD)	46 (n=1)	50 (n=1)	60 (12.3) (n=13)	55 (12.3) (n=6)	ND	30 (n=1)
		Minutes	Median (Range)			60 (30 to 90)	60 (30 to 90)		
	Nurse Band 5	Minutes	Mean (SD)	-	-	18.5 (28.8) (n=13	30.0 (30.9) (n=6)	ND	-
		Minutes	Median (Range)			0 (0 to 60)	30 (0 to 60)		
	Nurse Band 6	Minutes	Mean (SD)	-	-	27.7 (33.5) (n=13)	20.0 (31.0) (n=6)	ND	-
		Minutes	Median (Range)			0 (0 to 90)	0 (0 to 60)		
	Nurse Band 7	Minutes	Mean (SD)	28 (n=1)	30 (n=1)	13.9 (26.3) (n=13)	5.0 (12.3) (n=6)	ND	-
		Minutes	Median (Range)			0 (0 to 60)	0 (0 to 30)		
	Practice Nurse	Minutes	Mean (SD)	-	-	-	-	ND	30 (n=1)
		Minutes	Median (Range)						
	Consultant Physician	Minutes	Mean (SD)	18 (n=1)	20 (n=1)	-	-	ND	-
		Minutes	Median (Range)						
Follow up visits	Overall	Minutes	Mean (SD)	35 (n=1)	50 (n=1)	60 (0) (n=4)	30 (0) (n=2)	ND	15 (n=1)
		Minutes	Median (Range)			60 (60 to 60)	30 (30 to 30)		
	Nurse Band 6	Minutes	Mean (SD)	-	-	30.0 (34.6) (n=4)	15.0 (21.2) (n=2)	ND	-
		Minutes	Median (Range)			30 (0 to 60)	15 (0 to 30)		
	Nurse Band 7	Minutes	Mean (SD)	35 (n=1)	50 (n=1)	30.0 (34.6) (n=4)	15.0 (21.2) (n=2)	ND	-
		Minutes	Median (Range)			30 (0 to 60)	15 (0 to 30)		
	Practice Nurse	Minutes	Mean (SD)	-	-			ND	15 (n=1)
		Minutes							
Telephone follow up calls	Overall	Minutes	Mean (SD)	ND	9.2 (3.8) (n=5)	ND	10 (n=1)	ND	ND
		Minutes	Median (Range)		9 (5 to 15)				
	Nurse Band 7	Minutes	Mean (SD)	ND	9.2 (3.8) (n=5)	ND	10 (n=1)	ND	ND
		Minutes	Median (Range)		9 (5 to 15)				
	Practice Nurse	Minutes	Mean (SD)	ND	-	ND	-	ND	ND
		Minutes	Median (Range)						

ND Indicates where evaluation of time not undertaken
GLP-1 RA, glucagon-like peptide-1 receptor agonist; SD, standard deviation.

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RAs. Activities were shared between band-5, band-6 and band-7 nurses.

In secondary care, initiation visits were associated with ≈50 min of direct care time involving 20 min with the consultant and 30 min with the band-7 nurse. Follow-up visits ranged from 35 min to 50 min and a time per telephone follow-up call of 5–15 min. Initiation visit involved a consultant physician and a band-7 nurse, with all follow-up activity undertaken by a band-7 nurse.

NHS staff resources during the initiation period

In primary care, estimated costs for GLP-1 RA were £26.00 for an initiation visit and £13.00 for a follow-up visit (Table 4). In intermediate care, the costs were £117.17 for an initiation visit and £129.00 for a follow-up visit for basal insulin, and £101.25 for an initiation visit and £64.50 for a follow-up visit for GLP-1 RA. In secondary care, the per visit cost estimate was £125.17 for initiation and £81.08 for follow-up for basal insulin, and £136.50 for initiation and £115.83 for follow-up for GLP-1 RA. Costs for telephone follow-ups for GLP-1 RA were £21.31 in secondary and £23.17 in intermediate settings.

