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Sodium–glucose co-transporter 2 inhibitors (SGLT2Is) – The latest residents on the block: Impact on glycaemic control at a general practice level in England

Running head: Drug choice and its consequences for glycaemia year on year

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Abstract

Aims

Despite increasing spend on new Type 2 diabetes mellitus (T2DM) therapies, the proportion of people with T2DM achieving target glycaemia outcomes is declining. Our aim was to determine, using published General Practice level data, how differences in T2DM prescribing patterns relate to glycaemic target achievement levels.

Methods

Multiple linear regression modelling was used to link practice characteristics and defined daily dose (DDD) of class of medication in 2015/16 and changes to 2014/15 in medication to proportions achieving target glycaemic control (TGC; glycated haemoglobin A1c (HbA1c) ≤7.5%, 58 mmol/mol) and high glycaemic risk (HGR; HbA1c >10.0%, 86 mmol/mol) for practices in the National Diabetes Audit (NDA) with >100 T2DM on their register.

Results

Overall, HbA1c outcomes were not different between the years studied. Although in percentage terms most practices increased their use of Sodium–glucose co-transporter 2 inhibitors (SGLT-2Is) (96%), Dipeptidyl peptidase-4 inhibitors (DPP-4Is) (76%) and glucagon-like peptide 1 (GLP-1) analogues (53%), there was wide variation in use of older and newer therapies. For example, 12% of practices use >200% national average of some newer agents. In cross-sectional analysis: greater prescribing of metformin and analogue insulin were associated with a higher proportion achieving HbA1c ≤58 mmol/mol; SGLT-2Is and metformin were associated with reduced proportion of HbA1c >86 mol/mol; otherwise associations for sulphonylureas, GLP-1 analogues, SGLT-2Is and DPP-4Is were neutral or negative. In year-on-year analysis there was ongoing deterioration in glycaemic control which was offset to some extent by increased use of SGLT-2Is and GLP-1 analogues, which were associated with a greater proportion achieving HbA1c ≤58 mmol/mol and a less
proportion of people at >86mmol/mol. SGLT-2I prescribing was associated with significantly
greater improvements than those found for GLP-1 analogues.

**Conclusion**

Increased use of newer agents was associated with improvement of glycaemic outcomes
but not sufficient to compensate for prevailing decline. This may reflect wide variability in
the prescribing of newer agents. We have found that SGLTIs may display advantage vs
other oral agents in relation to HbA1C outcome. Serious consideration should be given to
their use.
Introduction

The report Prescribing for Diabetes England 2006/07 to 2016/17 [1] has documented a 70% increase in total expenditure on drugs used to treat Type 2 Diabetes Mellitus (T2DM) from 2010/11 to 2016/17 (£160 to £272 million/year). The main cost drivers have been new agents such as Glucagon-like peptide-1 agonists (GLP-1a), Dipeptidyl peptidase-4 inhibitors (DPP-4i) and sodium–glucose co-transporter 2 inhibitors (SGLT2Is).

The National Diabetes Audit (NDA) of England (2010/11–2015/16) reported that over this period, the diagnosed population of people with T2DM in England rose by 22% from 2.3 million to 2.8 million and the proportion of people with T2DM achieving target glycaemic control (TGC) with glycated haemoglobin A1c (HbA1c) ≤7.5% (58 mmol/mol) fell from 66.5% to 65.7% [2], whilst the number at higher glycaemic risk (HGR) with HbA1c >10.0% (86 mmol/mol) decreased from 7.0% to 6.7%.

These observations raise the important issue of whether the increased investments in the newer therapies for T2DM can deliver benefits in the real world. We have sought to determine whether practice-level differences in use of the individual medication classes relate to the proportions of T2DM individuals achieving TGC or at HGR.

We investigated whether General Practitioner Practice (GPP) level data for England and NDA HbA1c outcome data along with other epidemiological and service indicators for the years 2014–2016 are associated with rates of prescribing among the various classes of T2DM medications using a validated approach for combining large datasets [3] [4]. Our aim was to determine, using published General Practice level data, how differences in T2DM prescribing patterns relate to glycaemic target achievement levels. We have described our approach in previous recently published papers (3,4).

Methods

The NDA [2] includes, by type of diabetes, patient characteristics (age, ethnicity and social disadvantage) and treatment measurements (serum cholesterol levels, blood pressure (BP)) and stratified HbA1c. The NDA stratified HbA1c according to the UK National Institute for Clinical Excellence (NICE) clinical guideline HbA1c categories operational from 2010–2016 including HbA1c ≤7.5% (58 mmol/mol) and HbA1c ≤10.0% (86 mmol/mol). In this
study, the percentage of results \( \leq 7.5\% \) (58 mmol/mol) are defined as on TGC and of results >10\% (86 mmol/mol) as at HGR.

Data from general practices (GPs) in England that participated in 2014/15 and 2015/16 were included. However, to minimise outlier effects, practices that reported less than 100 T2DM individuals on their practice register were excluded.

