LANCET

Rosiglitazone reduces incidence of type 2 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓✓

1 The aim of the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) investigation was to assess the ability of rosiglitazone to prevent incidence of diabetes in high-risk individuals.

2 The trial investigated 5269 people over 30 years of age who had impaired fasting glucose, impaired glucose tolerance or both for a median of 3 years. They were randomised to receive either rosiglitazone (8 mg/day) or placebo.

3 By the end of the study 306 of the individuals taking rosiglitazone and 686 of those on placebo had reached the primary endpoint of incident of diabetes or death.

4 Normoglycaemia occurred in 1330 of the rosiglitazone group and 798 in the placebo group ($P<0.001$). Heart failure occurred in 14 (0.5%) of those taking the drug, compared with 2 (0.1%) of those taking placebo ($P=0.01$); however, other CV outcomes were similar between groups.

5 The study found that rosiglitazone at a dose of 8 mg daily over a mean period of 3 years will significantly reduce the incidence of type 2 diabetes in high-risk individuals. The drug also increased the likelihood of regression to normoglycaemia in the investigated population.

6 The authors conclude that for individuals at high risk of diabetes, early administration of rosiglitazone gives a relative risk reduction of 60% and an absolute risk reduction of 14.4%.

The DREAM (Diabetes Reduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators (2006) Effects of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet* **368:** 1096–105

Preventing diabetes: DREAM on?

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Even though my esteemed colleague, Ken MacLeod, discussed the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) study earlier in this issue (see page 16), I feel that the data are important enough to warrant a second commentary.

We already know from a Finnish study (Tuomilehto et al, 2001) and the American Diabetes Prevention Study (Diabetes Prevention Programme Research Group, 2002) that intensive lifestyle advice with increasing levels of physical activity and modest weight loss can reduce the development of diabetes in people with impaired glucose tolerance by 58%. In the American study a sub-group treated with metformin had a 37% reduction in the development of diabetes. The aim of DREAM (summarised on the left) was to see if either agent could prevent the development of diabetes in people with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG).

The DREAM study was a double blind, randomised clinical trial with a 2x2 factorial design. The study involved 5269 people with IGT or IFG or both but no cardiovascular disease who were given ramipril up to 15 mg/day or placebo or rosiglitazone or placebo and were followed for a median of 3 years. The results showed that those given rosiglitazone reduced their development of diabetes by 60%, those given ramipril were no different to placebo. The rosiglitazone group had more weight gain and seven times more heart failure.

The study showed that rosiglitazone reduces the risk of developing diabetes in people with IFG or IGT or both. It is not licensed for this indication (neither is metformin) and in view of the adverse events of weight gain and cardiac failure such an indication may not be forthcoming. Therapies that are to be given to people without diabetes to prevent the condition need to be proven to be very safe with very low levels of side effects.

Weight loss and exercise therefore remain the main treatments for people with IFG and IGT to prevent or delay progression to diabetes.

Tuomilehto J, Lindstrom MS, Eriksson J, et al (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine* **344**: 1343–9

Diabetes Prevention Programme Research Group (2002) Prevention of type 2 diabetes by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine* **346**: 393–403

ANNALS OF PHARMACOTHERAPY

A new option for type 2 diabetes

Readability	✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The aim of this study was to evaluate the efficacy, safety, pharmacology, drug interaction and pharmacokinetics of exenatide through a literature search.

2 The literature review was carried out by using the search term 'exenatide' on PubMed. The articles selected were in English and predominantly looked at clinical outcomes in type 2 diabetes.

3 The papers collected showed that while exenatide appeared to cause weight loss, patients also exhibited adverse gastrointestinal effects.

4 The clinical trials that were selected from the search seem to suggest that, alongside sulphonylurea and metformin, exenatide could be an alternative for people with type 2 diabetes who require additional therapy.

5 From the analysis of the papers the authors concluded that exenatide could be used as an alternative to insulin glargine and that further studies should elucidate the drug's impact on clinical areas such as vascular disease.

Yoo BK, Triller DM, Yoo DJ (2006) Exenatide: a new option for the treatment of type 2 diabetes. *Annals of Pharmacotherapy* **40:** 1777–84

'The Internet-based Chronic Disease Self Management Program appears to slow the effects of chronic diseases over a one year period.'

