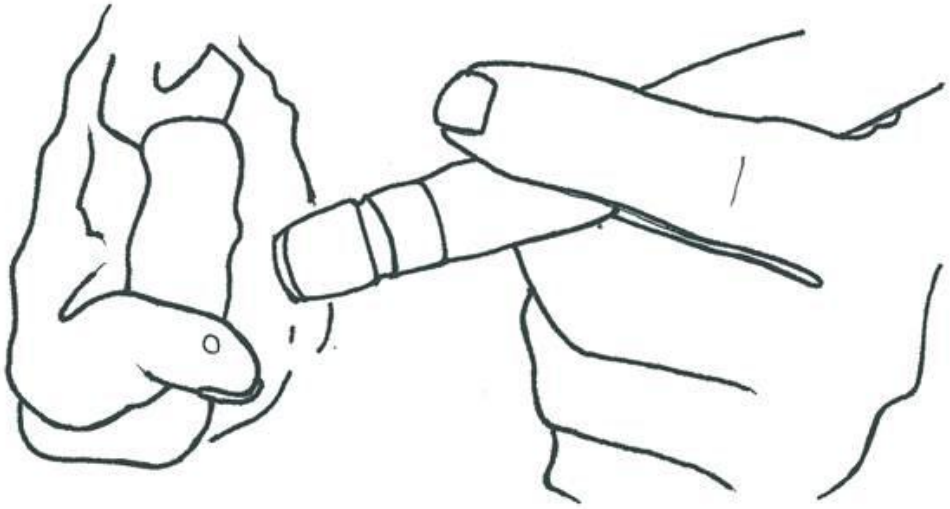
Diabetes Prescribing Strategy 2014 to 2016



NHS Scotland Diabetes Managed Clinical Network

Pharmacy and medicines division
Scottish Government Health and Social Care Directorates

Contents

The prescribing analysis included in this report has been reviewed by ISD Scotland. While every effort has been made to ensure the accuracy of the data, it is possible that there are inaccuracies. It is essential that any data, table, graph contained within this document is not used for any other purpose than this diabetes prescribing strategy, and that is not passed on to any other person or organisation.

This Diabetes Prescribing Strategy is intended for management purpose only

Acknowledgements

This diabetes prescribing strategy has been achieved through a short life working group that was facilitated by the Diabetes MCN Clinical leads in Scotland.

Group members are shown below:

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The group would also like to acknowledge the support from Sean-MacBride Stewart, John McKnight, Andy Gallagher, John Nugent and Gregor Smith

We also thank Professor Miles Fisher has also provided clinical expert feedback on the strategy

Foreword

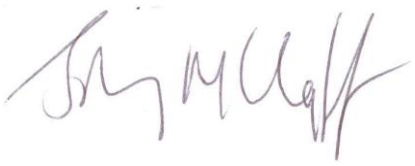
This prescribing strategy has been written with the support and input of the Lead Clinicians of the Diabetes Managed Clinical Networks in NHS Scotland. It is designed to promote appropriate, evidence-based, safe and cost-effective prescribing for the 227,967 people with Type 2 diabetes in Scotland, (88.6% of those with diagnosed diabetes) [1]. This strategy is important as NHS Scotland currently spends £73 million (ISD) [2] on antidiabetic drugs and glucose monitoring for people with diabetes. It is essential that this investment is used wisely to maximise the health benefit to patients.

The hope is that the strategy will help inform clinical practice in NHS Scotland. The advice is based largely on SIGN 116 (2010) [3]. Safe and Cost-effective prescribing involves both the appropriate selection of therapies for an individual patient, and consideration of when a treatment is no longer effective and should therefore be stopped. When introducing a new therapy for a patient with diabetes the prescriber should be clear about the advantages and disadvantages of any treatment and should also subsequently review whether or not that newly introduced therapy has been effective.

Type 2 diabetes is however a progressive condition that usually requires increased intensity of therapy over time. This fact creates an even greater challenge to the potential withdrawal of therapies that might not continue to be effective. A trial of stopping a medicine, with careful monitoring, should be considered when there are doubts regarding the continuing benefit to the patient.

It is recognised that the recommendations within this strategy cover the majority of hypoglycaemic agent prescribing for those with type 2 diabetes in Scotland. It is also recognised that there will be individual patients who require treatment different to these recommendations. In these cases it is important for the prescriber, usually the GP, to have a clear understanding of why these patients are exceptions. This is particularly important where the recommendation is to use a medicine outside of its licence agreement.

This NHS Scotland Diabetes Strategy is welcomed as an opportunity to further improve the already excellent care provided to patients with type 2 diabetes.



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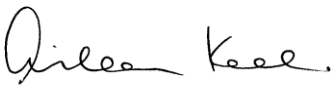


Aileen Keel CBE
Acting Chief Medical Officer

References:
1. **Scottish Diabetes Survey 2012** http://www.diabetesinscotland.org.uk/Publications/SDS%202012.pdf
2. **PRISMS accessed 17.03.14**
3. **SIGN 116 (2010)** ***Management of Diabetes*** http://www.sign.ac.uk/pdf/sign116.pdf

Executive Summary

The purpose of this strategy is to ensure person-centred, evidence-based, quality, safe and cost-effective prescribing for people living with type 2 diabetes. It has been developed through joint working between the Diabetes Managed Clinical Networks and the Scottish Government.

The recommendations are based on SIGN 116(2010) [3], subsequent clinical evidence, and Scottish medicines consortium (SMC) advice. It is accepted that there will be individual patients, under specialist management, for whom different clinical decisions may need to be made. In these situations the primary care practitioners will need to understand why this is the case, as they will be responsible for on-going prescribing and monitoring. Assessment of the continuing effectiveness of all treatments is recommended as part of regular patient review.

This strategy focuses on five broad areas of prescribing for people with diabetes. Each area is supported by prescribing data, which is presented by NHS Board to allow comparison of clinical practice.

The five areas are:

1. Oral Antidiabetic Drug prescribing:

- Metformin should be the first-line agent as this has been shown to provide a survival advantage [4]
- Sulfonylureas are recognised by SIGN 116 as second-line agents in patients who are not overweight or as a first-line agent for those who are intolerant of, or have contra-indications to, metformin. They have been shown to reduce clinically important microvascular complications. They remain the least expensive second line agent, but their use may be associated with weight gain and increased risk of hypoglycaemic episodes
- Thiazolidinediones (also known as glitazones) are alternative second or third-line agents. These are increasingly less expensive due to manufacturing licence patency expiry. Their use is associated with weight gain, and the European Medicines Agency has advised of a small increased risk of bladder cancer associated with pioglitazone use [5]
- Dipeptidyl petidase-4 (DPP-4) inhibitors (also known as gliptins) are alternative second or third-line agents. They are less cost-effective, but have a neutral effect on weight and no increased risk of hypoglycaemia. SIGN 116 recommends that their use is reserved for patients at particular risk of weight gain and/or hypoglycaemia
- Sodium-glucose co-transporter 2 (SGLT2) inhibitors are newer alternative second or third-line agents, accepted for restricted use by the SMC. They can promote weight-loss and their use is associated with increased risk of genital and urinary tract infections
- All of the second-line oral antidiabetic drugs have the potential to reduce the level of the surrogate disease marker, HbA_{1c}
- Unlike metformin, none of the other second or third-line agents have yet been shown to reduce the clinically important long-term complications of type 2 diabetes

References:

4. **UK Prospective Diabetes (UKPDS) Group http://www.dtu.ox.ac.uk/UKPDS/**
5. **Medicines and Healthcare Products Regulatory Agency, Drug Safety Update, August 2011, Volume 5, Issue 1**

2. Glucagon-like peptide-1 (GLP-1) agonist prescribing:

- GLP-1 agonists are alternative third-line agents that are injectable. They are more expensive than sulfonylureas or thiazolindinediones. They may promote weight-loss and are associated with no increased risk of hypoglycaemia
- SIGN 116 recommends consideration of third-line use of GLP-1 agonists to improve glycaemic control in obese adults (BMI ≥ 30kg/m^2). This will usually be for obese patients on metformin and a sulfonylurea, as an alternative to insulin
- GLP-1 agonist, like the oral second-line antidiabetic drugs, have the potential to reduce the level of the surrogate disease marker, HbA_{1c}
- Unlike metformin GLP-1 agonists have yet to be shown to reduce clinically important long-term complications of type 2 diabetes

3. Basal human* insulin versus basal analogue insulin use for type 2 diabetes:**

- Human insulin should be used as a first line for people with type 2 diabetes
- No clinically meaningful differences, have been found, between human and analogue insulins for HbA_{1c} level, severe hypoglycaemia or adverse events for those with type 2 diabetes [6]
- The rates of symptomatic and nocturnal hypoglycaemia are lower for analogue insulins, but at an incremental cost per quality adjusted life year (QALY) of around £300K [6]

4. Self-Blood Glucose Monitoring (SBGM) for type 2 diabetes:

- Routine SBGM for patients with Type 2 diabetes who are on metformin or diet alone is not recommended
- Patients using SBGM should be reviewed annually to assess the appropriateness of testing. Patient understanding of result interpretation, and their resulting actions should be reviewed
- Those with type 2 diabetes on insulin and or sulphonlyureas should be encouraged to monitor their blood glucose in line with SIGN 116
- Boards should aim to see a reduction in numbers of people testing that are on diet or metformin alone

5. Review of polypharmacy for frail patients and HbA1c targets

- Frail patients with type 2 diabetes require special consideration, particularly those with multiple morbidities and on multiple medications (polypharmacy). The potential advantage of tight glucose control must be viewed in the context of small potential health gain and increased risk of hypoglycaemia
- Scottish Government issued CEL (36) guidance to Health boards on appropriate prescribing and the polypharmacy guidance in October 2012. Full guidance can be found on: http://www.central.knowledge.scot.nhs.uk/upload/Polypharmacy%20full%20guidance%20v2.pdf

References:

6. **Horvath K et al. *Cochrane Database Syst Rev* 2007, issue2. Art No.:CD005613.DOI:10.1002/14651858.**

*** Human insulin: insulin zinc suspension, isophane insulin, protamine zinc insulin**

**** Analogue insulin: insulin degludec, insulin detemir, insulin glargine**

Recommendations

ONE Prescribing for patients with type 2 diabetes should be associated with on-going education and promotion of weight reduction and increased physical activity

TWO The increased importance of blood pressure and lipid control relative to glycaemic control should be recognised [7]

THREE Metformin remains the first-line antidiabetic drug

FOUR Second and third-line antidiabetic drugs (including insulin) are equivalent at improving glycaemic control, except in patients with very high HbA_{1c} when insulin is the only effective treatment

FIVE Second and third-line antidiabetic drugs (including insulin) should be selected based on their relative merits and cost-effectiveness

SIX Consideration of clinical effectiveness of all antidiabetic drugs should be an element of continued review. Medicines should be stopped when they no longer provide clinical benefit

References:

7. **Preiss D, et al.** ***Intensive glucose lowering treatment in type 2 diabetes*** ***BMJ*** **2011;343:d4243**

Introduction

The scope of this strategy includes review of the prescribing of antidiabetic medications, insulins, and diagnostic and monitoring reagents for adult patients with type 2 diabetes mellitus only. Though not the focus of the strategy, there are some comments regarding type 1 diabetes. The strategy is not intended to replace any current clinical guidance and should be read alongside SIGN 116.

