

Expert reviews of UKPDS – PROSE or POEMS?



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This sobering article suggests that expert reviews in general, and the plethora of expert reviews of the UKPDS in particular, are often highly selective, biased and misleading. It claims that experts tend to pick data that reinforce their own prejudices rather than offer a balanced review.

The message is simple – to get to the heart of Patient Oriented Evidence that Matters (POEMs), diabetes healthcare professionals need to read and critically evaluate original research – and not rely on the synthesis and interpretation of experts. Worryingly, the authors of this paper calculated an average validity score of 1.3 from a possible 15. If we accept this, then the authors of the review articles included in the study have failed miserably to provide accessible, applicable, evidence-based reviews and recommendations for management based on POEMs, but instead given us Prescriptive Recommendations based On Standard Evidence (PROSE).

I did not find the basis of the criticism entirely convincing. The authors define POEMs as evidence that tells clinicians directly that a diagnostic, therapeutic, or preventive procedure helps patients to live longer or better. It then rejects a study examining the use of digoxin in the treatment of heart failure. Digoxin use was associated with increased exercise tolerance but no survival advantage. I would guess that those who experienced improved exercise tolerance with digoxin appreciated this and felt that it was a real,

meaningful, worthwhile clinical advantage – in other words, that improved exercise tolerance was a POEM.

As Fitzmaurice points out, the striking paradox of this paper is that it uses ‘non-evidence based methods to discredit non-evidenced based reviews’. We have to remember that UKPDS started out as a trial to test the safety of glycaemic management strategies based primarily on lifestyle or oral agents or insulin. The conclusion – that all are safe but that metformin confers significant advantage in overweight patients – is robust. The trial did not test intensive vs conventional therapy as we now understand it, and while UKPDS is still the most significant evidence base for current practice, given the continuing advances in diabetes management, we are all, in daily diabetes care, extrapolating most of the time. Any interventional study can provide evidence for benefit or harm only for the questions that the study directly addresses.

The overall goal of the paper – to effect improvements in patient care and improved patient outcome by stressing clinically important hard end-points rather than surrogates – is vital. The encouragement that all those involved in clinical care need to get to grips with the evidence that tests the assumptions implicit in their clinical practice is one I endorse.

This still leaves a place for expert review articles, provided that we recognise them for what they are – summary opinions that give us an overview, provide another perspective, offer friendly advice, and lay themselves open to constructive criticism that advances the debate.

BRITISH MEDICAL JOURNAL



Review articles do not transmit research effectively

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

- 1 The UKPDS presented vital information that should be used to guide patient care, and contained both patient-oriented and disease-oriented outcomes.
- 2 This study evaluated how the findings of the UKPDS have been transmitted.
- 3 An inception cohort analysed 35 review articles on the treatment of type 2 diabetes, which had been written 2 years or more after the publication of the major findings of the UKPDS.
- 4 Of the 35 reviews analysed, six mentioned that tight control of blood glucose had no effect on diabetes-related or overall mortality, and seven mentioned that treatment with metformin was associated with decreased mortality.
- 5 Most reviews (30/35) did not report that people with diabetes and hypertension benefit more from good blood pressure control than from good blood glucose control.

- 6 No review stated that treatment of overweight people with type 2 diabetes with insulin or sulphonylurea drugs had no effect on microvascular or macrovascular outcomes; a total of 13 reviews recommended drugs as first-line treatment for which we do not have patient-oriented outcomes data.
- 7 The mean validity score for the 35 papers was 1.3 from a possible 15.
- 8 The current system of transmitting new research about type 2 diabetes to clinicians by review articles is less than optimal.

Shaughnessy AF, Slawson DC (2003) What happened to the valid POEMs? A survey of review articles on the treatment of type 2 diabetes. *British Medical Journal* **327**: 266–72

DIABETES CARE



Hypertension clinic led by nurses reduces CHD risk scores

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

- 1 This study compared the effectiveness of conventional community care in general practice with that of a nurse-led hypertension clinic, in the management of uncontrolled hypertension in people with type 2 diabetes.

- 2 Participants comprised 120 outpatients with type 2 diabetes

and seated blood pressure (BP) $\geq 140/80$ mmHg who were being treated for hypertension.

- 3 The nurse-led group were three times as likely to reach a target systolic BP < 140 mmHg than the conventional care group.

- 4 A significant fall in 10-year CHD and stroke risk scores occurred only in the nurse-led group, but there were no significant differences in the reduction of diastolic BP or any other secondary outcome measures at 6 months.

- 5 A nurse-led hypertension clinic is a more effective intervention for people with type 2 diabetes and hypertension than conventional care.

