Clinical *DIGEST 2*

Management & prevention of type 2 diabetes

Further evidence provided for patient-adjusted insulin



Roger Gadsby, GP and Senior Lecturer, Centre for Primary Healthcare Studies, Warwick University

he ideas of patient empowerment are affecting the way diabetes care is delivered in the UK. For example, healthcare professionals are becoming convinced that people with type 1 diabetes who understand

the principles of dose adjustment for normal eating can safely and usefully alter their short-acting insulin dose at mealtimes.

But do we have confidence that people with type 2 diabetes treated with once-daily long-acting insulin can safely up-titrate their insulin dose, or is up-titration better left to a healthcare professional?

Davies et al (see right) report on a prospective, multicentre, 24-week randomised trial in 4961 people with type 2 diabetes who were suboptimally controlled. Some were on tablets only, and others were on tablets and insulin. The study compared two treatment algorithms for initiation and titration of insulin glargine: one investigator-led and the other patient-led.

The patient-led treatment algorithm resulted in a greater drop in HbA_{1c} (1.22%, compared with 1.08% in the investigator-led one), with no difference in hypoglycaemia.

The paper concludes that insulin glargine is safe and effective in improving glycaemic control in a large, diverse population with longstanding type 2 diabetes. A simple patient-administered titration algorithm conferred significantly improved glycaemic control, with a low incidence of severe hypoglycaemia, compared with a physician-managed titration algorithm.

This is the largest study of insulin initiation in type 2 diabetes and it shows that once-daily insulin glargine plus tablets with up-titration of insulin dose by the patient is safe and effective. It also gives more evidence that patients who are educated and empowered can safely adjust their insulin treatment schedules.

DIABETES & METABOLISM

Insulin use in France trails that in other European countries

Readability	////
Applicability to practice	111
WOW! factor	1111

Results from the French National Sickness Insurance Fund surveys of 1998 and 2000 were extrapolated to get estimations of diabetes prevalence and treatment in France in 2002.

The estimation for the number of people with type 1 or type diabetes in 2002 was around

2 150 000 (or 3.4% of the French population); of these, 2 050 000 were treated with drugs, while 100 000 were treated with diet alone.

The percentage of people with type 2 diabetes on insulin (with or without an oral antidiabetic) rose from 12.3 % in 1998 to 16.5 % in 2002.

No data are available on monitoring in insulin users.

Despite the rise in insulin use in France, this nation has lower rates than other European countries.

It is possible that this difference could disappear in the coming years, as awareness of the importance of glycaemic control increases and the conditions for insulin use improve.

Detournay B, Raccah D, Cadilhac M, Eschwege E (2005) Epidemiology and costs of diabetes treated with insulin in France. *Diabetes & Metabolism* **31**(3 Pt 2): 3–18

DIABETES CARE



Patient-managed insulin regimen shows advantages

Readability	1111
Applicability to practice	1111
WOW! factor	11111

Attributes of insulin regimens include safety, dose titration and measures of glycaemic control (such as HbA_{1c}, fasting blood glucose and incidence of hypoglycaemia).

This 24-week, prospective, multicentre trial randomised people with poorly controlled type 2 diabetes to insulin glargine managed by healthcare professionals (algorithm 1; n=2493) or by themselves (algorithm 2; n=2468).

At the end of the study, the incidence of severe hypoglycaemia did not differ significantly between algorithms (0.9% for algorithm 1 and 1.1% for algorithm 2).

The reduction in HbA_{1c} was significantly greater for algorithm 2 (1.22%) than algorithm 1 (1.08%; P<0.001).

Similarly, the reduction in fasting blood glucose was significantly greater for algorithm 2 (62 mg/dl) than algorithm 1 (57 mg/dl; *P*<0.001).

There was also a significant difference in the increase of mean basal insulin dose between the algorithms (18.7 IU for algorithm 1 and 21.6 IU for algorithm 2; *P*<0.003).

No significant differences between algorithms were reported for adverse events.

An implication of the overall advantage of patient-managed insulin is the potential for a reduction in burden on healthcare professionals.