The monthly GP prescribing data reports [5], for each British National Formulary (BNF) code and practice, the prescriptions, quantity and costs prescribed were examined. From the BNF data, the amount of active chemical in each item of prescribed quantity was identified. Defined Daily Dose (DDD), which is the assumed average maintenance dose per day for a drug administered for its main indication in adults including insulin [6], was applied together with the amount prescribed to calculate the average daily number of T2DM individuals on each therapy during the year.

Other channels including hospital prescribers, prescribers not in the Quality and Outcomes Framework (QOF) and home delivery could not be captured with this analysis. The QOF [7] provides annual pay for performance data for all GPPs including the overall number of registered diabetes patients and levels of glycaemic control. However, there is no split between Type 1 Diabetes Mellitus (T1DM) and T2DM.

Public Health England (PHE) publish the theoretical expected percentage prevalence of overall diabetes based on age, gender and ethnicity [8] and these values for each GPP population, enabling calculation of the expected number of diabetes patients in each practice.

Datasets were combined into a single extract and several diabetes performance indicators were calculated for each GPP that took part in the NDA, for each of the two years. In order to ensure the sample was representative, the QOF reports from GPPs in the NDA were compared with those not in the NDA.

Practice characteristics measured were both socio-demographic (including age, gender, ethnicity and social deprivation, practice size, and expected disease prevalence) and GPP service determined (including case identification, completion of eight annual care checks (as reported in the NDA), percentage of annual new cases, the education provided to new
cases, the levels of NICE target BP and cholesterol achievement for T2DM, plus the level of HbA1c control being achieved within their T1DM population) [2].

The levels of medication use in each GPP were established for each class as the ratio of the total DDD to the T2DM register. The number of T2DM patients on insulin or using blood glucose meter (BGM) strips are not directly given, so we calculated these by deducting the estimated insulin and strips used by T1DM patients, based on NICE [9] recommended daily levels of 50 units of insulin and four BGM test strips, from the total insulin and BGM strips used, assuming the remainder were used by T2DM patients at a rate of 100 units of insulin/day and one test strip/day [10]. This number was then shown as a percentage of the T2DM population. Insulin analogue use was expressed as a percentage of total insulin.

The relation between practice characteristics, prescribing, and glycaemic outcomes (TGC, HGR) was examined both cross-sectionally for 2015/16 and longitudinally for those practices that had participated in the NDA both in 2014/15 and 2015/16, considering the relation between levels of change in measures for the same practice between the 2 years.

Due to the data structure, there was no information concerning the number of patients who managed with diet and lifestyle only or for whom combinations of multiple therapies were used.

**Patient involvement**

No patients, service users, carers or lay people were involved in the design or conduct of this study, which only used publically available data. The outcome measures were derived from NICE standards.

The analysis utilised publicly available data. The development of the research question and outcome measures were informed by patients’ priorities and experience in the everyday clinical setting.

**Analysis**

Figure 1 describes the methodology. For each practice, for 2015/16 and 2014/15, 17 performance indicators were used grouped into epidemiological, service and medication categories. Using 64-bit Microsoft Excel 2016 (with the Analyse-it add-in), the influence of these independent variables on the TGC and HGR patient outcome variables was
assessed using linear multiple regression analysis. Where practices had data for both years, linear multiple regression compared the annual changes in indicator values with annual changes in outcomes.

Step-wise regression was used to remove indicators with the highest p values sequentially from the model, until a set with p values all below 0.01 was reached. The 17 core indicator variables (Table 1) were reduced to 13 for both TGC and HGR for the cross-sectional analysis and to 7 for TGC and 6 for HGR for the longitudinal analysis.

The overall impact of longitudinal changes in prescribing on the changes in outcomes was assessed by applying the calculated linear regression factors to the changes in indicator values for each selected factor. Using the total England T2DM population as a denominator (2.8 million individuals), the annual average change in indicator value (DDD for medication) and the regression coefficient were applied to the total T2DM population to give an indication of the impact of that indicator on the TGC and HGR outcomes. The inverse of the regression coefficient was used to provide an approximation to the number needed to treat (NNT) to achieve 1 change in outcome.

This study was not funded by any external agencies and the analysis used only publicly available grouped data. Therefore, ethical approval was not sought.

**Results**

*Practice Characteristics*

Table 1 highlights the characteristics of the NDA participating and non-participating practices in the 2 years being considered. 7,618 GPP reported in the QOF in 2015/16. Of those that participated in the NDA, 353 Practices were excluded as their T2DM register was <100, and 5,733 were included (78% of total) who reported a total of 2.222 million on their T2DM register. Of these 3,762 practices (65% of this year’s total) had also participated in 2014/15 NDA and reported 1.502 million with T2DM, an increase of 5.8% on the 1.420 million they reported the previous year.
Comparing the GP Practices participating in the NDA with those not participating, showed the latter (non-participating) had an average practices list size of 6,543 compared to NDA 7,807 so were on average 19% smaller. The NDA practices reported overall diabetes prevalence of 5.23% compared to non-participating of 5.43%. Comparing their QOF overall diabetes reported HbA1c outcomes, the participating practices showed HbA1c ≤59 mmol/mol at 70.2% compared to 70.4% in non-participating, and HbA1c >75 mmol/mol at 12.4% compared to 12.7% in non-participating (note, the different cut points for QOF versus the NDA). All these are within +/-2% of the overall average figure. This suggests that apart from size, the UK NDA practices were broadly representative of all the GP practices in England.