The purpose of this strategy is to ensure person-centred, evidence-based, quality, safe and cost-effective prescribing for people living with type 2 diabetes.

The treatment and care of patients with diabetes is estimated to equate to 10% of total NHS costs. According to the Scottish Diabetes Survey 2012 [1] there were 227,967 people with type 2 diabetes recorded on the local diabetes registers in Scotland at the start of 2012, which is equivalent to a crude prevalence of 4.7% of the population. Type 2 diabetes generally has gradual onset and can be asymptomatic in the early stages. The Scottish Public Health Observatory [8] provides estimates for the number of people with type 2 diabetes, who have yet to be diagnosed.

Variation in the crude prevalence estimates between health boards (range 4.0% to 5.2%) can be explained by a number of factors including demographic changes, differing diagnostic criteria, deprivation and ethnic distribution.

Improved survival due to better control of glycaemia, blood pressure and dyslipidaemia, when coupled with earlier detection of people with type 2 diabetes, has resulted in significant resource pressure to both primary and secondary care services. This is within a finite financial envelope, and with restricted additional prescribing budget. These pressures are compounded by the emergence of new pharmaceutical therapies and devices for diabetes.

It is important that any strategy ensures that the recommendations are comprehensible, based on current guidance and are patient focused. Furthermore, it is essential that audits and reviews are put in place and applied to both secondary and primary care prescribers, including non-medical prescribers, to allow a change in long-term prescribing practices. The recommendations are based on SIGN 116. It must be accepted that guidelines are written to provide general advice and there may be some patients under specialist management who require a more individual approach. As general practitioners will be the main prescribers, it is important that they have a clear understanding as to why that patient requires an individualised approach.

References:

8. **The Scottish Public Health Observatory** http://www.scotpho.org.uk/health-wellbeing-and-disease/diabetes/key-points

Background

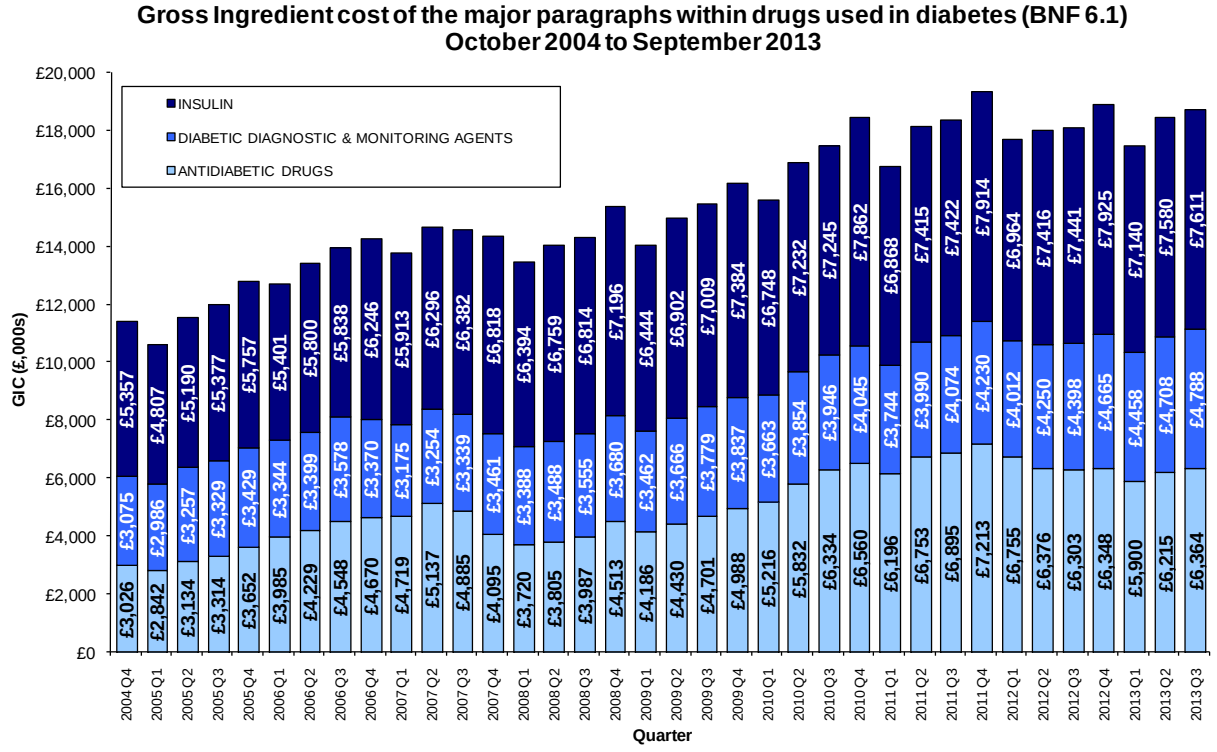
The context for this strategy is clearly defined by SIGN 116 and the financial situation into which NHS Scotland's prescribing budget sits. The primary care spend on drugs used in diabetes in 2012/13 was in excess of £73 million per annum and currently accounts for more than 7.6% of the total expenditure on prescriptions. This represents a decrease of 1.4% from the previous year. The spend in secondary care is just over £1.8 million representing approximately 0.5% of the total expenditure on medicines.

Table 1 summarises primary and secondary care diabetes prescribing costs for 2012/13

BNF Sub-section	NIC Primary Care	Cost Secondary Care
INSULIN	£29,921,185	£878,968
ANTIDIABETIC DRUGS	£24,925,821	£293,050
TREATMENT OF HYPOGLYCAEMIA	£492,561	£148,346
DIABETIC DIAGNOSTIC & MONITORING AGENTS	£16,678,429	£496,006
Sum:	**£71,323,558**	**£1,816,370**

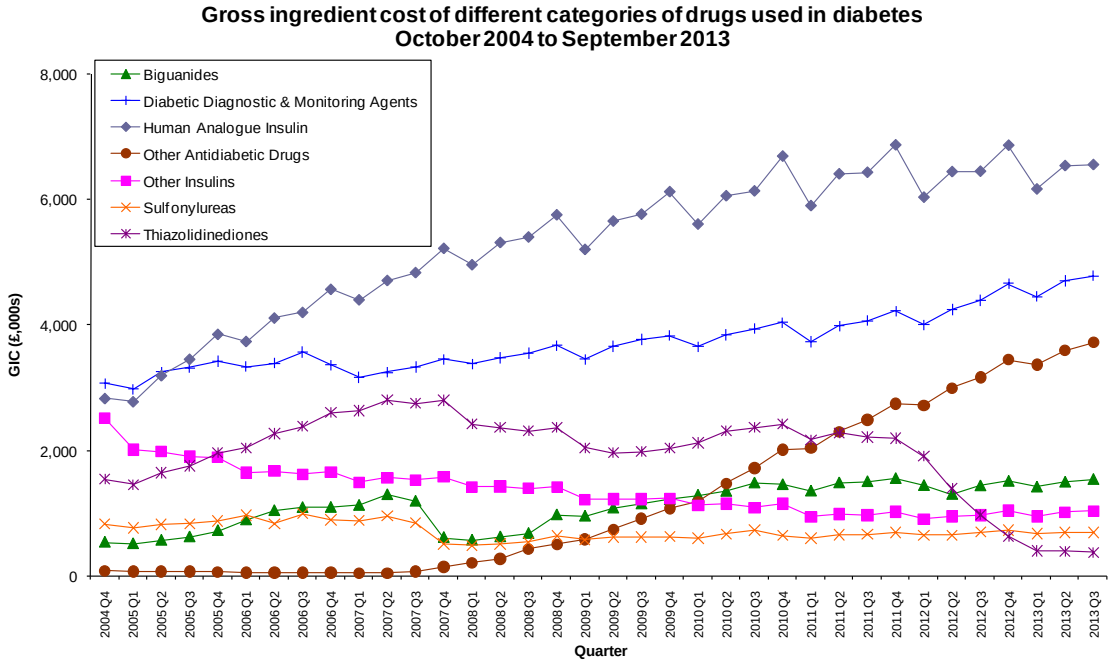
NOTES
a. Classification based on British National Formulary (BNF)
b. Primary Care costs use the gross ingredient cost (GIC) from PRISMS data
c. Secondary Care costs use HMUD data. NHS Tayside data is not currently available. HMUD extract 06.02.14

Figure 1 shows the increasing cost of prescribing for diabetes over the last nine years



NOTES
a. Primary Care costs use the gross ingredient cost (GIC) from PRISMS data
b. Classification based on British National Formulary (BNF)
c. Calendar Quarters: Q1 = January to March; Q2 = April to June; Q3 July to September; Q4 October to December