'The greatest risk of stroke in the group with type 2 diabetes was found in young women.'

MEDICAL CARE

Internet programme improves self-management

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 To date, the small-group Chronic Disease Self-Management Program has been shown to be effective in improving health status and related behaviours in people with chronic diseases, such as diabetes.

2 This study aimed to determine if an Internet-based Chronic Disease Self-Management Program was effective over 1 year.

3 This study randomised 958 patients who had chronic diseases and access to email and the Internet to usual care control or intervention.

4 The intervention consisted of an Internet-based, password-protected bulletin board with discussion groups and instructions. Participants were also given a book containing the entire content of the programme: while this was not a textbook, it contained details about the main chronic diseases and their associated medications and is referred to in the Internet-based programme.

5 After the investigation period of 1 year, the group of 457 who had been selected for intervention had significant improvement in their health status compared with those who had been selected for usual care (501).

6 The Internet-based Chronic Disease Self Management Program was shown to have a positive effect on health status over a 1 year period. As such, the authors recommend that it should be considered to help manage those with chronic diseases, such as diabetes.

Lorig KR, Ritter PL, Laurent DD, Plant K (2006) Internet-based chronic disease self-management: a randomized trial. *Medical Care* **44:** 964–71

DIABETES CARE

Insulin versus glitazone therapy in poorly controlled type 2 diabetes

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This paper reports on a study examining glycaemic control in people with type 2 diabetes that is poorly controlled by metformin plus sulphonylurea can be improved by the addition of insulin glargine or rosiglitazone.

2 The 20 participants had type 2 diabetes and no other chronic condition. Half received bedtime insulin glargine and half rosiglitazone BID. HbA_{1c}, oral glucose tolerance and a 3-h euglycaemic insulin clamp were performed at baseline and after 4 months.

3 It was concluded that both agents similarly reduced HbA_{1c} by suppressing hepatic glucose production.

Triplitt C, Glass L, Miyazaki Y et al (2006) Comparison of glargine insulin versus rosiglitazone addition in poorly controlled type 2 diabetic patients on metformin plus sulphonylurea. *Diabetes Care* **29:** 2371–7

DIABETOLOGIA

Women aged 35–54 with diabetes at higher risk of stroke

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The authors of this study investigated risk estimates for stroke and the association with type 2 diabetes, lifestyle and comorbidity in the UK in people aged 35-89 years.

2 The study group was identified from the General Practice Research Database and consisted of 41 799 individuals with type 2 diabetes. For each of these individuals there were approximately five comparison subjects of the same age and sex.

3 Stroke hazard ratios were calculated for the period January 1992–October 1999. Association with several other factors such as age, sex, BMI and smoking were also investigated.

4 The authors found that the greatest risk of stroke in the group with type 2 diabetes was found in young women. While this decreased with age, those over 75 were still at increased risk.

Mulnier HE, Seaman HE, Raleigh VS et al (2006) Risk of stroke in people with type 2 diabetes in the UK: a study using the general practice research database. *Diabetologia* **49:** 2859–65

METABOLISM CLINICAL AND EXPERIMENTAL

Walking 10 000 steps improves outcomes

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 This study looked at whether walking 10 000 steps per day would improve insulin sensitivity, glycaemic control and CV risk.

2 Thirty individuals with type 2 diabetes were randomised into a control group and an active group following 10 days of baseline activity. The control group continued with the same activity for 6 weeks while the active group walked at least 10 000 steps for at least 5 days a week for 6 weeks. This was measured using a pedometer.

3 Overall, there was a reduction in plasminogen activator inhibitor in the active group and an increase in HDL cholesterol and resting energy expenditure. The pedometer appears to help with exercise compliance which is a problem in diabetes management.

Arazia P, Hewes H, Gashetewa C et al (2006) Efficacy of a pedometer-based physical activity program on parameters of diabetes control in type 2 diabetes mellitus. *Metabolism Clinical and Experimental* **55:** 1382–7

'Acarbose significantly reduced postprandial hyperglycaemia compared with placebo.'

'Newer antipsychotic drugs can cause metabolic disturbances, including new-onset type 2 diabetes.'

