Primary care diabetes prescribing rates: latest analysis shows continued rise in volume and cost

The latest report on primary care prescribing for diabetes in England from NHS Digital (formerly from the Health and Social Care Information Centre) shows continued growth in prescribing volume and cost at a rate well in excess of that for all other medicines.1

In an in-depth analysis, Steve Chaplin here reports that, with support from management guidelines and emerging evidence, newer agents may after all reduce mortality, and there is clearly potential for an increase in prescribing for the foreseeable future.

The wider picture

According to data from the Quality and Outcomes Framework, 6.4% of people aged 17+ and registered with a GP in England have diabetes, of whom type 2 diabetes accounts for 89%. The region with the highest prevalence is the West Midlands (7.5%); South Central has the lowest (5.6%). These are probably substantial underestimates: figures from Public Health England put the 2016 prevalence of diagnosed and undiagnosed diabetes in England at 8.6% and higher than 12% in some clinical commissioning groups (CCGs).2

Prescriptions for medicines to treat diabetes have accounted for an increasing share of national prescribing during the past 10 years and now make up about one in every 22 items dispensed and over £1 in every £10 spent in primary care prescribing. In the past decade, volume and cost increased by well over 80%; the corresponding figures for all medicines are 49% for items and 16% for cost.

The average cost of prescribing per person on a diabetes register was £328 and half of CCGs lay within the range £310–353. The lowest spending CCG was Northumberland (£239); the highest was Warwickshire North (£415). Spending on diabetes medicines as a proportion of total net ingredient cost was highest in London (12.9%), where prevalence was 6.1%, and lowest in Cumbria (8.6%), where prevalence was 6.7%.

Not all diabetes drugs are equal

Volume and cost growth are not equally shared among the agents in BNF category 6.1 (‘Drugs used in diabetes’): (Figures 1 and 2). Volume has increased most for metformin, with a year-on-year increase that peaked at 13% in 2007/8 but since 2013/14 has fallen to 4.9%. The only category that has surpassed that growth rate has been ‘other antidiabetic drugs’, with volume growth peaking at 20% in 2010/11, falling back to 10% in 2012/13 and now returning to 19%.

Steady growth in the cost of diagnostic and monitoring products has
Primary care diabetes prescribing rates in England

continued but spending on sulphonylureas and ‘other insulins’ has fallen over the past decade. The rate of increase in volume and cost of analogue insulins looks to be reaching a plateau (albeit a very high one for cost), having doubled both volume and cost over the past 10 years. The year-on-year cost of metformin increased by 29% in 2014/15 and 14% in 2015/16. It now totals £119 million (compared with £71 million in 2012/13), due to higher cost per item (£5.94 vs £4.17).

The bulk of the NHS report focuses on ‘other antidiabetic drugs’ – the category that has seen most new medicines introduced. The cost of these agents was £273 million in 2015/16, almost matching that of the analogue insulins. Year-on-year cost growth was 6.3% in 2013/14, 16% in 2014/15, and 29% in 2015/16.

Other antidiabetic drugs

Other antidiabetic drugs are listed in Table 1. Figures 3 and 4 show the changes in prescribing volume and cost for the drugs in this category. The top five drugs by volume, cost and per item are listed in Table 2. Cost per item has changed little in the past four to five years for most drugs in this category, the exception being pioglitazone. In their prime during the late-2000s, the glitazones cost £44 per item. By 2014/15, rosiglitazone was a distant memory and the cost per item for pioglitazone was £4.80. However, in 2015/16, this increased to £15.67 – presumably following its classification as a Category M medicine, for which prices are set by the Department of Health as part of its mechanism to remunerate pharmacies.

DPP-4 inhibitors

The DPP-4 inhibitors have enjoyed enormous success: within the space of 10 years, annual volume has increased from 23 000 to 4.1 million items and the annual rate of growth in 2015/16 was 20%. Net ingredient cost increased from £0.9 million in 2007/08 to £147 million in 2015/16 but, by contrast with the GLP-1 agonists and SGLT2 inhibitors, average cost per item has fallen (from £40.95 to £35.69).