Denver EA, Barnard M, Woolfson RG, Earle KA (2003) Management of uncontrolled hypertension in a nurse-led clinic compared with conventional care for patients with type 2 diabetes. *Diabetes Care* **26**: 2256–60

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Acarbose reduces risk of CV disease

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

- The STOP-Noninsulin-Dependent Diabetes Mellitus (NIDDM) trial evaluated the effect of decreasing postprandial hyperglycaemia with acarbose (an α -glucosidase inhibitor) on the risk of cardiovascular (CV) disease and hypertension in people with impaired glucose tolerance (IGT).
- In this international, multicentre, double-blind, placebo-controlled randomised trial, 1368 people with IGT were placed in the acarbose or placebo group.
- The main outcome measures were the development of major CV events and hypertension.
- Decreasing postprandial hyperglycaemia with acarbose was associated with a 49% relative risk reduction and a 2.5% absolute risk reduction in the development of CV events.
- Acarbose was associated with a 34% relative risk reduction and a 5.3% absolute risk reduction in the incidence of new cases of hypertension.

Chiasson JL, Josse RG, Gomis R (2003) Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance. The STOP-NIDDM Trial. *Journal of the American Medical Association* **290**: 486–94

DIABETES

The role of PKC λ/ζ in insulin resistance

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

- This study set out to determine whether impaired protein kinase C (PKC) isoforms λ/ζ or phospho-inositide-dependent kinase-1 (PDK-1) activation impact on the pathogenesis of insulin resistance.

DIABETES CARE

70/30 mix vs triple oral therapy

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

- This study compared the efficacy, safety and cost of two approaches to the management of failure of combination therapy.
- A total of 188 people with type 2 diabetes and inadequate response to two oral medications were randomly assigned to treatment with a third oral medication or an insulin 70/30 mix twice daily plus metformin.
- Participants had clinic visits after 2, 6, 12 and 24 weeks' treatment, and kept blood glucose diaries.
- At the end of the study, A1C and fasting plasma glucose (FPG) values decreased in both groups; 31% (oral therapy) and 32% (insulin plus metformin) of people achieved target A1C values of < 7%.
- Cost analysis determined that insulin plus metformin (\$3.20/day) provided efficacy equal to that of a triple oral drug regimen (\$10.40/day).
- In the triple oral regimen group, 16.3% did not complete the study because of lack of efficacy or side-effects.
- Insulin 70/30 mix plus metformin is as effective as triple oral therapy in lowering A1C and FPG values. The triple oral regimen was not as cost-effective and may have side-effects.

Schwartz S, Sievers R, Strange P et al (2003) Insulin 70/30 mix plus metformin versus triple oral therapy in the treatment of type 2 diabetes after failure of two oral drugs. *Diabetes Care* **26**: 2238–43

- The activities of PKC λ/ζ and PDK-1 in vastus lateralis muscle of 15 lean, 16 obese and 21 obese people with type 2 diabetes were measured.
- Biopsies were taken after an overnight fast and after a 3-hour hyperinsulinaemic-euglycaemic clamp; obese participants were also studied after weight loss on a low-calorie diet.

METABOLISM

Metformin and diet improve metabolic syndrome features

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

- The first aim of this study was to assess the incidence of the metabolic syndrome and compare metabolic syndrome abnormalities in women with polycystic ovary syndrome (PCOS) with those in women in the National Health and Nutrition Examination Survey (NHANES) III.
- The second aim was to determine whether metformin and a diet of 1500 calories, 26% protein, 44% carbohydrate and 30% fat would ameliorate metabolic syndrome abnormalities in women with PCOS and metabolic syndrome.
- Of the 138 oligo-amenorrhoeic white women with PCOS participating in the study, 46.4% \pm 4.2% had metabolic syndrome vs 22.8% \pm 1.1% of 1887 white women in NHANES III.
- The PCOS group had more metabolic syndrome abnormalities than the 1887 women from the NHANES III cohort.
- Of the 64 women with PCOS and metabolic syndrome, 50 were followed-up with metformin and diet.
- Body weight, triglycerides, systolic and diastolic BP and insulin decreased; HDL-C increased.
- Metformin and diet ameliorate many of the features of metabolic syndrome, and should reduce the risk of atherothrombosis and type 2 diabetes in PCOS.

Glueck CJ, Papanna R, Wang P et al (2003) Incidence and treatment of metabolic syndrome in newly referred women with confirmed polycystic ovarian syndrome. *Metabolism* **52**: 908–15

- The researchers found that reduced insulin-stimulated PKC λ/ζ activity could play a part in the pathogenesis of insulin resistance in the muscle of people with obesity and type 2 diabetes.

Kim YB, Kotani K, Ciaraldi TP, Henry RR, Kahn BB (2003) Insulin-stimulated protein kinase C λ/ζ activity is reduced in skeletal muscle of humans with obesity and type 2 diabetes. *Diabetes* **52**: 1935–42

‘Acarbose was associated with a 34% relative risk reduction and a 5.3% absolute risk reduction in the incidence of new cases of hypertension.’

‘Reduced insulin-stimulated PKC λ/ζ activity could play a part in the pathogenesis of insulin resistance in the muscle of people with obesity and type 2 diabetes.’