In primary care, the mean (SD) overall cost of staff time for initiation and follow-up for GLP-1 RA was £43.81 (£12.04) per patient. No data were available for patients who underwent initiation for basal insulin. In intermediate care, the mean (SD) cost of staff time was £243.49 (£85.73) per patient for GLP-1 RA initiation and follow-up compared with £473.63 (£240.49) for basal-insulin initiation. In secondary care, the mean (SD) cost of staff time for initiation and follow-up was £518.99 (£150.44) per patient for GLP-1 RA and £571.11 (£57.33) for basal insulin.

NHS tariff cost analyses

In primary care, the mean (SD) cost of the total initiation period was £90.48 (£29.02) for basal insulin and £59.26 (£23.15) for GLP-1 RA (Table 5). In intermediate care, the mean (SD) cost of total initiation was £548.07 (£204.30) for basal insulin and £464.93 (£138.62) for GLP-1 RA. In secondary care, the mean (SD) cost of total initiation was £848.50 (£77.49) for basal insulin and £606.34 (£142.03) for GLP-1 RA.

Questionnaire on patient experiences

Questionnaires were completed by 20 patients. Not all respondents provided a response to each question and, in some instances, questions were not applicable for certain patients. There was little variation in the responses from patients in the three settings and these were, in general, positive. Respondents stated that: they found it easy to speak to a member of the diabetes team; if they had concerns they were always given the opportunity to discuss them; concerns were addressed adequately and questions answered in a way they could understand.

Discussion

The purpose of this series of service evaluations was to describe the current NHS staff resource use utilized in initiation of injectable T2DM therapies, pathways of care, clinical outcomes, and patient experiences across three care settings: primary, intermediate and secondary.

Retrospective review

This retrospective service evaluation aimed to describe the estimated number of patients that would be initiated over

Table 4. Micro-costing of resource use for initiation.

			Secondary Care		Intermediate Care		Primary Care	
			Insulin (n=2)	GLP-1 (n=31)	Insulin (n=29)	GLP-1 (n=21)	Insulin (n=21)*	GLP-1 (n=27)
Initiation visit cost	£	Mean	125.17	136.50	117.77	101.25	ND	26.00
Follow up visit costs	£	Mean (SD)	445.94 (57.33)	381.12 (150.11)	355.86 (240.49)	129.00 (81.59)	ND	17.81 (12.04)
Telephone follow up call costs	£	Mean (SD)	ND	1.37 (5.32)	ND	13.24 (15.67)	ND	ND
Total for initiation period	£	Mean (SD)	571.11 (57.33)	518.99 (150.44)	473.63 (240.49)	243.49 (85.73)	NA	43.81 (12.04)

Resource costs have been calculated by applying the healthcare staff costs per visit to the resource use data collected in the retrospective review of notes.
*Not available for 2 patients who were treated by district nurses
ND Indicates where evaluation of time not undertaken
GLP-1 RA, glucagon-like peptide-1 receptor agonist; SD, standard deviation.

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Table 5. Price for 3-month initiation period "top–down".

			Secondary Care		Intermediate Care		Primary Care	
			Insulin (n=2)	GLP-1 (n=31)	Insulin (n=29)	GLP-1 (n=21)	Insulin (n=21)*	GLP-1 (n=27)
Initiation visit cost	£	Mean (SD)	245.75	245.75	245.75	245.75	25.00	25.00
Follow up visit costs	£	Mean (SD)	602.75 (77.49)	360.59 (142.03)	302.32 (204.30)	219.18 (138.62)	65.48 (29.02)	34.26 (23.15)
Telephone follow up call cost	£	Mean (SD)	NA	NA	NA	NA	NA	NA
Total for initiation period	£	Mean (SD)	848.5 (77.49)	606.34 (142.03)	548.07 (204.30)	464.93 (138.62)	90.48 (29.02)	59.26 (23.15)