Of the five DPP-4 inhibitors available, sitagliptin has the highest

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipetidylpeptidase-4 inhibitors</td>
<td>Alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin</td>
</tr>
<tr>
<td>Glucagon-like peptide-1 receptor agonists</td>
<td>Dulaglutide, exenatide, lixisenatide, lixisenatide (albiglutide not included)</td>
</tr>
<tr>
<td>Insulin release stimulators</td>
<td>Nateglinide, repaglinide</td>
</tr>
<tr>
<td>Intestinal alpha-glucosidase inhibitor</td>
<td>Acarbose</td>
</tr>
<tr>
<td>Sodium-glucose co-transporter 2 inhibitors</td>
<td>Canagliflozin, dapagliflozin, empagliflozin</td>
</tr>
<tr>
<td>Thiazolidinedione</td>
<td>Pioglitazone</td>
</tr>
</tbody>
</table>

Table 1. ‘Other’ antidiabetic drugs

![Figure 3](https://example.com/figure3.png)  
**Figure 3.** Number of prescription items for other antidiabetic drugs by class of drug in England, 2007/08 to 2015/16.1 (Copyright © 2016, Health and Social Care Information Centre)

![Figure 4](https://example.com/figure4.png)  
**Figure 4.** Net ingredient cost (NIC) of other antidiabetic drugs by class of drug in England, 2007/08 to 2015/16.1 (Copyright © 2016, Health and Social Care Information Centre)
Primary care diabetes prescribing rates in England

average cost per item (£37.48) but accounts for 61% of items and 64% of spending on this group. Linagliptin (average cost per item £32.52) makes up 23% of items and 21% of spending. None of the others exceeds 10% of either volume or cost.

GLP-1 receptor agonists

The GLP-1 receptor agonists are the second largest group of other antidiabetic drugs. Introduced at about the same time as the DPP-4 inhibitors, prescribing has increased at about one-fifth of the rate for that group (Figure 3), but the rate of cost growth has been about half (Figure 4).

These agents are the most expensive of the other antidiabetic drugs, with average costs per item two to three times greater than the DPP-4 inhibitors and SGLT2 inhibitors. Of the four GLP-1 receptor agonists included, liraglutide is the most expensive but is the leader of this group by volume prescribed (58%) and cost (65%). Exenatide accounts for most of the remaining volume (30%) and cost (26%).

SGLT2 inhibitors

This, the newest group of other antidiabetic drugs, has also been a success. Items have risen from only 800 in 2012/13 to 778,000 in 2015/16 and annual spending now exceeds £33 million. Dapagliflozin, the first in class, still has the lion’s share of volume (71%) and spending (70%), followed by canagliflozin (23% and 24%, respectively).

Others

Compared with other groups in this category, repaglinide, nateglinide and acarbose were little used but they nonetheless account for substantial expenditure, with 135,000 items costing £1.5 million in 2015/16. These agents are not recommended in the latest NICE guidance on the management of type 2 diabetes (repaglinide is mentioned as an option for first intensification in patients who can’t take metformin but this is an unlicensed indication).3

Insulins

Prescribing of insulins has been growing at a rate of 3–4% annually since 2009/10, with cost growth of 2–3%. The 6.9 million items dispensed in 2015/16 cost a total of £344 million. Human analogue insulins (aspart, glulisine, lispro, degludec, detemir, glargine) account for about 87% of insulin prescribing and have done so for the past five to six years. They rank fourth by prescribing volume (after metformin, sulphonylureas and other antidiabetic drugs), but have the highest annual cost (Figures 1 and 2) and average net ingredient cost (by group, not individual product) of all. The statistics on insulin prescribing do not differentiate between their use for type 1 or type 2 diabetes.

Diagnostic and monitoring devices

The popularity of urine glucose testing continues to decline and prescribing volume (125,000 items) and cost (£400,000) are now about one quarter of their level a decade ago. Conversely, prescribing of ketone testing reagents is rising, with volume up 20% (to 132,000 items) and spending up 23% (to £5.4 million). The rate of increase in prescribing glucose testing reagents began to rise about five years ago and 2015/16 saw a 3% increase over the previous year to 6.8 million items at a cost of £181 million.

Prospects for future growth

Several indicators suggest that the growth in prescribing for diabetes is likely to continue. First, the population eligible for treatment will grow. The prevalence of diabetes in England is expected to increase to 9.5% by 2030; this is probably a low estimate because it takes into account the rising average age of the population but not an increase in the prevalence of obesity.2

Second, cost pressure will come from new drugs that have already been introduced but are not included in the current statistics (albiglutide, costing £923 per year) or are in the pipeline, such as omorglitapin, a weekly DPP-4 inhibitor, and etrogliuflozin, another SGLT2 inhibitor.

Finally, the indications for drug treatment may broaden, or certain classes of antidiabetic agents may be preferred for some subgroups of patients, as evidence emerges of their impact on long-term outcomes. Two trials have recently shown that treatment can reduce cardiovascular mortality in patients with type 2 diabetes who are at high cardiovascular risk (Table 3).4,5

In LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results), liraglutide significantly reduced the risk of the primary composite endpoint and the risk of all-cause and cardiovascular death. However, non-fatal myocardial infarction, non-fatal stroke and admission for heart failure were not significantly less common than with placebo. Liraglutide also significantly reduced the incidence of nephropathy but not retinopathy. Outcomes were superior, but not significantly so, in patients with shorter duration of diabetes (<11 years) and BMI >30, in patients without heart failure, and in those with established cardiovascular disease rather than having risk factors. The number of patients who would need to be treated (NNT) to prevent one primary endpoint event in three years was 66; the NNT for death from any cause was 98.

