Management & prevention of type 2 diabetes

Which country has the best guideline on oral medications for type 2 diabetes?

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We are not short of guidelines in diabetes! The main problem is often which guideline to use and which one is best. Clinical practice guidelines should ideally support patients and providers in making decisions about treatments, reduce inappropriate variation in treatments and ultimately improve the quality of diabetes care.

There has been increasing international concern about the low quality and highly variable guideline development processes. This can result in deficiencies in describing methods for identifying evidence, grading the strength of recommendations, and identifying conflicts of interest. Sometimes guidelines even give conflicting recommendations!

> **"There has been increasing international concern about the low quality and highly variable guideline development processes. This can result in deficiencies in describing methods for identifying evidence, grading the strength of recommendations, and identifying conflicts of interest."**

The authors of this paper, who are from the USA, conducted a systematic review on the comparative effectiveness of oral medications for adults with type 2 diabetes which was published in a peer-reviewed journal in 2007 (Bolen et al, 2007). They have used the results from this systematic review and the seven-item rigour of development domain of the Appraisal of Guidelines for Research and Evaluation (2012) instrument and the two items from its editorial independence domain to assess diabetes guidelines found from a comprehensive literature search looking at guidelines published between 2007 and 2010. This literature search (summarised alongside) yielded 11 guidelines from 22 publications, including seven updates, that met pre-specified inclusion criteria. Six of these guidelines were from the USA, one was from the International Diabetes Federation, and one was the American Diabetes Association/ European Association for the Study of Diabetes joint guideline. Seven out of 11 guidelines were consistent with the conclusion that metformin is favoured as first-line agent.

The summary scores of the rigour of development (median 28.6%, range 16.7–100%) and editorial independence (median 75%, range 8.3–100%) domains varied greatly across guidelines. Guidelines that received higher quality scores contained more recommendations that were consistent with the evidence-based conclusions. NICE clinical guidelines 66 and 87 (NICE, 2008; NICE, 2009) and the one from the Canadian Diabetes Association were the only ones to score 100% in both domains.

So who has the best guideline on oral medications for adults with type 2 diabetes – we here in the UK do! (Well, actually, Canada's are pretty good too!)

Appraisal of Guidelines for Research and Evaluation (AGREE) (2012) AGREE Instrument. Available at: www.agreetrust.org (accessed 21.05.12)

Bolen S, Feldman L, Vassy J et al (2007) Systematic review: comparative effectiveness and safety of oral medications for type 2 diabetes mellitus. *Ann Intern Med* **147**: 386–99

NICE (2008) *Type 2 Diabetes: The Management of Type 2 Diabetes.* Available at: www.nice.org.uk/cg66 (accessed 21.05.12)

NICE (2009) *Type 2 Diabetes – Newer Agents.* Available at: www.nice.org.uk/cg87 (accessed 21.05.12)

ANN INTERN MED

Evaluation of guidelines for oral therapy in T2D

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

1 Clinical guidelines have an important role in guiding choice of T2D medications, but little is known about the quality of the guidance.

2 The authors aimed to assess whether guidelines on oral medications for T2D are consistent with a systematic review of the current evidence and whether the consistency of the guidelines depends on the quality of guideline development.

3 Databases were searched to identify English-language guidelines on oral medications to treat T2D that were applied in the USA, the UK and Canada.

4 Reviewers assessed whether the guidelines agreed with seven evidence-based conclusions from a previous systematic review; they also rated guideline quality.

5 Seven of the 11 guidelines agreed that metformin is favoured as the first-line agent. Ten guidelines agreed that thiazolidinediones are associated with higher rates of oedema and congestive heart failure compared with other oral medications. One guideline addressed no evidence-based conclusions. The rigour of development and editorial independence varied greatly. Guidelines that received higher quality scores contained more recommendations that were consistent with the evidence-based conclusions.

6 The authors concluded that not all guidelines on oral treatment of T2D were consistent with available evidence and the quality of the development processes varied substantially.

Bennett WL, Odelola OA, Wilson LM et al (2012) Evaluation of guideline recommendations on oral medications for type 2 diabetes mellitus: a systematic review. *Ann Intern Med* **156**: 27–36

"T2D was associated with poorer cancer prognosis and metformin was associated with survival benefit."

DIABETES OBESITY AND METABOLISM

Lifestyle factors reduce risk of T2D

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

1 The authors compared clinical characteristics and treatment results in non-pharmacological treatment for T2D with the most commonly used pharmacological glucose-lowering treatment regimens.

2 In this population-based cross-sectional study, information was linked from three Swedish databases. T2D patients with non-pharmacological treatment and T2D patients using the 12 most common pharmacological treatment regimens were included in the study (n=163 121).

3 The proportion of patients reaching HbA_{1c} ≤53 mmol/mol varied between 70.1% (metformin) and 25.0% (premixed insulin plus sulphonylurea), while 84.8% of the patients with non-pharmacological treatment reached target. Compared with people using metformin, patients using other pharmacological treatments had a lower likelihood of having HbA_{1c} ≤53 mmol/mol. Patients on insulin-based therapy had the lowest likelihood, while non-pharmacological treatment was associated with an increased likelihood of having HbA_{1c} ≤53 mmol/mol.

4 It was concluded that there were significant differences in clinical characteristics as well as HbA_{1c} levels between the treatment groups.