Davies M, Storms F, Shutler S, Bianchi-Biscay M, Gomis R; ATLANTUS Study Group (2005) Improvement of glycemic control in subjects with poorly controlled type 2 diabetes: comparison of two treatment algorithms using insulin glargine. Diabetes Care **28**(6): 1282–8

Clinical *DIGEST*



Frequency of SMBG does not predict metabolic control

Readability Applicability to practice **WOW!** factor

Self-monitoring of blood glucose (SMBG) is a technique that has been recommended for improving blood glucose control in people with diabetes, although its role in people with non-insulin-treated type 2 diabetes is debated.

In this paper, as part of a nationwide outcomes research programme in Italy, the investigators examined the effect of SMBG on metabolic control over 3 years in people with type 2 diabetes not treated with insulin.

The study involved 1896 patients. Participants completed a questionnaire on their SMBG

activity at 6-monthly intervals. The questionnaire also included questions on hypoglycaemia, diabetes complications and SMBG support from the patients' families. Additional clincal data were collected at the same time points from clincians. Overall, 101 outpatient diabetes clinics and 103 GPs participated in the trial.

SMBG frequency was assessed in one question using a six-point scale (ranging from '>1 time/day' to 'never'). The validity of the answer to this question was assessed with a second question in a different part of the questionnaire which asked how many times the participant had measured his/her blood glucose in the last 2 weeks.

Multi-level statistical analysis was used to assess the predictive value of SMBG frequency on longterm metabolic control. A tree-based algorithm (recursive partitioning and amalgamation [RECPAM]) was used to identify distinct subgroups of patients with the same likelihood of performing SMBG. The impact of SMBG was then assessed within these groups.

Overall, 78 % of the particpants were treated with oral agents, and 22 % managed their diabetes by diet alone. Forty-one per cent of participants carried out SMBG at least once per week. The frequency of SMBG did not have a statistically significant impact on HbA_{1c} levels over the 3-year study. Furthermore, the investigators did not observe that changes in SMBG frequency resulted in significant impacts on HbA_{1c} level.

In none of the eight RECPAMidentified subgroups was increased SMBG frequency found to improve HbA_{1c} level over the 3-year follow-up. However, SMBG was associated with decreased hypoglycaemia in those RECPAM groups where SMBG was performed to avoid hypoglycaemia.

The authors concluded that SMBG frequency did not predict improved metabolic control in people with noninsulin-treated type 2 diabetes over a 3-year period.

Franciosi M, Pellegrini F, De Berardis G et al (2005) Self-monitoring of blood glucose in noninsulin-treated diabetic patients: a longitudinal evaluation of its impact on metabolic control. Diabetic Medicine 22(7): 900-6

Over the same time frame, the cost to society per QALY gained was predicted to be much higher for the lifestyle modification programme of the DPP, at US\$62600 (around £34500).

Moreover, in comparison with lifestyle modification beginning after the onset of diabetes, the marginal cost of beginning the DPP lifestyle modification programme immediately to society per QALY gained over 30 years was estimated to be US\$201 800 (around £111 000).

Even using this optimistic approach (for instance, the costs to society per QALY gained were higher over 5- and 10-year time frames), diabetes-related health costs were predicted to incur a net

Eddy DM, Schlessinger L, Kahn R (2005) Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. Annals of Internal Medicine 143(4): 251-64

SMBG frequency did not predict *improved* metabolic control in people with non-insulintreated type 2 diabetes over a 3-vear period.⁹

La Diabetes-related health costs were predicted to incur a net increase of around 25 % if a DPP-type programme were implemented.⁵



DPP-type lifestyle intervention may not be a costeffective strategy

Readability **Applicability to practice WOW!** factor

Studies such as that of the Diabetes Prevention Program (DPP) have shown that lifestyle modification can reduce the onset of diabetes, but the long-term costeffectiveness of such a strategy has not been fully investigated.

This analysis sought to address this need for research by using the Archimedes model, which is a

high-level simulation that includes diabetes, coronary artery disease, congestive heart failure, hypertension and stroke.