The data for the 3,762 practices that completed both years in the NDA showed a decline in local service indicators, e.g. completion of the 8 NICE care processes 57.5% falling to 53.9% (a relative 6.5% reduction) and BP ≤140/80 mm/Hg falling from 74.3% to 73.7%, a relative 0.8% decline.

Variation between practices

There is wide practice level variation in use of therapies as measured by DDD/person with T2DM. Figure 2a shows the distributions of the relative levels of use of the principally prescribed agents. The x-axis shows the variation around the national mean for prescribing by GP practice with the y-axis showing the proportion of practices at each 5th centile of prescribing for each agent.

Application of medication varies considerably by class across the practices. Here, it was measured by the % of practices falling within +/-30% of the overall class mean. Metformin was the most consistently used. The DDD/T2DM register mean was 0.514 and 95% of practices fell within +/-30% of this. Sulphonylureas were the most widely used with DDD/T2DM register of 0.65 but with significantly more variation only 62% falling within +/-30%. The declining use of the thiazolidinedione (TZD) pioglitazone had mean DDD/T2DM register of 0.035 and even more variation in prescribing, only 26% falling within +/-30%.

While the use of newer agents is growing, it remains small with overall DDD/T2DM 0.16 and variation in use is large: DPP-4I mean DDD/T2DM 0.11, 46% of practices within +/-30%; GLP-1a mean DDD/T2DM 0.030, 41% within +/-30%; and SGLT2I mean DDD/T2DM 0.022, 24% within +/-30% of the mean.
With newer agents and also with pioglitazone there were significant practice outliers with 4%—14% of practices using more than 200% of the overall mean and between 1%—5% of practices not using them at all.

*Year-on-year Prescribing Change*

For each class of medication, the distribution of net overall change between 2014/15 and 2015/16 in DDD/T2DM register was calculated and shown as a percentage (%) of the current value in each practice. Figure 2b shows the amount of this change and its distribution in principally prescribed agents across the 3,762 practices.

It shows an overall reduction in use of standard medications as measured by DDD/T2DM register with 56% of practices reducing their use of biguanide (overall national reduction 1%), 79% of practices reducing their use of sulphonylureas (overall reduction 6%) and 75% of practices reducing their use of pioglitazone (overall reduction 19%).

In contrast, use of more recently introduced medications increased with 96% of practices increasing their use of SGLT2I (overall national increase 62%), 76% of practices increasing their use of DPP-4I (overall increase 11%) and 53% of practices increasing their use of GLP-1a (overall increase 3%).

*Cost Impact of Changes*

Table 1 shows that the total annual spend in England on T2DM medication during 2014—15 to 2015—16 increased by 20% (£320 million to £386 million, £66 million). The 3,856 practices reporting in both years of the NDA recorded a 6% increase in the number of people with T2DM. If this was reflected across the total population this would have increased cost by £19 million. However, total DDD of medication prescribed increased only by 3%, reflecting a 3% reduction in level of medication prescribing/person equivalent to a £10 million cost reduction due to less use per head. The changes in unit cost during the year as £/DDD (including 8% increase in metformin, 9% fall in sulphonylurea and 330% increase in TZD) accounts for £21 million increase). The remaining £36 million is due to switching from lower cost to higher cost medication. Based on an estimated increase in annual prescribing costs of around £420/switched patient this is equivalent to overall additional 86,000 patients being moved to higher cost medication. With this level of
additional investment, the overall proportion within the NDA of patients at TGC decreased (66.4% to 65.9%) while the proportion at HGR improved (6.6% to 6.4%).

**Multi-variant analysis – cross sectional including comparison to previous years analysis**

Figure 3 shows the standardised beta coefficients determined from multivariate analysis of 5,733 practices in 2015–16 compared to the 7,883 practice years in 2013–14 and 2014–15 used in our previous paper [4]. Where figures are absent, there was no significant relation with either proportion at TGC or proportion at HGR.

The new results closely match the previous findings: a higher proportion of older people in the practice was associated with higher proportions of TGC and higher levels of social disadvantage, with higher proportions of HGR; higher local services factors including completion of all 8 Care Processes, greater proportions of people achieving target cholesterol and BP control and a higher proportion of T1DM individuals achieving TGC were all associated with better levels of TGC (increased) and HGR (reduced). The new results also continue to show the positive association of prescribing more metformin and the negative association of higher sulphonylurea prescribing with both TGC and HGR.