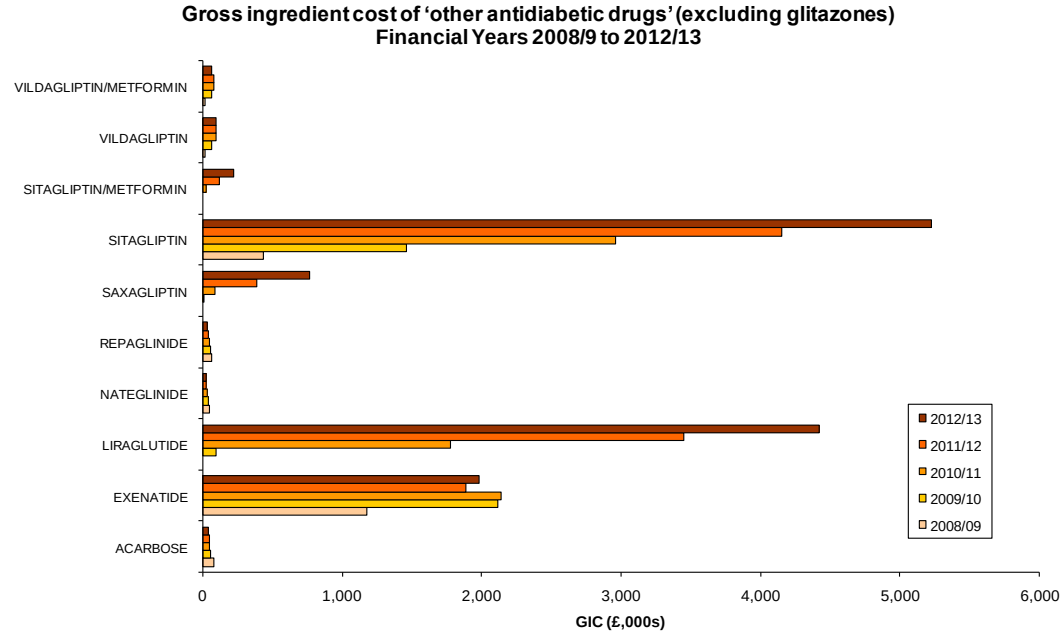
Figure 2 shows the change in cost for the different categories of drugs used to treat type 2 diabetes over the last nine years



NOTES

a. Primary Care costs use the gross ingredient cost (GIC) from PRISMS data
b. Classification based on MeReC Bulletin Vol.22 No.05 March 2012
c. Calendar Quarters: Q1 = January to March; Q2 = April to June; Q3 July to September; Q4 October to December

Figure 3 shows changing net ingredient cost of antidiabetic drugs (excluding metformin, sulfonylureas and glitazones) for each financial year from 2008/09 to 2012/13



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors
b. Goss Ingredient Cost = the list price of medicines and medical devices for prescriptions dispensed by community pharmacies

The Diabetes Prescribing Strategy

The purpose of this strategy is to ensure person-centred, evidence-based, quality, safe and cost-effective prescribing for people living with type 2 diabetes. The strategy highlights areas of prescribing for type 2 diabetes that should be considered for review at NHS board level. It is important that review includes both primary and secondary care, and involves all prescribers. This is essential to ensure positive long term prescribing behaviours.

The recommendations are based on SIGN 116(2010) [3], subsequent clinical evidence and Scottish medicines consortium (SMC) advice. The strategy should also be used in the context of local joint formularies and other local clinical guidance.

It is accepted that there will be individual patients, under specialist management, for whom different clinical decisions may need to be made. In these situations the primary care practitioners will need to understand why this is the case, as they will be responsible for on-going prescribing and monitoring.

Evaluating the continuing effectiveness of all treatment options is recommended as part of regular patient review.

The strategy has been developed from consensus of the diabetes MCN leads, prescribing advisers and the Scottish Government multidisciplinary short life working group. Patient representation and Diabetes UK have also been involved.

This strategy focuses on five prescribing areas.

1. Antidiabetic Drugs

The therapeutic use of antidiabetic drugs must be supported by the use of an appropriate diet for people with diabetes and increased physical activity. In addition the relative importance of lipid lowering and blood pressure control, when required, should be recognised,

'The emphasis in type 2 diabetes should remain on tight control of lipids and blood pressure with reasonable but not exaggerated attempts to control glycaemia.' [7]

SIGN 116 (**Summary table SIGN 116 Quick Reference Guide**) provides guidance on HbA_{1c} targets that should be set for patients. When dealing with frail patients also consider polypharmacy advice (see section 5).

1a. Oral antidiabetic drugs

Metformin should be the first-line agent with proven evidence of survival advantage. Metformin modified release (MR) should be reserved for those who do not tolerate the immediate release preparation in line with SMC restricted approval for Glucophage® (see SMC Advice Glucophage SR Oct 2009). The prescribing of combination preparations that include metformin may have the advantage of improving compliance, however this must be in line with any SMC advice and restrictions such as those for Janumet® (see SMC Advice Janumet Aug 2010) and Competact® (see SMC Advice Competact Sep 2006).

Sulphonlyureas are recognised by SIGN 116 as second-line agents in patients who are not overweight or as a first-line agent for those who are intolerant of, or have contra-indications to, metformin. It remains the least expensive second line agent, but its use may be associated with weight gain and increased risk of hypoglycaemic episodes.

Thiazolidinediones (also known as glitazones) are alternative second or third-line agents. These are increasingly less expensive due to manufacturing licence patency expiry, but their use is associated with weight gain, and the European Medicines Agency has advised of a small increased risk of bladder cancer associated with pioglitazone use (see http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON125962 and http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON105746). Pioglitazone should be used with caution in patients with heart failure. The increased risk of hip fracture should also be considered. The MHRA recommends careful, regular monitoring of elderly patients when prescribed glitazones.

Dipeptidyl petidase-4 (DPP-4) inhibitors (also known as gliptins) are alternative second or third-line agents. They are more expensive, but have a neutral effect on weight and no increased risk of hypoglycaemia. SIGN 116 recommends that their use is reserved for patients at particular risk of weight gain and/or hypoglycaemia.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are newer alternative second or third-line agents, accepted for restricted use by the SMC. Prescribers are advised to refer to the SMC web site for the current recommendations for the use of SGLT2 inhibitors. They are more expensive, but can promote weight-loss. Their use is associated with increased risk of genital and urinary tract infections.

Comparative data

All of the second-line oral antidiabetic drugs have a similar potential effect on the surrogate disease marker, HbA_{1c}. Unlike metformin, none of the second or third-line agents have yet been shown to reduce the clinically important long-term complications of type 2 diabetes, either for microvascular or macrovascular events. For the DPP-4 inhibitors (gliptins) and SGLT2 inhibitors we do not yet have long term safety outcomes data.

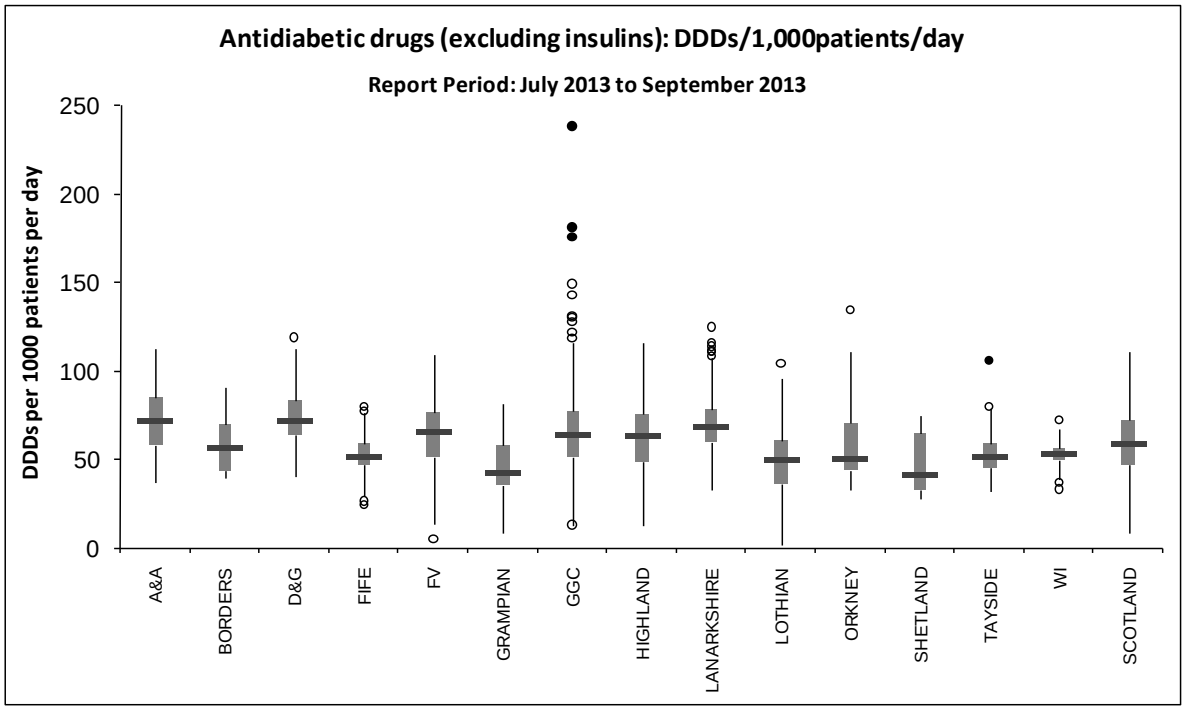
Response to treatment should be assessed, and SIGN 116 advises that **a reduction in HbA_{1c} of 0.5% (5.5mmol/mol) is expected and if this is not achieved after six months or maintained thereafter, consideration should be given to trial without therapy to determine if substitution or add on therapy is appropriate.**

A national therapeutic indicator (NTI) has been developed for 2014-15, which will allow boards to measure the use of metformin as a proportion of all oral anti diabetic drugs. Review of prescribing should focus on those type 2 diabetic patients prescribed antidiabetic medication without metformin. This is especially important for patients prescribed second or third line agents before metformin.

The following four pages present the comparative NHS Board use of metformin, sulfonylureas, glitazones and gliptins. Comparative data for the use of SGLT2s is not available at this time in any meaningful quantity.