DIABETES CARE

Progression of early diabetes may not be delayed by treating postprandial hyperglycaemia

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓

1 This investigation looked at whether progression of type 2 diabetes could be delayed or prevented by using acarbose to treat postprandial hyperglycaemia in those with early type 2 diabetes.

2 Two hundred and nineteen individuals were randomised to receive either acarbose 100 mg or placebo. Follow-up lasted for 5 years or until the primary outcome of two consecutive fasting plasma glucose measurements of ≥140 mg/dl (7.8 mmol/l) were reached.

3 Participants were excluded from the study if they had a BMI 27<kg/m^2, had had a cardiac event in the previous 6 months, hypertension or any significant disease or medication that would interfere with tolerance or outcome.

4 In years 1 and 2 acarbose significantly reduced postprandial hyperglycaemia compared with placebo (P<0.01). However, there did not appear to be any effect on the cumulative rate of reaching the primary endpoint.

5 The authors concluded that there may be other factors that could be more useful as markers of the progression of diabetes, and that while acarbose may have slowed the rate of progression to an FPG of ≥126 mg/dl, upon reaching this concentration it may be too late to have any significant effect on ß-cell decline.

Kirkman MS, Shankar RR, Shankar S et al (2006) Treating postprandial hyperglycemia does not appear to delay progression of early type 2 diabetes: the Early Diabetes Intervention Program. *Diabetes Care* **29:** 2095–101

THE AMERICAN JOURNAL OF CLINICAL NUTRITION

Breast-fed children at less risk of type 2 diabetes in later life

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓

1 The authors set out to investigate whether breast-feeding during infancy reduces the occurrence of type 2 diabetes in adulthood.

2 Twenty-three studies and reports that investigated a possible correlation between infant breast-feeding and prevalence of type 2 diabetes, identified by an EMBASE, MEDLINE and Web of Science search, were reviewed and seven were included in the final analysis.

3 Formula-fed babies were significantly more likely to develop type 2 diabetes later in life than those who were fed on breast milk (P=0.003). They were also marginally more likely to have higher fasting insulin levels but showed no difference in fasting blood glucose levels compared to the breast-fed comparators.

4 The lower levels of fasting insulin in adults who were breast-fed as infants suggests that there may be differences in the degree of insulin resistance experienced between the two groups.

5 While only a few studies were available for review, these results show no evidence of a publication bias. However, a bias may be present from other factors such as the influences on the likelihood of a mother breast-feeding her child, such as maternal weight and low birthweight.

Owen CG, Martin RM, Whincup PH et al (2006) Does Breastfeeding influence risk of type 2 diabetes in later life? A quantitative analysis of published evidence. *The American Journal of Clinical Nutrition* **84**: 1043–54

AMERICAN JOURNAL OF EPIDEMIOLOGY

Risk of type 2 diabetes increased by 2nd-generation anti-psychotic medications

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 It has been identified previously that the newer antipsychotic drugs can cause metabolic disturbances, including new-onset type 2 diabetes.

2 The aim of this study was to investigate this association in four second-generation antipsychotics.

3 In a US national sample of 15 767 people diagnosed with schizophrenia without any pre-existing diabetes were followed for 1-year after initiation of olanzapine, quetiapine, risperidone or the first-generation drug haloperidol.

4 Compared to haloperidol, the three second-generation antipsychotics increased the risk of type 2 diabetes by between 60 and 70%.

5 The authors estimate that in those patients taking one of the three new-generation medications, up to a third of cases of new type 2 diabetes may have resulted from this treatment. However, it should be noted that these drugs were studied only in the context of schizophrenia.

6 Findings were validated by using people who were naive to the treatment they would be receiving and who only received one drug during the 1-year follow-up period.

7 While the authors tried to minimise selection bias, exclude multiple medication use and adjust for a host of multiple confounding factors, it was not possible to consider any contraindications that may have formed part of the prescribers' decision making. Thus, the sample may include a bias.

Lambert BL, Cunningham FE, Miller DR et al (2006) Diabetes risk associated with use of olanzapine, quetiapine, and risperidone in veterans health administration patients with schizophrenia. *American Journal of Epidemiology* **164**: 672–81