The analysis related to adults who were deemed to be at high risk of diabetes, which meant fulfilling the eligibility criteria for the DPP study (body mass index >24 kg/m²; fasting plasma glucose of 5.27-6.94 mmol/l; 2-hour glucose tolerance test of 7.77-11.04 mmol/l).

Three interventions were examined: metformin; lifestyle modification beginning after the onset of diabetes; and the lifestyle modification programme of the DPP.

Over a 30-year time frame, the cost to society per quality-adjusted life year (QALY) gained was predicted to be US\$35400 (around £19500) for metformin and US\$24500 (around £13500) for lifestyle modification beginning after the onset of diabetes.

increase of around 25% if a DPP-type programme were implemented.

Diabetes Digest Volume 4 Number 4 2005

Type 2 diabetes



Data lend support to need for physical activity programmes

Readability	1111
Applicability to practice	/////
WOW! factor	11111

- The impact of different levels of physical activity on health and expenditure in type 2 diabetes is an area where more research is needed.
- Post hoc analysis was performed on 179 people with type 2 diabetes who received physical activity counselling and were followed for 2 years.
- Six groups were defined on the basis of increase in energy expenditure (in metabolic equivalents [METs] per hour per week): group 0, group 1–10, group 11–20, group 21–30, group 31–40 and group >40.
- In group 11–20, group 21–30, group 31-40 and group >40, there were significant improvements at 2 years in HbA_{1c}, total cholesterol, triglycerides, blood pressure and estimated improvement in 10-year risk of coronary heart disease (all P<0.05); there were no such significant changes for group 0 and group 1–10.
- Medical costs at 2 years significantly increased in group 0 (P=0.008), did not change significantly in group 1–10, and significantly decreased in group 11–20 (P=0.01), group 21–30 (P=0.009), group 31–40 (P=0.003) and group >40 (P=0.001).
- Increased energy expenditure through voluntary physical activity can thus have health and cost benefits.
- The study's threshhold for full benefits was in group 21–30; the authors thus recommend this group's average increase in expenditure, 27 METs per hour per week, as a reasonable target for previously sedentary patients (equivalent to a 5 km daily walk).

Di Loreto C, Fanelli C, Lucidi P et al (2005) Make your diabetic patients walk: long-term impact of different amounts of physical activity on type 2 diabetes. *Diabetes Care* **28**(6): 1295–302

DIABETIC MEDICINE



Study suggests need for improved patient-oriented material on the Internet

Readability	////
Applicability to practice	1111
WOW! factor	111

- Using the Internet is one means for patients to become involved in the process of making decisions about their health care.
- This investigation aimed to evaluate the provision of patient-oriented evidence that matters (POEMs) on the Internet.
- A partially random sampling method was used to find 66 websites with health information on type 2 diabetes, 15 of which had the 'Health on the Net' seal.
- The DISCERN instrument was used to judge the quality of written information about treatment choices on the websites.
- Of the items searched for (based on the UK Prospective Diabetes Study), the statement that tight blood pressure control reduced complications or mortality was the most common (occurring on 36 [55%] of the websites).
- Less common statements included those about metformin's effect on mortality or morbidity in overweight people and the lack of effect of tight blood glucose control on premature mortality (occurring on 12 [18%] and 1 [2%] of the websites, respectively).
- The provision of POEMs was more common on websites with the 'Health on the Net' seal and those rated highly using the DISCERN instrument.
- Overall, the provision of POEMs on the Internet was deemed to be poor.
- The authors suggest the need for efforts to update the information provided on the Internet, if the challenge of helping patients to become involved in decision-making is to be met.

Gimenez-Perez G, Caixas A, Gimenez-Palop O, Gonzalez-Clemente JM, Mauricio D (2005) Dissemination of 'patient-oriented evidence that matters' on the Internet: the case of Type 2 diabetes treatment. *Diabetic Medicine* **22**(6): 688–92

negotiation was less common in practices which carried out annual reviews with the practice nurse alone than in those where a GP was involved.

DIABETES CARE



SCI-R shows good psychometric properties

Readability	111
Applicability to practice	111
WOW! factor	11

The psychometric properties of the Self-Care Inventory-revised (SCI-R) – a patient-reported measure of adherence to diabetes self-care

interventions - were investigated in this study, which looked at data from adults with type 1 or type 2 diabetes.