Antidiabetic Drugs

Figure 4 shows the antidiabetic drugs excluding the insulins



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

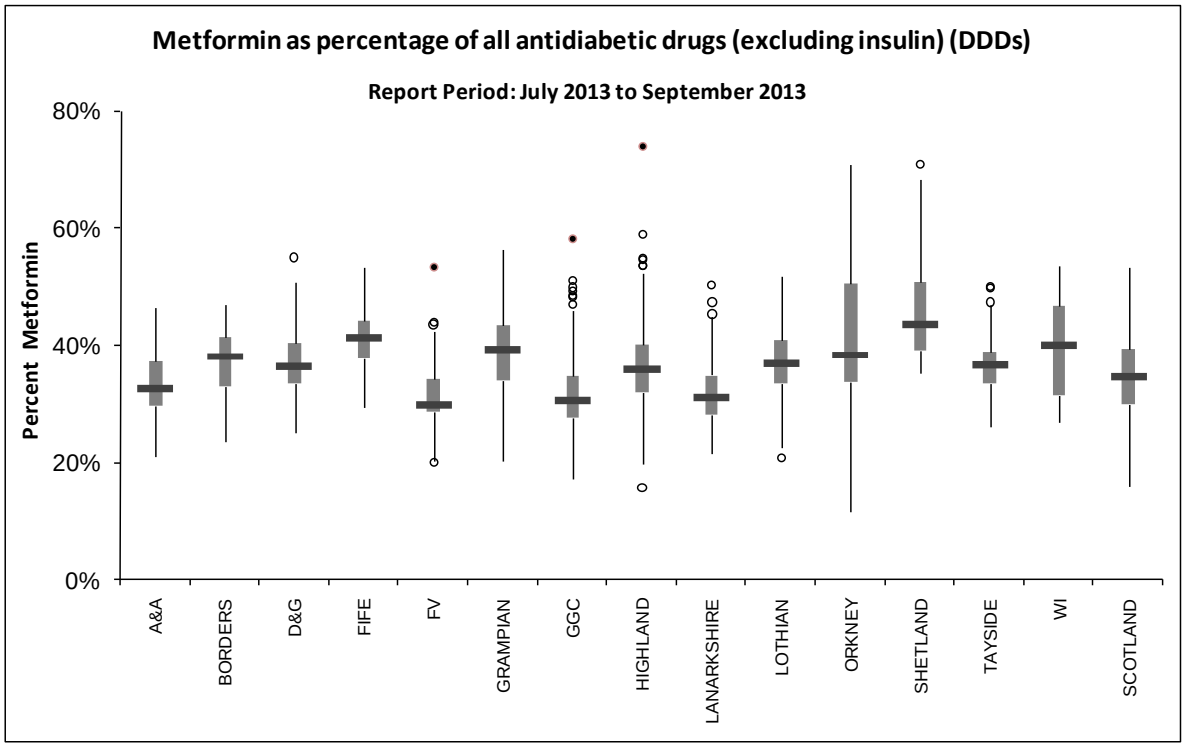
b. DDDs (defined daily doses) the assumed average maintenance dose per day for a drug used for its main indication in adults

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Antidiabetic drugs (excluding insulin) (DDDs/1,000 patients/day)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	37.29	58.47	71.51	84.91	112.58
NHS BORDERS	39.33	44.08	56.33	70.28	90.68
NHS DUMFRIES & GALLOWAY	40.23	63.79	71.21	83.35	118.72
NHS FIFE	24.41	47.02	51.30	58.74	79.63
NHS FORTH VALLEY	4.94	51.36	65.58	76.29	109.56
NHS GRAMPIAN	8.22	35.61	41.91	57.92	81.63
NHS GREATER GLASGOW & CLYDE	12.88	52.07	64.69	77.51	238.15
NHS HIGHLAND	13.09	48.62	63.05	75.59	116.02
NHS LANARKSHIRE	32.70	59.56	68.64	78.68	124.70
NHS LOTHIAN	2.03	36.55	50.09	60.42	104.34
NHS ORKNEY	32.86	43.84	50.23	70.80	134.34
NHS SHETLAND	27.64	32.74	41.59	65.07	74.69
NHS TAYSIDE	32.07	45.69	51.74	59.11	105.91
NHS WESTERN ISLES	33.20	49.43	53.27	56.72	72.21
SCOTLAND		47.07	59.23	72.79	

Metformin

Figure 5 shows metformin as proportion of all antidiabetic drugs excluding insulins



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

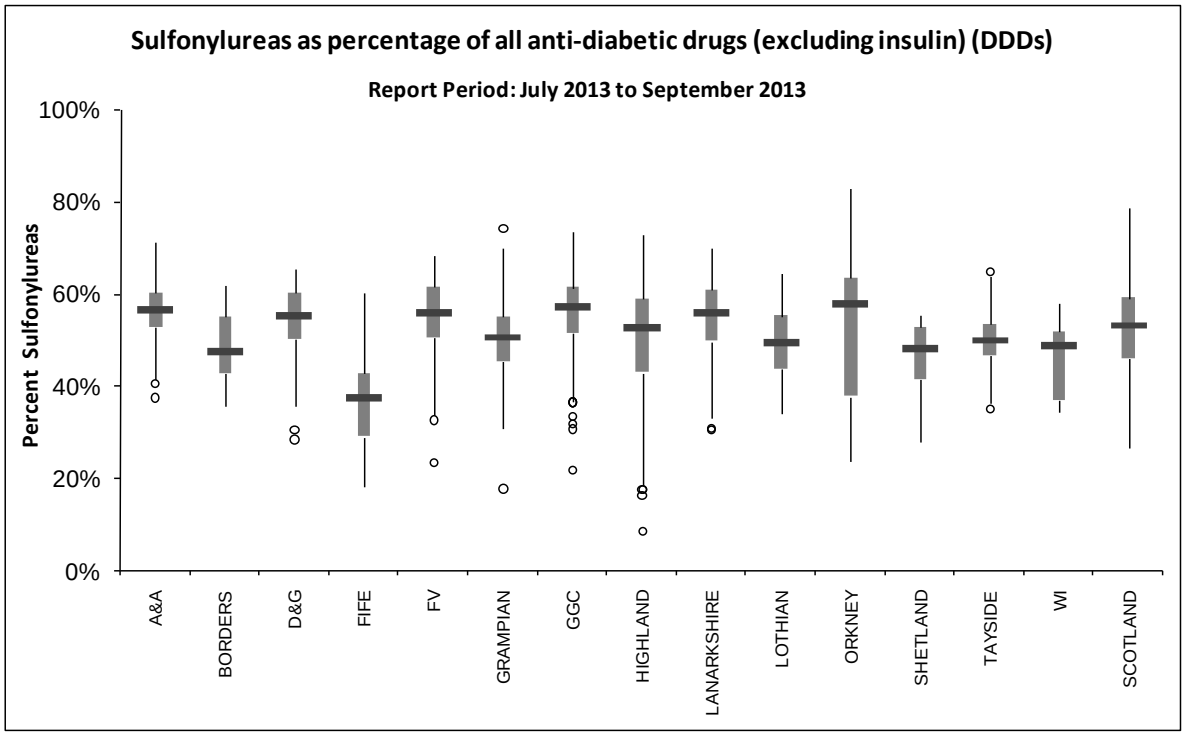
b. DDDs (defined daily doses) the assumed average maintenance dose per day for a drug used for its main indication in adults

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Metformin as percentage of all anti-diabetic drugs (excluding insulin) (DDDs)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	20.99%	29.66%	32.54%	37.25%	46.38%
NHS BORDERS	23.61%	32.95%	38.06%	41.41%	47.01%
NHS DUMFRIES & GALLOWAY	25.15%	33.53%	36.32%	40.42%	55.03%
NHS FIFE	29.31%	37.89%	41.22%	44.25%	53.42%
NHS FORTH VALLEY	20.14%	28.65%	29.76%	34.19%	53.41%
NHS GRAMPIAN	20.30%	33.95%	39.20%	43.41%	56.46%
NHS GREATER GLASGOW & CLYDE	17.17%	27.54%	30.39%	34.90%	58.14%
NHS HIGHLAND	15.65%	32.00%	35.92%	40.14%	73.96%
NHS LANARKSHIRE	21.63%	28.21%	30.99%	34.92%	50.40%
NHS LOTHIAN	20.76%	33.48%	36.91%	40.80%	51.78%
NHS ORKNEY	11.65%	33.74%	38.31%	50.53%	70.82%
NHS SHETLAND	35.31%	39.14%	43.53%	50.79%	70.95%
NHS TAYSIDE	26.18%	33.41%	36.70%	38.80%	50.02%
NHS WESTERN ISLES	26.94%	31.54%	39.96%	46.79%	53.66%
SCOTLAND		29.88%	34.55%	39.27%	

Sulfonylureas

Figure 6 shows sulfonylureas as a proportion of all antidiabetic drugs excluding insulins



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

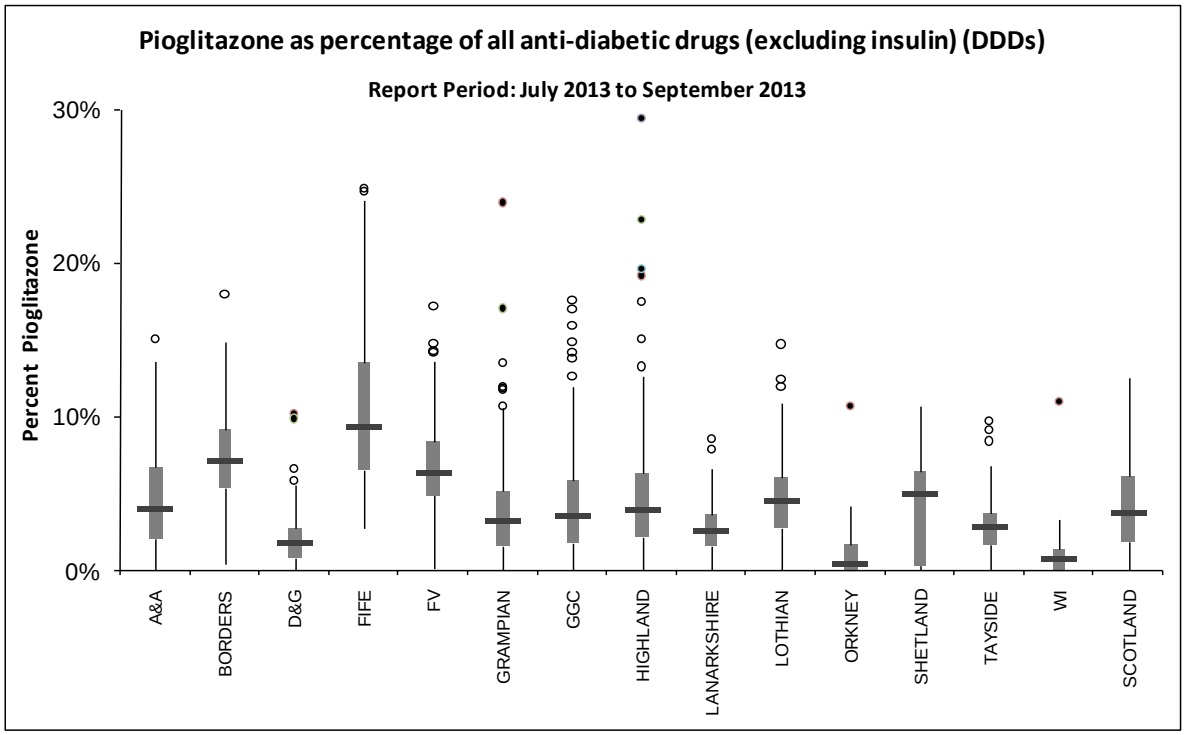
b. DDDs (defined daily doses) the assumed average maintenance dose per day for a drug used for its main indication in adults