Ekström N, Miftaraj M, Svensson AM et al (2012) Glucose-lowering treatment and clinical results in 163 121 patients with type 2 diabetes: an observational study from the Swedish national diabetes register. *Diabetes Obes Metab* Feb 24 [Epub ahead of print]

DIABETES CARE

T2D linked with poor cancer prognosis

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

1 The authors examined cancer survival in individuals who had developed a first tumour (n=112 408).

2 Mortality was increased in those with T2D (n=8392), and was increased relative to non-diabetes in those on sulphonylurea monotherapy, but reduced in those on metformin.

3 The authors concluded that T2D was associated with poorer cancer prognosis and that metformin was associated with survival benefit.

Currie CJ, Poole CD, Jenkins-Jones S (2012) Mortality after incident cancer in people with and without type 2 diabetes: impact of metformin on survival. *Diabetes Care* **35**:299–304

COCHRANE DATABASE SYSTEMATIC REVIEW

Little evidence for SMBG in T2D not treated with insulin

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

1 Self-monitoring of blood glucose (SMBG) has been found to be effective for people with T2D using insulin. There is much debate on the effectiveness of SMBG as a tool in the self-management of people with T2D who are not using insulin.

2 The authors reviewed randomised controlled trials investigating the effects of SMBG compared with usual care, self-monitoring of urine glucose (SMUG) or both in people with T2D who were not using insulin

3 Twelve trials were included (n=3259). Intervention duration ranged from 6 to 12 months. Nine trials compared SMBG with usual care without monitoring, one study compared SMBG with SMUG, one study was a three-armed trial comparing SMBG and SMUG with usual care and one study was a three-armed trial comparing less intensive SMBG and more intensive SMBG with a control group.

4 Meta-analysis showed a statistically significant SMBG-induced decrease in HbA_{1c} at up to 6 months' follow-up, yet an overall statistically non-significant SMBG induced decrease was seen at 12-month follow-up.

5 Qualitative analysis of the effect of SMBG on well-being and quality of life showed no effect on patient satisfaction, general well-being or general health-related quality of life.

6 It was concluded that when diabetes duration is over 1 year, the overall effect of SMBG on glycaemic control in people with T2D who are not using insulin is small up to 6 months after initiation and subsides after 12 months.

Malanda UL, Welschen LM, Riphagen II et al (2012) Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. *Cochrane Database Syst Rev* 1:CD005060

DIABETIC MEDICINE

Restrictive regimens lead to insulin non-compliance

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

1 The authors examined patient and clinician beliefs regarding insulin therapy and the level of patient compliance with insulin regimens.

2 An internet survey of 1250 physicians and telephone survey of 1530 insulin-treated patients (180 with T1D, 1350 with T2D) in China, France, Japan, Germany, Spain, Turkey, the UK and the USA was undertaken.

3 One third (33.2%) of patients reported insulin non-adherence at least 1 day in the last month, with an average of 3.3 days, while 72.5% of physicians reported non-compliance. Both groups indicated the same five reasons: too busy, travelling, skipped meals, stress/emotional problems and public embarrassment.

4 The authors concluded that there is a need for insulin regimens that are less restrictive and burdensome.

Peyrot M, Barnett AH, Meneghini LF, Schumm-Draeger PM (2012) Insulin adherence behaviours and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. *Diabet Med* Feb 7 [Epub ahead of print]

DIABETES OBESITY AND METABOLISM

Fractures associated with hypoglycaemia

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

1 This retrospective observational study examined the association between outpatient hypoglycaemic events and fall-related fractures in T2D.

2 Patients selected for study were at least 65 years of age with T2D.

3 Of 361 210 included patients, 16 936 had hypoglycaemic events during the evaluation period. Patients with hypoglycaemic events had 70% higher regression-adjusted odds of fall-related fractures than patients without hypoglycaemic events.

4 It was concluded that outpatient hypoglycaemic events were independently associated with an increased risk of fall-related fractures. Further studies are warranted.

Johnston SS, Conner C, Aagren M et al (2012) Association between hypoglycaemic events and fall-related fractures in Medicare-covered patients with type 2 diabetes. *Diabetes Obes Metab* Feb 15 [Epub ahead of print]

BMJ

SMBG does not affect glycaemia

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

1 The researchers assessed the effectiveness of self-monitoring of blood glucose (SMBG) in people with non-insulin-treated T2D compared with clinical management without SMBG.

2 They examined data from randomised controlled trials. A total of 2552 patients were included.

3 A mean reduction in HbA_{1c} level of –2.7 mmol/mol (95% confidence interval, –3.9 to –1.6) was observed for those using SMBG compared with no self-monitoring at 6 months. The mean reduction in HbA_{1c} level between groups was –2.0 mmol/mol (–3.2 to –0.8) at 3 months (five trials) and –2.5 mmol/mol (–4.1 to –0.9) at 12 months (three trials).

4 It was concluded that evidence from this meta-analysis of individual patient data was not convincing for a clinically meaningful effect of clinical management of non-insulin-treated T2D by SMBG compared with management without self-monitoring, although the difference in HbA_{1c} level between groups was statistically significant.

Farmer AJ, Perera R, Ward A et al (2012) Meta-analysis of individual patient data in randomised trials of self monitoring of blood glucose in people with non-insulin treated type 2 diabetes. *BMJ* **344**: e486

> "Patients with hypoglycaemic events had 70% higher regression-adjusted odds of fall-related fractures than patients without hypoglycaemic events."