Cross-sectional analysis (2015–16) showed that practices using more SGLT2I achieved a reduction in the proportion at HGR. By contrast, practices using more DPP-4I and GLP-1a prescribing was associated with increased HGR while GLP-1a use was associated with lower TGC attainment at a GP practice level.

**Multi-variant Analysis: longitudinal year-on-year change**

A regression analysis across the 3,762 practices with data for both 2014/15 versus 2015/16 outcomes showed a standardised β-coefficient with regard to year-on-year comparison of 0.75 for is strongly dependant on their previous year’s performance.

Further analysis considered changes in net overall indicator values and the impact on the changes to the TGC and HGR outcomes. As this approach cannot identify levels of internal switching in and out within the same year, it is more effective for assessing the impact of growing and declining medication use where levels of overall change might reflect local changes in behaviours.
Figure 4 shows for the year-on-year changes in prescribing and other measures the standardised beta values for the multi-variant linear regression factors that link to the proportion of patients at TGC or at HGR.

Practices where T1DM HbA1c control or T2DM cholesterol improved, showed improvement in both the T2DM TGC and HGR outcomes, reinforcing the cross-sectional finding regarding importance of local service organisation and illustrating how service improvements can have relatively rapid impacts.

Increased use of SGLT2I and GLP-1a use at a GP practice level was associated both with an increase in those at TGC and decrease in those at HGR. The slight association of increased use of metformin to increase HGR requires more work to explain.

Impact of prescribing changes on outcomes

If one assumes that changes in prescribing are linked causatively to changes in glycaemic outcomes, Table 2 shows, using linear regression analyses, the impact of the change between 2014/15 and 2015/16. We extrapolated from the NDA to the total England T2DM population. This suggests that in 2014/15 around 1.81 million achieved TGC; the regression constant year on year of -0.76% suggests that there is an expected annual decline of 20,800 in the next year and for the 178,000 at HGR an expected increase +0.06% equal to 1,600, due to the growing numbers and generally progressive natural history of T2DM.

The number failing to achieve TGC was reduced by 6,800 due to the increase in SGLT2I and GLP-1a prescribing while reported reduction in service level factors had the effect of decreasing the number with TGC by 1,400. This leaves an overall, modelled, net fall of 15,400 or 0.56%, which is similar to the actual 0.6% fall recorded in the NDA.

For HGR, the corresponding extrapolated increased use of SGLT2I and GLP-1a is estimated to have reduced the total by 4,400, with some other factor leaves a net reduction of 3,200 or 0.12% similar to the actual 0.13% change recorded in the NDA.

The analysis also suggests the growth in prescribing of SGLT2I (0.13 DDD/T2DM) had an impact of 0.25% on the percentage at TGC. This is reflected in estimated NNT of 5. The increase in use by 38,000 of this therapy can be implied to have resulted in an additional 6,800 patients achieving TGC. The implications for HGR were similar with reduction in HGR...
of -0.17% for SGLT2I an estimated NNT of 8 so the additional prescribing decreased the number of individuals at HGR by 4,200.

Discussion

Previously [4], we used cross-sectional analysis within a 2-year period to assess the impact of practice epidemiology, local services and major medications on glucose control in T2DM. This follow-on study, using the latest published practice level NDA and prescribing data, confirms those findings and uses longitudinal year-on-year analysis to assess the impact of the more recent medications, specifically SGLT2Is, DPP4Is and GLP-1 agonists. We found that SGLT-2Is and GLP-1 analogues were associated with a greater proportion achieving HbA1c ≤58 mmol/mol; SGLT-2I prescribing was associated with greater improvements in HGR than those found for GLP-1 analogues in year-on-year analysis.

The differences between the results of cross-sectional and longitudinal analysis (Figures 3 and 4) may relate at least in part to the fact that patients moving onto a new therapy often change most at the start. For TGC and HGR comparing 2014/15 to 2015/16 increased use of both SGLT2Is and GLP-1a were associated with improvement.

In the cross-sectional analysis of use of newer therapies, there were some low level correlations including using more GLP-1a associated with poorer outcomes for TGC and HGR while more DDP-4I led to poorer HGR. Maybe this highlights how timely review of the effectiveness of agents is a way of overcoming treatment inertia by reducing the numbers of people on ineffective pharmacotherapy. A caveat is that our analysis cannot take account of the rationale underlying individual patient level prescribing decisions in relation to initiation and discontinuation of specific pharmacotherapies. Nevertheless the overall findings do have implications for the way that over time T2DM treatment is modified (or not as the case may be).

In the longitudinal 2014/15 to 2015/16 analysis, SGLT2I use was associated both with an increase in those at TGC and a decrease in those at HGR. The estimated NNT to bring one person into TGC was 5 and to take one person out of HGR was 8. This is in keeping with the EMPA-REG Outcome Study [11] and was the most beneficial association identified. However, despite increased use and increased spend on newer therapies, for which there
is clinical trial and real world evidence of effectiveness, the overall scorecard was balanced rather than improved with percentage at TGC falling by 0.8% and percentage at HGR falling by 1.9%. This accords with health economic analysis in the USA [12].