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Sulfonylureas as percentage of all anti-diabetic drugs (excluding insulin) (DDDs)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	37.46%	52.74%	56.50%	60.23%	71.35%
NHS BORDERS	35.77%	42.72%	47.58%	54.98%	61.90%
NHS DUMFRIES & GALLOWAY	28.52%	50.29%	55.25%	60.12%	65.51%
NHS FIFE	18.09%	29.01%	37.46%	42.69%	60.39%
NHS FORTH VALLEY	23.58%	50.40%	55.90%	61.41%	68.36%
NHS GRAMPIAN	17.83%	45.36%	50.60%	55.15%	74.08%
NHS GREATER GLASGOW & CLYDE	21.76%	51.42%	57.25%	61.38%	73.61%
NHS HIGHLAND	8.72%	42.89%	52.70%	59.04%	72.73%
NHS LANARKSHIRE	30.59%	49.69%	56.03%	60.79%	69.87%
NHS LOTHIAN	34.10%	43.82%	49.54%	55.24%	64.42%
NHS ORKNEY	23.86%	37.70%	57.95%	63.47%	82.75%
NHS SHETLAND	27.90%	41.37%	48.10%	52.86%	55.44%
NHS TAYSIDE	35.03%	46.67%	49.97%	53.48%	64.87%
NHS WESTERN ISLES	34.51%	37.05%	48.71%	51.85%	57.90%
SCOTLAND		46.04%	53.22%	59.09%	

Pioglitazones

Figure 7 shows pioglitazone as a proportion of all antidiabetic drugs excluding insulins



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

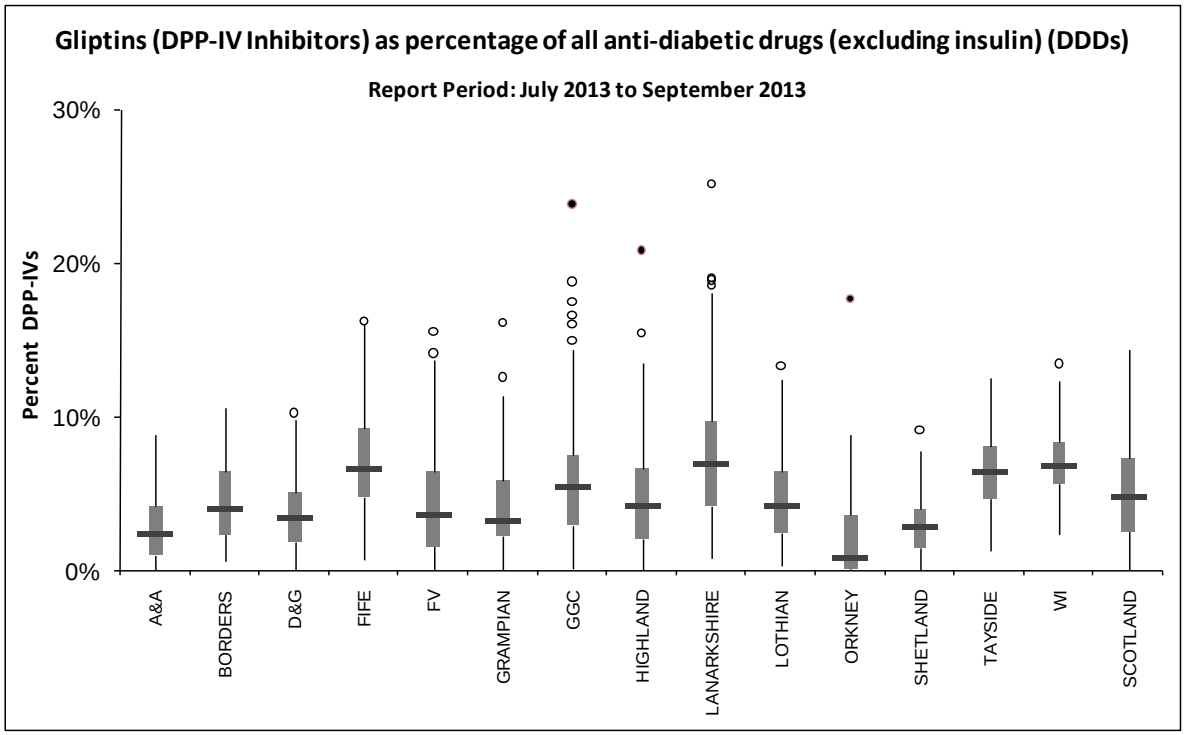
b. DDDs (defined daily doses) the assumed average maintenance dose per day for a drug used for its main indication in adults

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Pioglitazone as percentage of all anti-diabetic drugs (excluding insulin) (DDDs)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	0.00%	2.09%	4.01%	6.70%	15.01%
NHS BORDERS	0.44%	5.39%	7.14%	9.20%	17.96%
NHS DUMFRIES & GALLOWAY	0.00%	0.81%	1.74%	2.72%	10.18%
NHS FIFE	2.79%	6.51%	9.32%	13.54%	24.83%
NHS FORTH VALLEY	0.17%	4.90%	6.32%	8.39%	17.19%
NHS GRAMPIAN	0.00%	1.56%	3.24%	5.17%	23.93%
NHS GREATER GLASGOW & CLYDE	0.00%	1.73%	3.52%	5.81%	17.54%
NHS HIGHLAND	0.00%	2.20%	3.89%	6.37%	29.38%
NHS LANARKSHIRE	0.00%	1.57%	2.57%	3.59%	8.55%
NHS LOTHIAN	0.00%	2.77%	4.45%	6.02%	14.71%
NHS ORKNEY	0.00%	0.00%	0.38%	1.70%	10.67%
NHS SHETLAND	0.00%	0.33%	5.00%	6.47%	10.74%
NHS TAYSIDE	0.00%	1.72%	2.82%	3.76%	9.70%
NHS WESTERN ISLES	0.00%	0.07%	0.75%	1.37%	10.94%
SCOTLAND		1.90%	3.71%	6.15%	

Dipeptidyl peptidase-4 (DPP-4) inhibitors ('gliptins')

Figure 8 shows 'gliptins' as a proportion of all antidiabetic drugs excluding insulins



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

b. DDDs (defined daily doses) the assumed average maintenance dose per day for a drug used for its main indication in adults

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Gliptins as percentage of all anti-diabetic drugs (excluding insulin) (DDDs)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	0.08%	1.01%	2.37%	4.23%	8.86%
NHS BORDERS	0.58%	2.33%	3.99%	6.39%	10.56%
NHS DUMFRIES & GALLOWAY	0.00%	1.84%	3.45%	5.03%	10.24%
NHS FIFE	0.69%	4.78%	6.60%	9.28%	16.18%
NHS FORTH VALLEY	0.00%	1.54%	3.58%	6.40%	15.53%
NHS GRAMPIAN	0.00%	2.28%	3.21%	5.90%	16.14%
NHS GREATER GLASGOW & CLYDE	0.10%	2.91%	5.47%	7.57%	23.83%
NHS HIGHLAND	0.00%	2.04%	4.17%	6.63%	20.79%
NHS LANARKSHIRE	0.83%	4.25%	6.90%	9.78%	25.10%
NHS LOTHIAN	0.31%	2.46%	4.19%	6.45%	13.27%
NHS ORKNEY	0.00%	0.17%	0.82%	3.64%	17.63%
NHS SHETLAND	0.00%	1.47%	2.88%	4.00%	9.11%
NHS TAYSIDE	1.30%	4.71%	6.45%	8.12%	12.51%
NHS WESTERN ISLES	2.36%	5.66%	6.79%	8.35%	13.43%
SCOTLAND		2.59%	4.79%	7.30%	

1b. Glucagon like Peptide-1 (GLP-1) agonists

GLP-1 agonists are alternative third-line antidiabetic agents that are injectable. They are more expensive than sulfonylureas or thiazolindinediones, but they may help weight-loss and are associated with no increased risk of hypoglycaemia. As third-line agents they should be used following the trial of at least two other antidiabetic medicines where medication adherence and dose optimization was assessed. Refer to local joint formulary for the preferred GLP-1 agonist.

SIGN 116 recommends consideration of third-line use of GLP-1 agonists to improve glycaemic control in obese adults (BMI ≥ 30kg/m^2). This will usually be for obese patients on metformin and a sulfonylurea, as an alternative to insulin.

An exception to this is the acceptable use of GLP-1 agonists for non-obese type 2 diabetics with group 2 DVLA driving licenses, (Large goods vehicle or passenger carrying vehicle). The DVLA would require informing of the GLP-1 agonist treatment, but there shouldn't be the need for self-blood glucose monitoring, unless there was co-prescribing of a sulfonylurea.

GLP-1 agonists have a statistically similar effect to the oral second-line and third-line antidiabetic drugs on the surrogate disease marker, HbA_{1c}. Individual patient response is hard to predict, with some having no response, and others having an enhanced fall in HbA_{1c} and weight. Some patients cannot tolerate GLP-1 agonists due to gastrointestinal side-effects.

Unlike metformin, GLP-1 agonists have yet to be shown to reduce clinically important long-term complications of type 2 diabetes.

There is to date limited long-term safety data, but severe pancreatitis and renal failure have been reported with exenatide, as highlighted by the MHRA, (http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON088117).