- The SCI-R was reported to have high internal consistency as well as concurrent and convergent validity (which relate to correlation with measures of known quality).
- The SCI-R had a positive correlation with self-esteem and self-efficacy (both P < 0.0001), while its negative correlations included those with anxiety and distress (both P < 0.0001).

Weinger K, Butler HA, Welch GW, La Greca AM (2005) Measuring diabetes self-care: a psychometric analysis of the Self-Care Inventory-Revised with adults. *Diabetes Care* **28**(6): 1346–52

diabetes was reported in 88 (89%) of the practices that responded.

> Forty-five (46 %) of the practices carried out annual diabetes reviews with the practice nurse alone for at least some patients.

Target negotiation was less common in these practices (43 %) for blood pressure and 39 % for HbA_{1c}) than in practices where a GP was involved in the annual review (64% and 60 %, respectively; P=0.04 and P=0.03 for the respective differences).

A need for further work to establish reasons for the reported differences is acknowledged.

Stewart J, Kendrick D; Nottingham Diabetes Blood Pressure Study Group (2005) Setting and negotiating targets in people with Type 2 diabetes in primary care: a cross sectional survey. Diabetic Medicine 22(6): 683-7

Clinical trials, however, have not properly controlled for other glucose

or lipid-lowering therapies.

- This study aimed to examine these agents' lipid and glucose effects.
- After 4 weeks' wash-out on placebo, participants were randomised to 24 weeks of pioglitazone (n=400) or rosiglitazone (n=402).
- Pioglitazone led to significant improvements in HDL cholesterol, LDL cholesterol and triglyceride levels relative to rosiglitazone.

Goldberg RB, Kendall DM, Deeg MA et al (2005) A comparison of lipid and glycemic effects of pioglitazone and rosiglitazone in patients with type 2 diabetes and dyslipidemia. Diabetes Care **28**(7): 1547–54

DIABETES CARE

Combination weight loss programme is beneficial in diabetes

Readability	111
Applicability to practice	111
WOW! factor	11

- Optimal long-term strategies for the treatment and prevention of obesity need clarification.
- This 2-year trial assessed the effect of a combination of weightloss interventions on glycaemic control and weight loss in people with a body mass index of 27-50 kg/m² and type 2 diabetes.
- Of 48 people who completed the study, 25 were on standard therapy for the first year (which involved a tailored calorie-reduced diet and exercise plan) and combination therapy for the second year (which involved the standard therapy as well as meal replacement products and daily sibutramine).
- The other 23 participants were on combination therapy for 2 years.
- The mean weight loss in those The mean weight on combination therapy for 2 years was 4.6 kg (P < 0.001); HbA_{1c} decreased non-significantly in this
- For individuals on standard therapy for the first year, changes in weight and HbA_{1c} in the second year were deemed similar to those seen in the first year in people on just combination therapy.
- The study design did not allow for discrimination between the components of the combination therapy with regard to their contribution to the weight loss.
- The weight loss seen with 2 years' combination therapy can, according to the authors, lead to improvements in diabetes control of clinical significance.

Redmon JB, Reck KP, Raatz SK et al (2005) Two-year outcome of a combination of weight loss therapies for type 2 diabetes. Diabetes Care

DIABETIC MEDICINE

Target negotiation is less frequent where reviews involve just a practice nurse

Readability Applicability to practice **WOW!** factor

- An aim of this study was to determine the frequency of target setting and negotiating for people with diabetes in primary care.
- Of 123 general practices surveyed, 99 (80%) responded.
- Target setting for HbA_{1c} and blood pressure in people with type 2

Pioglitazone led to significant improvements in

HDL cholesterol. LDL cholesterol and triglycerides relative to

rosiglitazone."

DIABETES CARE



Pioglitazone shows better lipid effects than rosiglitazone

•		
Readability	111	
Applicability to practice	111	
WOW! factor	111	

There is evidence to suggest that pioglitazone and rosiglitazone differ in their effect on lipids in people with type 2 diabetes.