It is recognised that only a relatively small proportion of the variance in glycaemia is accounted for in these analyses. The major factor is the inexorable progression of dysglycaemia year-on-year possibly related to changes in population characteristics such as age (younger), duration (longer) and lifestyle [13]. The small variance in prescribing of metformin across the NDA GP practices [14] and the progressive decline in pioglitazone use despite its clinical efficacy [15] are not surprising in relation to acknowledged prescribing trends in the UK.

Previously, we showed through cross-sectional analysis, which we confirmed in this paper, that moving levels of local service performance and prescribing of metformin and sulphonylureas from the median to the 90th percentile level might be associated with 210,000 additional patients in TGC and 62,000 fewer in HGR. The associations between change in SGLT2I and DPP4I prescription at a practice level and the proportions at TGC and HGR may be important, if the link is causative [16]. Improving glucose control by using new drugs would be costly although the findings here suggest, for example, that an investment of £50 million in additional SGLT2i in those practices prescribing around or below the national average would include an additional 100,000 patients and could bring as many as 12,500 out of HGR and 20,000 people into TGC.

Limitations

Due to the data structure, there was no information concerning the number of patients who were only on diet and lifestyle or for whom combinations of multiple therapies were used. The number of GPP in 2014/15 was less than in 2015/16. Nevertheless, the number of practices compared year on year is sufficient for valid and nationally relevant conclusions to be drawn. Furthermore, we accept that there is lack of precise information on time span between exposure and outcome. We have recently also described this in relation to (different) treatment variables in T1DM individuals using a similar methodology (17).

We have in this paper focussed on glycaemic outcomes. Prescribing has additionally to take into account many other contributors including patient reaction, patient tolerance and drug side effects.
Results from clinical trials have shown that the drugs, which lowered HbA1c to similar levels, had different effects on patient outcomes (18,19). The link between diabetes treatment drug and cardiovascular disease / mortality as an outcome would have to include another set of practice variables, including their use of cardiovascular medication as well as cardiovascular events and mortality, with inclusion of Hospital Episode Statistics (HES) data. This will be the subject of future work.

Conclusion

We have shown that greater prescribing of the newer therapies is associated at practice level with more people at target HbA1c (TGC) and fewer with high risk HbA1c (HGR). At the same time, at a national level, fewer are achieving TGC although there are also fewer at HGR. We suggest that the group of SGLTis as the latest class of oral hypoglycaemic agent, must be considered earlier rather than later in the treatment pathway for individuals with T2DM.

Contributorship statement and guarantor:

Adrian Heald is the first author and was the instigator of the work done to bring this paper to fruition. Mark Livingston provided invaluable scientific advice and helped with manuscript preparation. Dr Gabriela Moreno contributed to the writing of the manuscript and literature review. Statistical analysis was performed by Mike Stedman and Simon Anderson who also compiled the results section. Mark Lunt gave statistical advice and reviewed the analysis results. Mark Davies provided editorial guidance. Anthony Fryer reviewed all sections of the paper in relation to scientific relevance and provided support to the research group. Robert Young and Roger Gadsby provided senior review of all sections of manuscript and gave invaluable assistance in writing the discussion section.

Transparency declaration:
Adrian Heald is the guarantor of the paper:

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Author positions:

Adrian Heald is a Consultant Physician at Salford Royal Hospital and Honorary Research Fellow at Manchester University. Mark Livingston is Consultant Clinical Biochemist at Walsall Manor Hospital and Honorary Research Fellow at Manchester University. Gabriela Moreno is a Visiting Research Fellow at Manchester University. Mike Stedman is a Health Consultant based with RES Consortium, Andover. Mark Davies is a Health Consultant based with RES Consortium, Andover. Mark Lunt is a Senior Statistician at Manchester University. Simon Anderson is a Lecturer in Cardiology at Manchester University. Anthony Fryer is the Professor of Biochemistry at Keele University School of Medicine and the University Hospital of North Staffordshire. Roger Gadsby is the GP Clinical Lead for the National Diabetes Audit. Robert Young is the Speciality Clinical Lead for the National Diabetes Audit.

Ethics committee approval: Not required.

Clinical trials registration: Not required.

Funding statement:

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Role of the sponsor:

Not required.

Data sharing statement/author access to data:
Not required. Data is freely available publically.

**Patient consent:**

Not required.

**Declaration**

No author has any conflict of interest in relation to contribution to this paper.
Figure Legends:

**Figure 1:** Flow chart describing the methodology

**Figure 2a:** Distribution among English General Practices of 2015/16 blood glucose lowering medication use as measured by defined daily dose of each agent per person with diagnosed diabetes as a percentage of the overall average for each medication.