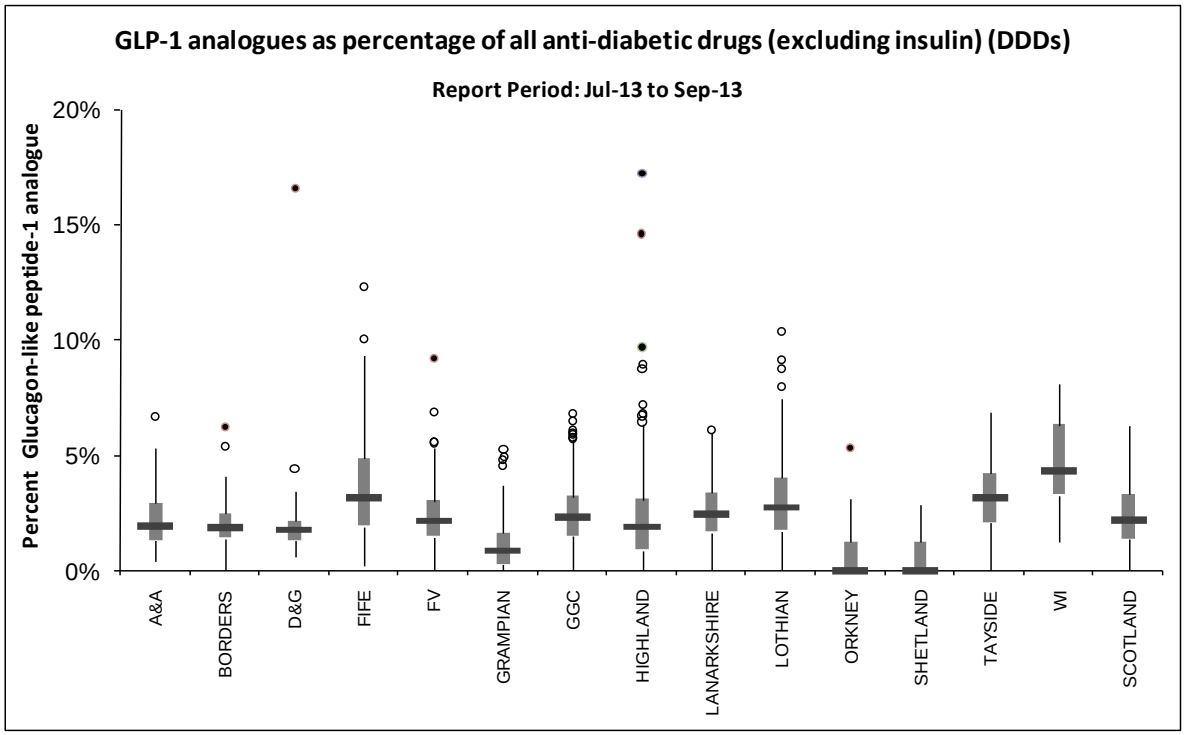
It is recommended that initiation of co-prescribing with GLP-1 agonists is undertaken by specialists, and for people in whom there can be shown the additional benefit.

As with all antidiabetics, GLP-1 agonists should be reviewed every six months for on-going effectiveness and tolerability. **It is important to recognise that this medicines only work whilst there is residual production of insulin by the pancreatic beta cells**. As the disease progresses there will come the time when the endogenous insulin production fails, and the GLP-1 agonists no-longer work. At this stage it is recommended that there is a trial of stopping the GLP-1 in combination with careful patient monitoring.

It should be noted that as newer products are marketed, SMC and local formulary recommendations are likely to change, and these should be used to inform choice.

Glucagon-like peptide-1 (GLP-1) agonists

Figure 9 shows the GLP-1 agonists as a percentage of all antidiabetic drugs



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

b. DDDs (defined daily doses) are the assumed average maintenance dose per day for a drug used for its main indication in adults

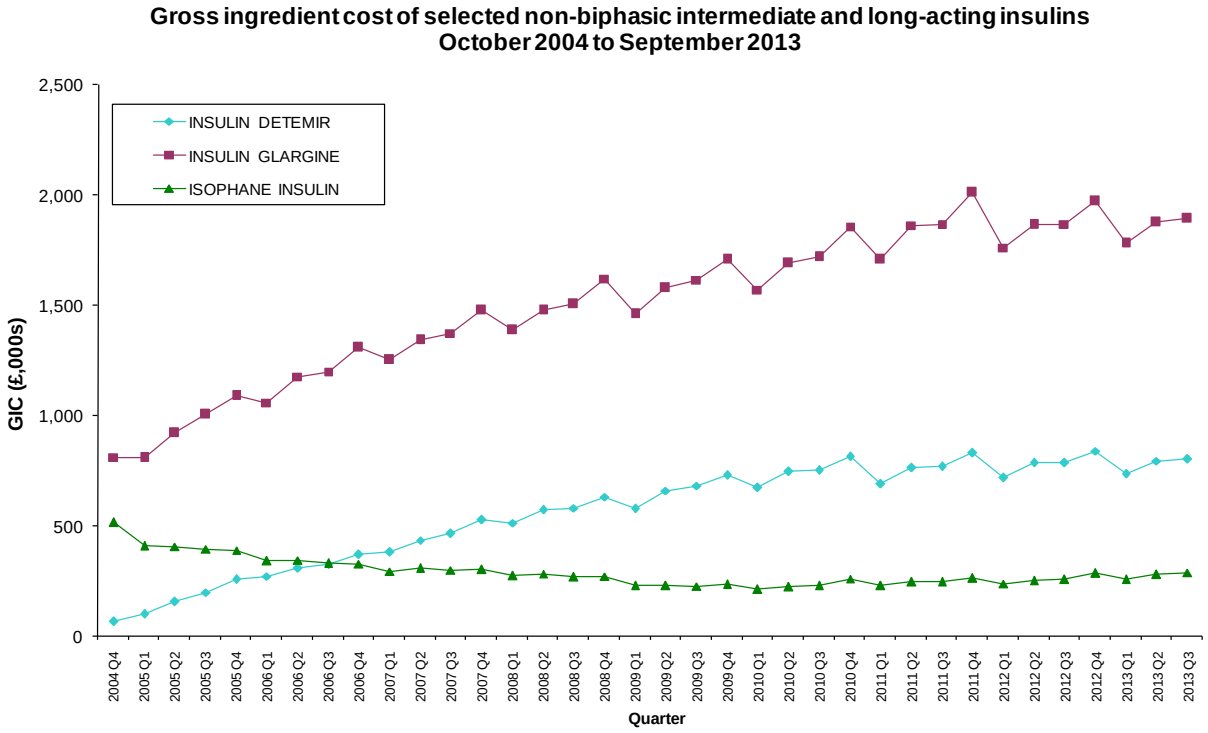
c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

GLP-1s as percentage of all anti-diabetic drugs (excluding insulin) (DDDs)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	0.43%	1.29%	1.93%	2.91%	6.66%
NHS BORDERS	0.00%	1.39%	1.86%	2.48%	6.23%
NHS DUMFRIES & GALLOWAY	0.57%	1.31%	1.76%	2.16%	16.57%
NHS FIFE	0.21%	1.91%	3.14%	4.87%	12.32%
NHS FORTH VALLEY	0.00%	1.47%	2.15%	3.02%	9.20%
NHS GRAMPIAN	0.00%	0.29%	0.87%	1.65%	5.25%
NHS GREATER GLASGOW & CLYDE	0.00%	1.54%	2.30%	3.21%	6.80%
NHS HIGHLAND	0.00%	0.88%	1.89%	3.08%	17.20%
NHS LANARKSHIRE	0.00%	1.66%	2.41%	3.38%	6.08%
NHS LOTHIAN	0.00%	1.73%	2.72%	4.03%	10.38%
NHS ORKNEY	0.00%	0.00%	0.00%	1.25%	5.32%
NHS SHETLAND	0.00%	0.00%	0.00%	1.26%	2.87%
NHS TAYSIDE	0.00%	2.08%	3.12%	4.23%	6.87%
NHS WESTERN ISLES	1.26%	3.27%	4.30%	6.32%	8.08%
SCOTLAND		1.35%	2.20%	3.32%	

2. Insulins

For many with type 2 diabetes the disease will progress and require a third-line agent for glycaemic control. For most non-obese patients (BMI ≤30Kg/m^2) insulins remains the preferred third-line therapy following optimal use of first and second-line agents. SIGN 116 advises that analogue insulins offer no advantage over human insulins for most patients with type 2 diabetes.

Figure 10 shows the rising costs of detemir (analogue) and largine (analogue) vs isophane (human) insulin



NOTES

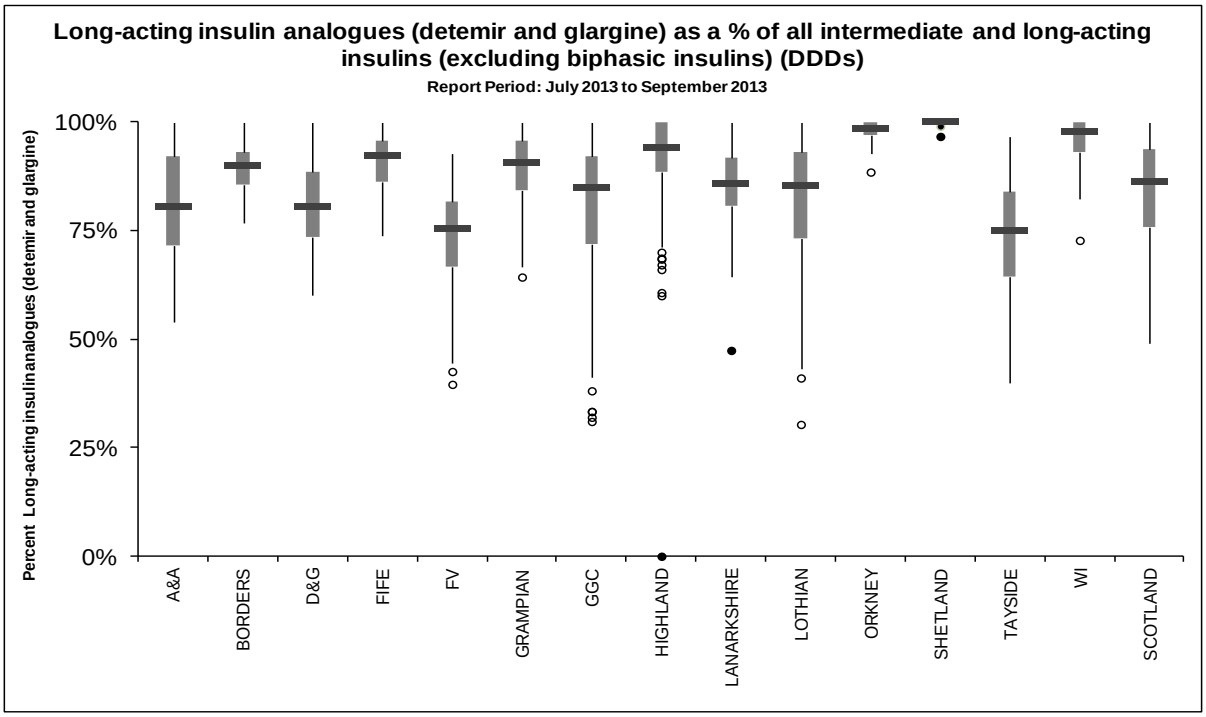
a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors. Net Ingredient Cost = price paid by NHS Scotland for medicines dispensed by community pharmacies and refers the price after discounts and does not include any dispensing costs or fees.