In EMPA-REG OUTCOME, empagliflozin significantly reduced the risk of the primary composite

<table>
<thead>
<tr>
<th>No. of items (000s)</th>
<th>Cost (£ million)</th>
<th>Mean cost per item (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Sitagliptin</td>
<td>2500</td>
<td>94</td>
</tr>
<tr>
<td>2 Pioglitazone</td>
<td>1105</td>
<td>48</td>
</tr>
<tr>
<td>3 Linagliptin</td>
<td>965</td>
<td>31</td>
</tr>
<tr>
<td>4 Dapagliflozin</td>
<td>550</td>
<td>23</td>
</tr>
<tr>
<td>5 Liraglutide</td>
<td>464</td>
<td>19</td>
</tr>
</tbody>
</table>

Table 2. Top 5 ‘other antidiabetic drugs’ 2015/16 (includes combinations with metformin)
### Table 3. Summary of the LEADER and EMPA-REG OUTCOME trials

<table>
<thead>
<tr>
<th>Eligibility criteria</th>
<th>LEADER (n=9340)</th>
<th>EMPA-REG OUTCOME (n=7020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c ≥53mmol/mol (7.0%); mean BMI 72≥50 years + ≥1 cardiovascular (CV) condition*. Median follow up 3.8 years. DPP-4 inhibitors not permitted</td>
<td>HbA1c ≤53mmol/mol (7.0–9.0%) without treatment or 53–86mmol/mol (7.0–10.0%) despite treatment (mean 64mmol/mol, 8.0%). Established CV disease***</td>
<td>BMI ≤45 (mean 31). HbA1c 53–75mmol/mol (7.0–9.0%) and all-cause death, and admission to hospital for heart failure. There was little difference between active treatment and placebo or empagliflozin 10 or 25mg/day. HbA1c target decided locally. Median follow up 3.1 years</td>
</tr>
<tr>
<td><strong>Microalbuminuria or proteinuria, hypertension and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction, or an ankle–brachial index &lt;0.9.</strong></td>
<td><strong>Coronary heart disease, cerebrovascular disease, peripheral vascular disease, chronic kidney disease of stage 3 or greater, or chronic heart failure (New York Heart Association class II/III).</strong></td>
<td><strong>Microalbuminuria or proteinuria, hypertension and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction, or an ankle–brachial index &lt;0.9.</strong></td>
</tr>
<tr>
<td>Primary endpoint</td>
<td>Composite of death from CV causes, non-fatal myocardial infarction (including silent MI) or non-fatal stroke</td>
<td>Composite of death from CV causes, non-fatal myocardial infarction (excluding silent MI) or non-fatal stroke</td>
</tr>
<tr>
<td>Outcome</td>
<td>Incidence of primary endpoint: liraglutide 13.0% vs placebo 14.9%. Hazard ratio 0.87 (95% CI 0.78–0.97); p&lt;0.01</td>
<td>Incidence of primary endpoint: all empagliflozin 10.5% vs placebo 12.1%. Hazard ratio 0.86 (95% CI 0.74–0.99); p=0.04</td>
</tr>
</tbody>
</table>

*Coronary heart disease, cerebrovascular disease, peripheral vascular disease, chronic kidney disease of stage 3 or greater, or chronic heart failure (New York Heart Association class II/III). **Microalbuminuria or proteinuria, hypertension and left ventricular hypertrophy, left ventricular systolic or diastolic dysfunction, or an ankle–brachial index <0.9. ***Mostly coronary artery disease, history of myocardial infarction or stroke.

Table 3. Summary of the LEADER and EMPA-REG OUTCOME trials

---

**Call for your diagnostic dilemmas in diabetes in young people**

Practical Diabetes is planning a themed issue on the topic of ‘What type of diabetes do I have?’ We would welcome a short description (around 500–800 words) of your unusual diabetes presentations in young people which the Practical Diabetes Genetics Expert will endeavour to discuss. We are planning to publish the short cases and practical approaches to investigating and treating them in an article to appear in the themed issue.

Please email your cases to the Managing Editor, Helen Tupsy htupsy@wiley.com by 20th March 2017 and we will be pleased to offer a payment of £100.00 to the authors of any of the published cases.

---

**References**