**Figure 2b:** Distribution among English General Practices of the change in use between 2014/15 and 2015/16 of blood glucose lowering medication defined daily dose per person with diagnosed diabetes expressed as a percentage of the 2015/16 value current value versus 2014/15. GP: general practitioner; NDA: National Diabetes Audit; DDD: defined daily dose; T2DM: typer 2 diabetes mellitus; TZD: thiazolidinedione; GLP-1: glucagon-like peptide 1; DPP4I: dipeptidyl peptidase-4 inhibitors; SGLT2I: sodium-glucose co-transporter 2 inhibitor.

**Figure 3:** Factors associated at General Practice level with the proportions of patients with type 2 diabetes mellitus in a) target glycaemic range (TGC; glycated haemoglobin A1c (HbA1c) \(\leq 58 \text{ mmol/mol} \)) and b) a decreased number at high glycaemic risk (HGR; HbA1c \(>86 \text{ mmol/mol} \)) as identified by cross-sectional regression analysis for selected indicator factors for the year 2015-16 and for 2013-15 (displayed as diamonds). T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; IMD: index of multiple deprivation; DDD: defined daily dose; GLP-1: glucagon-like peptide 1; DPP4I: dipeptidyl peptidase-4 inhibitors; SGLT2I: sodium-glucose co-transporter 2 inhibitor; BGM: blood glucose meter; BP: blood pressure.

**Figure 4:** Factors associated at General Practice level with the change in proportions of patients with type 2 diabetes mellitus in a) target glycaemic range (TGR; glycated haemoglobin A1c (HbA1c) \(\leq 58 \text{ mmol/mol} \)) and b) a decreased number at high glycaemic risk (HGR; HbA1c \(>86 \text{ mmol/mol} \)) as identified by longitudinal regression analysis where change in for selected indicator factors since 2014/15.
References


Table 1: Data on general practitioner (GP) practices that reported in the National Diabetes Audit (NDA) for cross-sectional and longitudinal from total quality outcomes framework (QOF) England practices

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<tr>
<td>DM HbA1c % &gt; 75 mmol/mol</td>
<td>QOF</td>
<td>12.3</td>
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<tr>
<td>OUTCOMES</td>
<td>66.5</td>
<td>-0.8</td>
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<tr>
<td>T2DM HbA1c % ≤58 mmol/mol</td>
<td>NDA</td>
<td>6.4</td>
</tr>
<tr>
<td>T2DM HbA1c % &lt; 86 mmol/mol</td>
<td>NDA</td>
<td></td>
</tr>
<tr>
<td>EPIDEMIOLOGY FACTORS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2DM % Age &gt;65 years</td>
<td>NDA</td>
<td>55.5</td>
</tr>
<tr>
<td>T2DM % Minority Ethnicity</td>
<td>NDA</td>
<td>20.4</td>
</tr>
<tr>
<td>T2DM IMD % Most Deprived</td>
<td>NDA</td>
<td>22.7</td>
</tr>
<tr>
<td>T2DM % Prevalence</td>
<td>NDA</td>
<td>4.8</td>
</tr>
<tr>
<td>LOCAL SERVICE FACTORS</td>
<td>5.3</td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>MEDICATION FACTORS</th>
<th>Total DDD,000</th>
<th>Total Costs £,000</th>
<th>Total DDD,000</th>
<th>Total Costs £,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>METFORMIN DDD/T2DM Register</td>
<td>0.519</td>
<td>0.530</td>
<td>1,422</td>
<td>109,319</td>
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<tr>
<td>SULPHONYLUREA DDD/T2DM Register</td>
<td>0.661</td>
<td>0.640</td>
<td>1,779</td>
<td>29,134</td>
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<tr>
<td>T2D DDD/T2DM Register</td>
<td>0.035</td>
<td>0.036</td>
<td>96</td>
<td>15,920</td>
</tr>
<tr>
<td>GLP1 DDD/T2DM Register</td>
<td>0.030</td>
<td>0.031</td>
<td>82</td>
<td>66,312</td>
</tr>
<tr>
<td>DPP4I DDD/T2DM Register</td>
<td>0.113</td>
<td>0.126</td>
<td>320</td>
<td>134,905</td>
</tr>
<tr>
<td>SGLT2I DDD/T2DM Register</td>
<td>0.021</td>
<td>0.024</td>
<td>60</td>
<td>30,199</td>
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<tr>
<td><strong>Sub Total</strong></td>
<td><strong>3,759</strong></td>
<td><strong>385,789</strong></td>
<td><strong>3,642</strong></td>
<td><strong>320,171</strong></td>
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<tr>
<td>T2DM Estimate % on Insulin</td>
<td>12.0</td>
<td>11.6</td>
<td>12.2</td>
<td>-2.1</td>
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<tr>
<td>Insulin Analogue % Overall</td>
<td>80.7</td>
<td>83.1</td>
<td>81.5</td>
<td>-1.0</td>
</tr>
<tr>
<td>T2DM Estimate % Using BGM</td>
<td>15.5</td>
<td>14.9</td>
<td>15.0</td>
<td>3.1</td>
</tr>
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</table>