Costs for intermediate and secondary care have been taken from the National Tariff[12] an MFF of 1.08 applied and a CQUIN payment of 2.5% added. Initiation visit total cost £245.75. Follow up visit total cost £109.59. Costs for primary care have been taken from the PSSRU 2013 and a nurse led surgery consultation cost of £25 applied for both initiation and follow up visits.
*Data not available for 2 patients
NA Tariff costs are not available for telephone calls and do not apply to services delivered within the primary care setting
GLP-1 RA, glucagon-like peptide-1 receptor agonist; SD, standard deviation.

a 3-year period in each setting. Despite the relatively small numbers of patients included in the evaluation, baseline characteristics and clinical measurements for the basal insulin group were similar to those for large cohort studies [24]. Mean age of patients initiated on basal insulin was not similar across the three settings (P=0.02) with those in primary care being (on average) 7 years older than those in intermediate care; however, patients initiated on a GLP-1 RA were (on average) 5 years younger than patients initiated on basal insulin (P=0.014). This difference may be due to GLP-1 RA being a displaced therapy in the prescribing hierarchy, often being introduced to patients before the option of basal insulin therapy. Hypertension was the most commonly listed comorbidity for patients on basal insulin and GLP-1 RA therapies. Patients were taking various oral DM medications before initiation of basal insulin or GLP-1 RA, with a sulphonylurea and metformin being the most common.

At initiation, the mean level of HbA_{1c} tended to be slightly (but not significantly) higher for patients taking basal insulin than for those taking GLP-1 RA across all settings. Overall, there was a reduction in the mean level of HbA_{1c} 3 months after initiation for both types of injectable therapy in all settings (basal insulin: intermediate and primary care; GLP-1RA: all settings). For those initiated on basal insulin, 60% initiated in intermediate care and 78% in primary care achieved a reduction in HbA_{1c} level of ≥1%. Achievement of reduction of a HbA_{1c} level of ≥1% (11 mmol/mol) was assessable in only 28 patients due to missing data. Due to small sample sizes, these differences were not significant.

In addition to reduction in HbA_{1c} level, patients on GLP-1 RA also experienced the added benefit of weight loss. Patients initiated on GLP-1 RA were (on average) heavier than those initiated on basal insulin. This weight difference at initiation may be due to the acknowledged weight-loss effect of GLP-1 RA, meaning that these therapies are used primarily in patients with higher weight, in accordance with NICE guidance [2].

Three months after initiation with GLP-1 RA, 55% in primary care, 25% in intermediate care, and 42% of patients in secondary care saw a weight reduction of ≥3%. These results reflect findings from a nationwide audit of liraglutide use that showed an average weight loss of –3.1 kg at 3 months [25]. Unexpectedly, 1 patient initiated on basal insulin had a weight reduction of ≥3%. However, for most of the patients initiated on basal insulin, average weight increased in all three settings. Basal insulin is anabolic in nature, so this is an expected outcome and consistent with other evidence that has shown weight gain after initiation of basal insulin [25,26].

Similarly, the baseline BMI was higher for patients taking GLP-1 RA than those on basal insulin. NICE recommends that GLP-1 RA should be considered if the BMI is ≥35 kg/m^2 and patients do not have glycaemic control [2]. This strategy suggests that NICE guidance is being considered when initiating a patient on a GLP-1 RA in all settings. After GLP-1 RA, the mean reduction in the BMI was lower in secondary, intermediate and primary (–1.7 and –0.7 *vs.* –2.4 kg/m^2) settings. Analyses of the proportion of patients who experienced a reduction in the BMI showed that approximately one-third of patients initiated on basal insulin and at least two-thirds of those initiated on GLP-1 RA had this benefit.

Patients on basal insulin were more likely to experience hypoglycaemia during their first 3 months of treatment than patients on GLP-1 RA. However, the number of other adverse events experienced during the first 3 months of treatment was higher for GLP-1 RA patients, and included nausea/vomiting/diarrhoea and gastrointestinal discomfort. These observations are consistent with findings from clinical trials which report a higher incidence of gastrointestinal-related adverse events with GLP-1 RA [27]. These findings highlight the importance of the education and support of patients for the known side effects of these therapies.