b. Calendar Quarters: Q1 = January to March; Q2 = April to June; Q3 July to September; Q4 October to December

Despite the rise in the use of insulin detemir and insulin glargine no clinically meaningful differences, have been found, between human and analogue insulins for HbA_{1c} level, severe hypoglycaemia or adverse events. [6] The rates of symptomatic and nocturnal hypoglycaemia are lower for analogue insulins, but at an incremental cost per quality adjusted life year (QALY) of around £300K. [6] Analogue insulins should be reserved for patients where there is a significant problem with nocturnal hypoglycaemia.

Insulin

Figure 11 shows the Long-acting insulin analogues (detemir and glargine) as a % of all intermediate and long-acting insulins (excluding biphasic insulins) (DDDs)



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors

b. DDDs (defined daily doses) are the assumed average maintenance dose per day for a drug used for its main indication in adults

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Long-acting insulin analogues (detemir and glargine) as a % of all intermediate and long-acting insulins (excluding biphasic insulins) (DDDs)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	53.91%	71.44%	80.40%	92.15%	100.00%
NHS BORDERS	76.89%	85.48%	90.00%	92.90%	100.00%
NHS DUMFRIES & GALLOWAY	60.00%	73.61%	80.54%	88.36%	100.00%
NHS FIFE	73.97%	86.18%	92.19%	95.64%	100.00%
NHS FORTH VALLEY	39.58%	66.67%	75.43%	81.48%	92.86%
NHS GRAMPIAN	64.29%	84.18%	90.70%	95.78%	100.00%
NHS GREATER GLASGOW & CLYDE	31.04%	71.70%	84.92%	92.06%	100.00%
NHS HIGHLAND	0.00%	88.44%	94.13%	100.00%	100.00%
NHS LANARKSHIRE	47.40%	80.77%	85.78%	91.70%	100.00%
NHS LOTHIAN	30.35%	73.02%	85.39%	92.89%	100.00%
NHS ORKNEY	88.46%	97.08%	98.55%	100.00%	100.00%
NHS SHETLAND	96.67%	100.00%	100.00%	100.00%	100.00%
NHS TAYSIDE	40.00%	64.29%	75.00%	83.98%	96.55%
NHS WESTERN ISLES	72.73%	92.97%	97.84%	100.00%	100.00%
SCOTLAND		75.86%	86.34%	93.70%	

3. Glucagon

Glucagon (GlucaGen® Hypokit) is indicated for the treatment of severe hypoglycaemia reactions which might occur in **insulin treated** persons with diabetes mellitus. As it requires subcutaneous, intramuscular or intravenous injection it should only be prescribed to those who have someone (relative, carer or health care professional) who is able to reconstitute and administer correctly when required.

GlucaGen® Hypokit has a shelf life of 3 years when stored in a fridge (2°C to 8°C) and 18 months at room temperature (25°C).

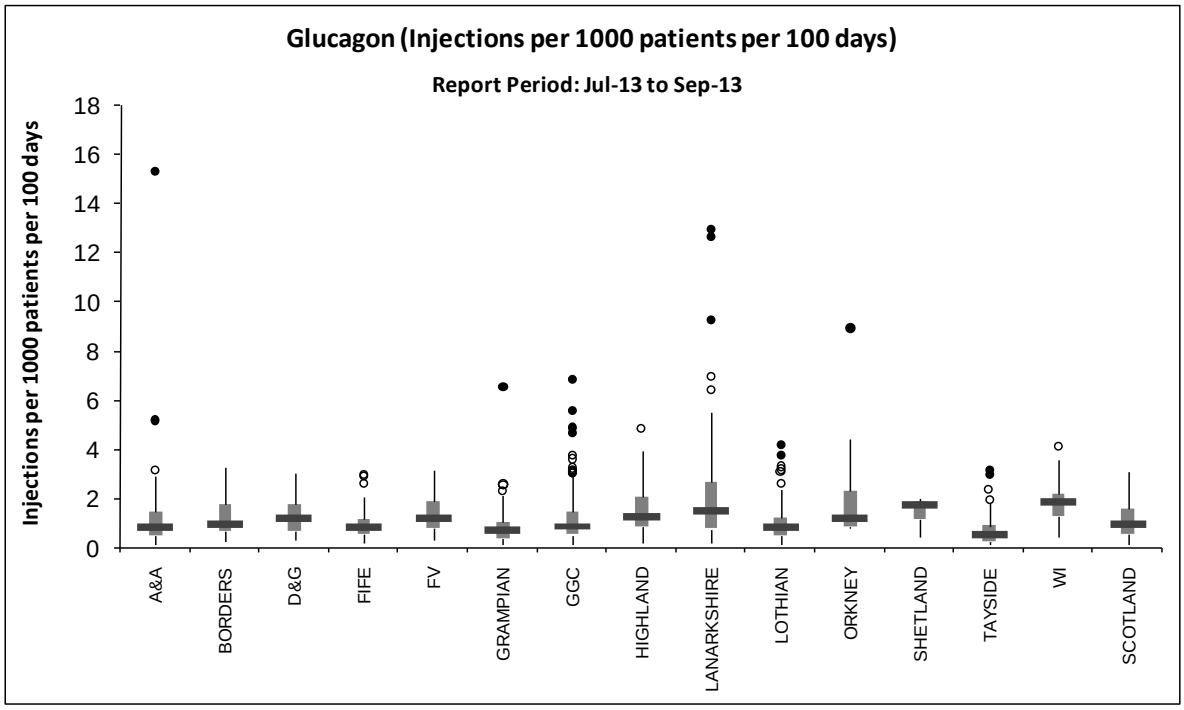
Table 2 shows the number and cost of GlucaGen® Hypokits prescribed by NHS Board

GlucaGen® kits: number of items and spend	Items		Cost per Item (NIC)		Cost (NIC)	
	2011-12	2012-13	2010-11	2011-12	2010-11	2011-12
NHS AYRSHIRE & ARRAN	878	923	£19.91	£19.03	£17,479	£17,568
NHS BORDERS	406	411	£14.38	£14.21	£5,839	£5,839
NHS DUMFRIES & GALLOWAY	389	404	£15.05	£14.51	£5,853	£5,863
NHS FIFE	890	843	£15.51	£15.80	£13,807	£13,317
NHS FORTH VALLEY	1096	1207	£15.14	£14.47	£16,595	£17,468
NHS GRAMPIAN	991	1096	£15.15	£15.33	£15,015	£16,807
NHS G. GLASGOW & CLYDE	3172	3146	£15.33	£15.42	£48,614	£48,510
NHS HIGHLAND	844	843	£15.56	£15.46	£13,137	£13,030
NHS LANARKSHIRE	2913	3213	£14.89	£14.75	£43,375	£47,378
NHS LOTHIAN	2315	2204	£16.07	£15.98	£37,198	£35,228
NHS ORKNEY	48	46	£14.60	£13.46	£701	£619
NHS SHETLAND	92	90	£16.83	£14.87	£1,549	£1,338
NHS TAYSIDE	521	493	£17.16	£16.57	£8,938	£8,167
NHS WESTERN ISLES	118	130	£14.19	£13.53	£1,675	£1,760
Total	14673	15049			£229,773	£232,892

It is advocated that a GP practice based review is undertaken of all patients prescribed glucagon to ensure that the individual's circumstances allow for reconstitution and injection when required in an emergency situation. This should also be addressed at the patient's annual review to ensure that all prescribing remains appropriate.

Glucagon

Figure 12: Glucagon: GlucaGen HypoKit® (DDDs/1,000patients/100days)



NOTES

a. From PRISMS which details the prescriptions dispensed by community pharmacists and appliance contractors.

b. DDDs (defined daily doses) are calculated using the assumed average maintenance dose per day for a drug used for its main indication in adults (http://www.whocc.no/ddd/definition_and_general_considera/)

c. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

Glucagon (Injections per 1000 patients per 100 days)	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	0.10	0.48	0.84	1.46	15.34
NHS BORDERS	0.23	0.65	0.93	1.74	3.26
NHS DUMFRIES & GALLOWAY	0.29	0.69	1.20	1.76	3.04
NHS FIFE	0.18	0.54	0.83	1.16	2.99
NHS FORTH VALLEY	0.33	0.80	1.18	1.86	3.13
NHS GRAMPIAN	0.13	0.35	0.72	1.06	6.54
NHS GREATER GLASGOW & CLYDE	0.11	0.52	0.85	1.48	6.85
NHS HIGHLAND	0.20	0.86	1.24	2.09	4.85
NHS LANARKSHIRE	0.22	0.76	1.46	2.67	12.98
NHS LOTHIAN	0.11	0.50	0.82	1.24	4.19
NHS ORKNEY	0.78	0.86	1.18	2.28	8.95
NHS SHETLAND	0.44	1.15	1.70	1.87	2.02
NHS TAYSIDE	0.11	0.24	0.51	0.88	3.15
NHS WESTERN ISLES	0.46	1.27	1.85	2.19	4.14
SCOTLAND		0.53	0.92	1.57	

4. Diagnostic and Monitoring Agents

4a. Self-Blood Glucose Monitoring (SBGM)

Self-monitoring of blood glucose is essential in type 1 diabetes to manage glycaemic control and monitor for hypoglycaemia. SBGM is not suitable or recommended for all those with type 2 diabetes and there are clear recommendations for specific groups of patients. SBGM is essential for people with type 2 diabetes:

- who are treated with insulin
- who are group 2 DVLA (lorry and bus) drivers taking a sulfonylurea or glinide***

SBGM could be considered for type 2 diabetics who:

- who are at risk of hypoglycaemia due to sulfonylurea or glinide***
- **Short-term** to monitor glycaemic control during lifestyle or medication change

SBGM should be prescribed in line with local MCN guidance and the local joint formulary. SBGM is not recommended for patients with 'diet only' diabetes, or taking metformin as the only therapy. It is noted that short-term use for those undergoing the DESMOND [9] programme is an exception to this rule.