DM: diabetes mellitus; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; HbA1c: glycated haemoglobin A1c; TGC: target glycaemic control; HGR: high glycaemic risk; IMD: index of multiple deprivation; DDD: defined daily dose; GP prescr: general practitioner prescribing data; T2D: thiazolidinedione; GLP-1: glucagon-like peptide 1; DPP4I: dipeptidyl peptidase-4 inhibitors; SGLT2I: sodium-glucose co-transporter 2 inhibitor; BGM: blood glucose meter.
## Table 2: Extrapolation of expected impact of individual longitudinal correlation factors onto total glycaemic control (TGC) and higher glycaemic risk (HGR) outcomes

<table>
<thead>
<tr>
<th></th>
<th>Year-on-year Change</th>
<th>Regression Coefficient</th>
<th>% TGC Impact</th>
<th>NNT England basis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T2DM 2014–15 ESTIMATED POPULATION</strong></td>
<td></td>
<td></td>
<td></td>
<td>2,730,496</td>
</tr>
<tr>
<td><strong>PROJECT TGC IMPACT:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous Year TGC 2014–15</td>
<td></td>
<td></td>
<td>66.46</td>
<td>1,814,700</td>
</tr>
<tr>
<td>Expected Constant</td>
<td></td>
<td>-0.76</td>
<td>-20,800</td>
<td></td>
</tr>
<tr>
<td>Year-on-year Change in SGLT2I DDD/T2DM Register</td>
<td>0.013</td>
<td>0.192</td>
<td>0.25</td>
<td>5 6,800</td>
</tr>
<tr>
<td>Year-on-year Change in GLP1 DDD/T2DM Register</td>
<td>0.001</td>
<td>0.264</td>
<td>0.02</td>
<td>4 500</td>
</tr>
<tr>
<td>Year-on-year Change in NDA T2DM % Age &gt;65 yrs</td>
<td>0.001</td>
<td>0.131</td>
<td>0.02</td>
<td>8 400</td>
</tr>
<tr>
<td>Year-on-year Change in NDA T2DM % Cholesterol &lt;4 mmol/L</td>
<td>0.000</td>
<td>0.118</td>
<td>0.00</td>
<td>100</td>
</tr>
<tr>
<td>Year-on-year Change in NDA T1DM % HbA1c ≤58 mmol/mol</td>
<td>-0.003</td>
<td>0.073</td>
<td>-0.02</td>
<td>-700</td>
</tr>
<tr>
<td>Year-on-year Change in % T2DM using BGM</td>
<td>0.005</td>
<td>-0.053</td>
<td>-0.02</td>
<td>-700</td>
</tr>
<tr>
<td>Year-on-year Change in NDA T2DM % BP &lt;140/80 mm/Hg</td>
<td>-0.005</td>
<td>0.049</td>
<td>-0.03</td>
<td>-700</td>
</tr>
<tr>
<td>Overall Expected by Regression</td>
<td></td>
<td></td>
<td>-0.55</td>
<td>-15,000</td>
</tr>
<tr>
<td><strong>PROJECTED 2015–16 TOTAL</strong></td>
<td></td>
<td></td>
<td>65.91</td>
<td>1,799,700</td>
</tr>
<tr>
<td><strong>PROJECT HGR IMPACT:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous Year HGR 2014–15</td>
<td></td>
<td></td>
<td>6.52</td>
<td>178,000</td>
</tr>
<tr>
<td>Expected Constant</td>
<td></td>
<td>0.06</td>
<td>1,200</td>
<td></td>
</tr>
<tr>
<td>Year-on-year Change in SGLT2I DDD/T2DM Register</td>
<td>0.013</td>
<td>-0.119</td>
<td>-0.15</td>
<td>8 4,200</td>
</tr>
<tr>
<td>Year-on-year Change in NDA T2DM % Age &gt;65 yrs</td>
<td>0.001</td>
<td>-0.068</td>
<td>-0.01</td>
<td>15 -200</td>
</tr>
<tr>
<td>Year-on-year Change in GLP1 DDD/T2DM Register</td>
<td>0.001</td>
<td>-0.091</td>
<td>-0.01</td>
<td>11 -200</td>
</tr>
<tr>
<td>Year-on-year Change in Metformin DDD/T2DM Register</td>
<td>-0.005</td>
<td>0.012</td>
<td>-0.01</td>
<td>-200</td>
</tr>
<tr>
<td>Year-on-year Change in NDA T2DM % Cholesterol &lt;4 mmol/L</td>
<td>0.000</td>
<td>-0.052</td>
<td>0.00</td>
<td>19 0</td>
</tr>
<tr>
<td>Overall Expected by Regression</td>
<td></td>
<td></td>
<td>-0.12</td>
<td>-3,200</td>
</tr>
<tr>
<td><strong>PROJECTED 2015–16</strong></td>
<td></td>
<td></td>
<td>6.40</td>
<td>174,800</td>
</tr>
</tbody>
</table>

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; HbA1c: glycated haemoglobin A1c; DDD: defined daily dose; GLP-1: glucagon-like peptide 1; SGLT2I: sodium-glucose co-transporter 2 inhibitor; BGM: blood glucose meter; BP: blood pressure; NDA: National Diabetes Audit; NNT: number needed to treat.