Service outcomes

Times from referral to initiation were similar whether initiation was for basal insulin or GLP-1 RA. However, patients experienced longer referral times in intermediate care (4.5 and 4.1 weeks, respectively) than in primary care (1.3 and 2.0 weeks, respectively).

A higher proportion of patients attended ≥5 times during the initiation period when initiated on basal insulin compared with GLP-1 RA. Data were not collected regarding the nature of these visits. However, GLP-1 RA initiations may have been less resource-intensive than basal-insulin initiations in terms of numbers of visits due to the absence of a requirement to titrate to the optimal dose in relation to carbohydrate load. However, due to the small sample size and lack of statistical analyses, these results should be viewed with caution.

The mean number of follow-up clinic visits per patient during the 3 months post-initiation period was broadly similar whether initiation was for basal insulin or GLP-1 RA. In contrast, primary-care patients had more telephone follow-up calls than those in other settings, with 2.5 calls for insulin and 1.0 for GLP-1 RA in primary care, 1.6 for insulin and 0.6 for GLP-1 RA in intermediate care, and 0 calls for insulin and 0.1 calls for GLP-1 in secondary care.

Evaluation of NHS staff time

Where data were available, the mean NHS staff time required for an initiation visit was 30–60 min, with little difference in the amount of time required for initiation using GLP-1 RA or basal insulin across all three settings. Time taken for follow-up visits was similar to the initiation visit, with mean NHS staff time of 15–60 min. Telephone follow-up calls were considerably shorter and, in secondary and intermediate care centres, the mean nurse time was 9.2–10 min.

Staff involved in the initiation visit varied across the three centres: practice nurse in primary care; nurse bands 5, 6 and 7 in intermediate care; consultant physician and nurse band 7 in secondary care. For follow-up visits, a practice nurse was involved in primary care, nurse bands 6 and 7 in intermediate care, and nurse band 7 in secondary care. Telephone follow-up calls were conducted by nurse band 7 in intermediate and secondary care.

Resource use

Using micro-costing methods, for the overall initiation period for which data regarding time taken for care episodes was available, the mean per patient cost for basal insulin and GLP-1 RA initiations was higher in secondary care than in other settings. Where data were available, the mean per patient initiation cost was lowest in primary care for GLP-1 RA patients. As noted in the evaluation of secondary care, GLP-1 RA initiations were more costly than those for basal insulin. This finding may be unexpected, particularly with existing support to indicate that initiations of basal insulin may be more complicated. However, this finding may be due to the small sample of patients in this evaluation and because information regarding initiations may not have been captured adequately in medical notes.

Differences in cost according to setting were driven largely by differences in staff cost with involvement of a mixture of specialist nurse and consultant physician in secondary care, specialist nurses of varying grades in intermediate care, and a diabetes practice nurse in primary care. In addition, the primary-care service tended towards fewer clinic visits and a higher number of telephone follow-up calls.

For "top–down" costing, the NHS England outpatient tariff for Diabetic Medicine in 2014/2015 has been applied to the number of care episodes identified in the retrospective review of records for secondary and intermediate care. No such data are available for primary care, so costs for primary care were taken from *Unit Costs of Health and Social Care* (2013 edition) [13]. Primary-care costs were lower than intermediate and secondary care (£90.48 for GLP-1 RA and £59.26 for basal insulin). Tariff prices used for secondary and intermediate care visits are identical, so differences between services were due to numbers of follow-up visits in the initiation period. Hence, secondary-care costs were greater than those for intermediate care, and basal-insulin initiations were greater than those for GLP-1 RA: £848.50 for basal insulin in secondary care, £606.34 for GLP-1 RA in secondary care, £584.07 for basal insulin in intermediate care, and £464.93 for GLP-1 RA in intermediate care. In some cases, intermediate-care costs were derived from block contracts and so may vary depending on locality and contract negotiations.

Questionnaire on patient experiences

Fewer patients completed the questionnaire than expected. Responses in the three settings were, in general, positive, but these results should be interpreted with caution due to the low number of respondents. Future studies aiming to capture patient experiences should consider an alternative methodology for capturing feedback and achieving a higher response rate. Uptake of patient questionnaires could be better if patients were asked to complete the survey while they are visiting the centre as part of their routine care rather than taking it home to complete.