Appendix A contains examples of where the appropriateness of SBGM has been reviewed in the context of current evidence, guidance and local joint formulary.

Evidence based medicine supports the restricted use of SBGM in type 2 diabetes. A Cochrane review found a poor correlation between HBGM and overall glycaemic control for type 2 diabetics. [10] Evidence to date suggests that SBGM does not improve patient satisfaction, general well-being or health related quality of life. The ESMON study, which looked at newly diagnosed patients with type 2 diabetes, showed that SBGM did not improve control and was associated with increased depression scores.[11] The DiGEM study reports that SBGM reduces quality of life, increases anxiety scores and costs a lot per patient.[12]

4b. Ketone monitoring

Ketone testing is not necessary for those with type 2 diabetes, so strips should not be prescribed. Although not recommended as a routine measurement, ketone monitoring (urine or blood) is accepted as an integral component in the management of type 1 diabetes and can be critical to prevent or detect diabetic ketoacidosis. For most type 1 patients urine ketone testing is entirely appropriate however particular groups of patients may benefit from blood ketone monitoring. SIGN recommends that this is done in conjunction with increased input from the primary healthcare team. Every patient should be educated in frequency of ketone monitoring and how to interpret results

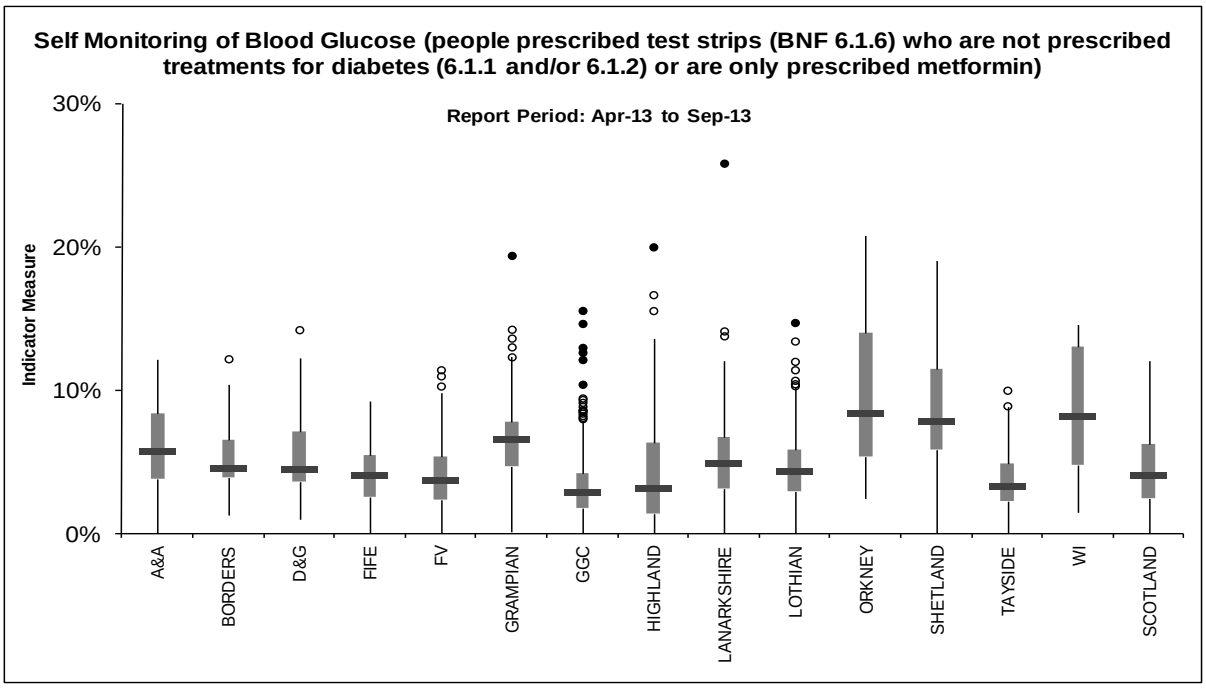
References:

9. **DESMOND programme (2008) http://www.desmond-project.org.uk/locationmap.html#scotland**
10. **Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin *Cochrane Database of Systematic Reviews. 2012, Issue 1. Art. No.:CD005060.DOI:10.1002/14651858.CD005060.pub3.***
11. **Efficacy of self-monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study) *BMJ*2008;336:1174**
12. **Cost-effectiveness of self-monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial *BMJ*2008:336:177-80**

***** Glinides are not mentioned elsewhere in the strategy, but included here to reflect DVLA guidance**

Self-Blood Glucose Monitoring (SBGM)

Figure 13 People prescribed SBGM who are not prescribed treatments for diabetes or who are only prescribed metformin (NB data includes <u>all</u> patients with diabetes)



NOTES

a. From PIS which details the prescriptions dispensed by community pharmacists and including the unique patient identifier CHI

b. Community Health Index (CHI) was recorded from ?% of the prescription items for the selected medicines in the time period

c. Count of distinct patients dispensed testing strips (BNF 6.1.6) who were either not prescribed an oral antidiabetic agent or insulin or if they were they were only prescribed metformin in the timeframe November 2012 to April 2013

d. Box plot showing distribution of GP practices within each health board: median (central bar), inter-quartile range (grey box), minimum/maximum (whiskers) and outliers if greater than 1.5 (○) or 3 (●) of inter-quartile range from lower or upper quartile.

SBGM: people prescribed test strips (BNF 6.1.6) who are not prescribed treatments for diabetes (6.1.1 and/or 6.1.2) or are only prescribed metformin	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
NHS AYRSHIRE & ARRAN	0.00%	3.82%	5.68%	8.38%	12.16%
NHS BORDERS	1.26%	3.90%	4.56%	6.50%	12.20%
NHS DUMFRIES & GALLOWAY	1.03%	3.65%	4.49%	7.09%	14.22%
NHS FIFE	0.00%	2.51%	4.02%	5.49%	9.26%
NHS FORTH VALLEY	0.00%	2.33%	3.67%	5.33%	11.43%
NHS GRAMPIAN	0.00%	4.72%	6.52%	7.76%	19.40%
NHS GREATER GLASGOW & CLYDE	0.00%	1.77%	2.87%	4.21%	15.56%
NHS HIGHLAND	0.00%	1.44%	3.13%	6.32%	20.00%
NHS LANARKSHIRE	0.00%	3.14%	4.85%	6.69%	25.84%
NHS LOTHIAN	0.00%	2.92%	4.33%	5.82%	14.72%
NHS ORKNEY	2.44%	5.41%	8.33%	14.04%	20.83%
NHS SHETLAND	0.00%	5.81%	7.78%	11.47%	19.00%
NHS TAYSIDE	0.00%	2.25%	3.30%	4.89%	10.00%
NHS WESTERN ISLES	1.49%	4.79%	8.15%	13.06%	14.58%
SCOTLAND		2.45%	4.05%	6.29%	

5. Polypharmacy

The Scottish Government issued CEL (36) guidance to Health boards on appropriate prescribing and the polypharmacy guidance in November 2012. Full guidance can be found on http://www.central.knowledge.scot.nhs.uk/upload/Polypharmacy%20full%20guidance%20v2.pdf

When treating type 2 diabetes particular consideration needs to be given to HbA_{1c} targets set for frail and elderly, noting that hypoglycemia can predispose a patient to falls.

The potential of adverse events for all type 2 diabetes prescribed treatments for frail and elderly patients requires careful consideration. Sulfonylureas are associated with weight gain and increased risk of hypoglycaemia. Glitazones may also cause weight gain and should not be used in patients with heart failure, a history of fragility bone fractures or bladder cancer. There is as yet no long term safety data for either gliptins or GLP-1s.

The polypharmacy guidance also considers **anticipatory care during intercurrent illness,** where there should be consideration of stopping certain medicines for the duration of the illness. It is recommended that for dehydrated frail patients suffering from moderate to severe vomiting and/or diarrhoea the following medicines should be stopped:

- ACE inhibitors
- A2RAs
- NSAIDs
- Diuretics
- Spironolactone or eplerenone
- Metformin

This applies for the duration of the illness and is separate from decisions relating to the long term use of these drugs.

Appendix A

Case Studies from Scotland and England:

a. NHS Glasgow

NHS GG&C encouraged GP practices to audit their prescribing of blood glucose test strips against MCN guidance which included recommendations for the frequency of SBGM for each treatment option. Ninety-seven practices (of a total of 270) reviewed the prescribing of blood glucose test strips in 2010/11. For these practices growth in prescribing costs for blood glucose test strips in 2010/11 compared to the previous year was 0.86% compared to 1.86% for the other GP practices in the health board area. In the following year the difference in growth was more marked (1.33% versus 7.30%). This equates to differences in prescribing costs of £11,156 in 2010/11 and £67,332 in 2011/12. The main outcome of the audit work was ensuring people with a clinical need for self-monitoring were appropriately prescribed blood glucose tests strips. The audit help to identify people with diabetes provided test strips unnecessarily but more importantly it highlighted the many people not provided sufficient test strips for the self-monitoring that is recommended by the MCN.

b. Aston PCT

The Aston healthcare practice based commissioning group developed a programme to improve the appropriateness of SBGM[4]. The approach included the implementation of local testing guidelines and formulary and the education of patients on appropriate testing. There was a 25.4% reduction in use of SBGM and an improvement in HbA1c target achievement.

Timelines for Actions

It is acknowledged and agreed that prescribing for this patient group should reflect the current SIGN guideline 116: Management of diabetes (March 2010)

Prescribing should also be in line with Scottish Medicines Consortium (SMC) approval and local Formularies whenever possible. Further guidance and support is contained in that provided by health boards through their MCNs.