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Figure 1: Flow chart describing the methodology

Total England 2015/16 QOF
- 7,618 Practices
- 57.53 Million registered population
- 3.03 Million DM register
- 7,552 List/Practice
- 398 Diabetes/Practice

Practices Participating in NDA
- 6,086 Practices
- 47.51 Million registered population
- 2.49 Million DM register
- 2.22 Million T2 Register
- 7,806 List/Practice
- 409 Diabetes/Practice
- 365 T2/Practice

Not Participating
- 1,532 Practices
- 10.02 Million registered population
- 0.55 Million DM register
- 6,540 List/Practice
- 356 Diabetes/Practice

With T2 Register ≥ 100
- 5,733 Practices
- 46.06 Million registered population
- 2.44 Million DM register
- 2.22 Million T2 Register
- 8,034 List/Practice
- 426 Diabetes/Practice
- 388 T2/Practice

With T2 Register < 100
- 353 Practices
- 1.45 Million registered population
- 0.04 Million DM register
- 0.03 Million T2 Register
- 4,110 List/Practice
- 125 Diabetes/Practice
- 85 T2/Practice

Also participated in 2014/15
- 3,762 Practices
- 31.37 Million registered population
- 1.66 Million DM register
- 1.50 Million T2 Register
- 8,339 List/Practice
- 440 Diabetes/Practice
- 399 T2/Practice

Newly participated in 2015/16
- 1,971 Practices
- 14.69 Million registered population
- 0.79 Million DM register
- 0.72 Million T2 Register
- 7,452 List/Practice
- 400 Diabetes/Practice
- 365 T2/Practice

USED IN CROSS-SECTIONAL ANALYSIS
USED IN LONGITUDINAL ANALYSIS
Figure 2: Distribution of a) use of medication within practices in 2015–16 and b) relative change to the previous year

a) Distribution of Use of Medication

b) Distribution of Year on Year Change in Use of Medication

GP: general practitioner; NDA: National Diabetes Audit; DDD: defined daily dose; T2DM: type 2 diabetes mellitus; TZD: thiazolidinedione; GLP-1: glucagon-like peptide 1; DPP4I: dipeptidyl peptidase-4 inhibitors; SGLT2I: sodium-glucose co-transporter 2 inhibitor.
Figure 3: Standardised Beta Coefficients for 2015–16 Cross-sectional analysis of selected regression factors linked to a) total glycaemic control (TGC) and b) a decreased number at higher glycaemic risk (HGR)

T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; HbA1c: glycated haemoglobin A1c; IMD: index of multiple deprivation; DDD: defined daily dose; GLP-1:
glucagon-like peptide 1; DPP4I: dipeptidyl peptidase-4 inhibitors; SGLT2I: sodium-glucose co-transporter 2 inhibitor; BGM: blood glucose meter; BP: blood pressure.
Figure 4: Standardised Beta Coefficients for year on year change between 2014–15 and 2015–16 longitudinal analysis of selected regression factors linked to a) total glycaemic control (TGC) and b) a decreased number at higher glycaemic risk (HGR)

a)

![Graph showing standardised β values for HGR](image)

Factors Included into Regression:
- NDA T2 % Cholesterol <4mmol/l
- NDA T1 % HbA1c ≤58mmol/mol
- SGLT2i DDD/T2 Reg (NNT = 8)
- % NDA T2 % Age >65
- GLP1 DDD/T1 Reg (NNT = 11)
- METFORMIN DDD/T2Reg (NNT = 87)

- EPIDEMIOLOGY
- LOCAL SERVICE
- PRESCRIBING

b)

![Graph showing standardised β values for TGC](image)

Factors Included into Regression:
- NDA T1 % HbA1c ≤58mmol/mol
- NDA T2 % Cholesterol <4mmol/l
- NDA T2 % Blood Pressure <140/80
- SGLT2i DDD/T2 Reg (NNT = 5)
- GLP1 DDU/tri Reg (NNT = 4)
- % NDA T2 % Age >65
- % T2 Using 3GM (NNT = 19)

NDA: National Diabetes Audit; T1: type 1 diabetes mellitus; T2: type 2 diabetes mellitus; HbA1c: glycated haemoglobin A1c; DDD: defined daily dose; NNT: number needed to treat; GLP-1: glucagon-like peptide 1; SGLT2i: sodium-glucose co-transporter 2 inhibitor; BGM: blood glucose meter.