Limitations

This is a series of local-service evaluations aimed to describe initiation services in three healthcare settings. These results are examples of costs and, as such, are not designed to be statistically representative beyond the scope of the services evaluated. By its nature the sample was small and the aim was to provide a descriptive analysis: statistical analyses were not conducted. Retrospective data were derived from clinical

records so the accuracy and completeness of evaluation data relies on the quality of clinical records. In many cases, data regarding weight, the BMI and HbA_{1c} level at 3–5 months post-initiation were missing, making it difficult to describe changes that had taken place over the first 3 months of treatment.

Overall, patient numbers were skewed towards more patients being initiated on GLP-1 RA rather than basal insulin at some of the centres. Unequal numbers of patients on basal insulin and GLP-1 meant that it is not possible to compare across therapy groups effectively. Low uptake of basal insulin at some centres may have been due to the choice and involvement of patients in discussions regarding the types of therapy available. Given the high prevalence of obesity of patients with T2DM, the benefits of weight loss and low incidence of hypoglycaemia are particularly appealing to some patients, and could explain this discrepancy.

Data were not available for the time from referral to initiation from secondary care because referrals are conducted by telephone (which are not documented). In addition, data from evaluation of NHS staff time were received on fewer episodes of care than expected. This phenomenon may have been due to the low number of patients that attended clinics during the evaluation period and the demanding workload of clinical staff conducting the evaluation, thereby not allowing time to adequately record data for this evaluation. Where data regarding staff time needed for episodes of care were not available from staff evaluation (e.g., telephone follow-up calls for basal-insulin initiations in secondary care and all care episodes for basal-insulin initiations in primary care), no assumptions regarding staff time were made. Therefore, where data were available for some (but not all) aspects of the initiation period, resource use may have been underestimated and under-reported for basal insulin and GLP-1 RA. However, with the exception of basal-insulin initiations in primary care, missing data were limited to time for telephone follow-up calls. Telephone calls may not have a great impact on resource use as they are often shorter than visits in person. However, a series of telephone calls over a period of time may have a greater impact on resource use.

Conclusion

Despite the limitations acknowledged in this evaluation, retrospective data showed that basal insulin and GLP-1 RA were effective therapies in the treatment of T2DM. All three services, with both types of injectable therapies, achieved a reduction in HbA_{1c} level after initiation, with patterns of weight gain/loss and adverse events as expected. Adverse events and known side effects experienced by patients in evaluations highlight the need for patient support if a new medication is initiated.

Initiation of GLP-1 RA was associated with less staff time than initiation of basal insulin and this was a consistent difference across the three service settings. Primary care provided a less resource-intensive and less costly setting, driven largely by lower staff costs and fewer face-to-face clinic visits, with similar outcomes achieved. As a result, the intermediate service has adapted its services to include greater use of remote follow-ups for patients.

Findings from this evaluation can be used as a guide for local diabetes services to evaluate their service delivery. Future research could expand upon these findings to produce generalizable results and explore outcomes over a longer term beyond the 3-month initiation period covered in this evaluation.

Contributions

Dr Richard Brice, Ms Sharon Shelley, and Dr Pankaj Chaturvedi were involved in the planning and conduct of the research study, interpretation and reporting of results, and met the criteria of authorship. Novo Nordisk UK were involved in the planning, design and interpretation of results and facilitated conduction of the study. pH Associates provided support with the design, conduction, analyses and reporting of study results and scientific editorial support.

Potential conflicts of interest

The International Committee of Medical Journal Editors' (ICMJE) Potential Conflicts of Interests forms for the authors are available for download at: http://www.drugsincontext.com/wp-content/uploads/2015/01/dic.212269-COI.pdf

All named authors meet the ICMJE criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for this version to be published. All authors (excluding the study sponsor) had full access to all data in this study and take complete responsibility for the integrity of the data and accuracy of the data analyses.

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