

## A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO DIABETES MELLITUS: ESSENTIALS FOR BEST PRACTICE

Selection of readings made by A/Prof Goh Lee Gan

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### Reading 1 - Therapy for new onset type 2 diabetes mellitus

Klam C, Neher JO, Mayo H, Lo V. Clinical inquiries. What is the best medical therapy for new-onset type 2 diabetes? J Fam Pract. 2006 Nov;55(11):998-1000.

URL: <http://www.jfponline.com/Pages.asp?AID=4514> (payment required for full text)

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#### ABSTRACT

Sulfonylureas, metformin, thiazolidinediones, and non-sulfonylurea secretagogues differ little in their ability to decrease glycosylated hemoglobin (HbA1c) levels when used as initial monotherapy for diabetes mellitus type 2 (strength of recommendation [SOR]: A, based on systematic reviews); alpha-glucosidase inhibitors may also be as effective (SOR: B, based on systematic reviews with inconsistent results). Metformin is generally indicated in obese patients because it improves all-cause mortality and diabetes related outcomes (SOR: B, based on a single high-quality randomised controlled trial [RCT]). Insulin is generally not recommended as an initial agent (SOR: C, expert opinion).

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### Reading 2 - Combination therapy

Esken S, Kelsberg G, Hitchcock K, Lo V. Clinical inquiries. What is the role of combination therapy (insulin plus oral medication) in type 2 diabetes? J Fam Pract. 2006 Nov;55(11):1001-3.

URL: <http://www.jfponline.com/Pages.asp?AID=4515&UID=21348> (payment required for full text)

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#### ABSTRACT

Combination therapy using insulin plus metformin (Glucophage), a sulfonylurea, or both produces glycaemic control comparable with using insulin alone, but there is less weight gain when metformin is used (strength of recommendation [SOR]: B, based on systematic review of randomized controlled trials [RCTs] with some heterogeneity). Combination therapy using insulin and pioglitazone (Actos) reduces glycosylated hemoglobin (HbA1c) more than either insulin alone or adding pioglitazone to a sulfonylurea, but results in more weight gain (SOR: A, based on RCT). Using insulin glargine (Lantus) in combination therapy produces fewer nocturnal hypoglycemic events than using neutral protamine Hagedorn (NPH) insulin, while producing equivalent HbA1c reduction (SOR: B, based on RCT). When the HbA1c is high (above 9.0% to 9.5%) on 1 or 2 oral agents, beginning combination therapy is more effective than adding another oral agent (SOR: B, based on subpopulation analysis in RCTs).

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### Reading 3 - Control of type 2 diabetes mellitus

Brewer D. Are alpha-glucosidase inhibitors effective for control of type 2 diabetes? *Am Fam Physician*. 2006 Feb 1;73(3):433-4.

URL: <http://www.aafp.org/afp/20060201/cochrane.html#c1> (free full text)  
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#### SUMMARY

**Clinical Scenario.** A 55-year-old man with diabetes has used diet to control his glucose levels for the past six years. His HbA1c level gradually has risen to 7.5 percent, and he wants to discuss options for medical therapy.

**Clinical Question.** Is monotherapy with alpha-glucosidase inhibitors effective in reducing complications and improving glucose control in patients with diabetes?

**Evidence-Based Answer.** The use of alpha-glucosidase inhibitors has a modest effect on intermediate diabetes-control endpoints such as postprandial blood glucose, postprandial insulin levels, and HbA1c levels. There is no evidence, however, of improvement in mortality, morbidity, or quality of life. In comparisons with sulfonylureas, alpha-glucosidase inhibitors had less effect on intermediate diabetes-control endpoints and had a greater incidence of adverse effects. The use of alpha-glucosidase inhibitors had no effect on plasma lipid levels or body weight.

### Reading 4 - Starting insulin therapy

Mooradian AD, Bernbaum M, Albert SG. Narrative review: a rational approach to starting insulin therapy. *Ann Intern Med*. 2006 Jul 18;145(2):125-34.

URL: <http://www.annals.org/cgi/content/full/145/2/125> (payment required till 6 months after publication)  
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#### ABSTRACT

**BACKGROUND:** The emergence of multiple insulin products has provided new opportunities to achieve diabetes control. However, the number of options has raised concerns about the optimal choices of products.

**PURPOSE:** To briefly review the pharmacologic characteristics of currently available insulin products and to suggest an initial insulin regimen based on common blood glucose profiles among patients with diabetes.

**DATA SOURCES:** Relevant manuscripts were identified through a MEDLINE search (1996 to 25 February 2006) of the English-language literature. The key phrase used was therapeutic use of insulin. The literature search was limited to core clinical journals that have accessible full texts.

**STUDY SELECTION:** Clinical trials and authoritative reviews published between 1996 and February 2006 were selected. A total of 420 manuscripts was reviewed.

**DATA EXTRACTION:** The authors independently reviewed the relevant available literature. This literature, along with the authors' clinical experience, was used to construct practical suggestions.

**DATA SYNTHESIS:** Several new insulin and insulin analogue preparations are now available for clinical use. Used as prandial insulin (for example, insulin lispro, insulin aspart, or insulin glulisine) and basal insulin (for example, insulin glargine or insulin detemir), the analogues simulate physiologic insulin profiles more closely than the older conventional insulins. There is currently no strong rationale favoring glargine, neutral protamine Hagedorn insulin, insulin detemir, or fixed-ratio insulin preparations as the preferred agent for initiating insulin therapy.

**LIMITATIONS:** This was a retrospective review of previously published manuscripts chosen at the authors' discretion.

**CONCLUSIONS:** The advent of recombinant DNA technology made it possible to overcome limitations in the time-action profiles of conventional insulins. Insulin therapy must be individualized. Nevertheless, certain subgroups of patients with diabetes can be differentiated from each other according to the pattern of blood glucose changes during the day. On the basis of the blood glucose profile, the authors suggest an initial insulin regimen that can be used to evaluate individual responsiveness and plan a long-term regimen.

### Reading 5 - Gestational diabetes is worth finding and treating

Phillips PJ, Jeffries B. Gestational diabetes – worth finding and actively treating. *Aust Fam Physician*. 2006 Sep;35(9):701-3.

URL: <http://www.racgp.org.au/Content/NavigationMenu/Publications/AustralianFamilyPhys/2006issues/20060906/20060906phillips.pdf> (free full text)

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#### ABSTRACT

Gestational diabetes affects around 5% of pregnant women, however the value of screening women for gestational diabetes has been hotly debated. On the positive side there has been potential benefits for the baby and, on the negative side, the costs of managing gestational diabetes to the mother. This controversy has largely been settled with the publication of the Australasian Carbohydrate Intolerance Study (ACHOIS). This article reviews the implications of ACHOIS for Australian women and their general practitioners.

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### Reading 6 - Prevention of diabetic nephropathy

Dressler RL. Antihypertensive agents for prevention of diabetic nephropathy. *Am Fam Physician*. 2006 Jul 1;74(1):77-9.

URL: <http://www.aafp.org/afp/20060701/cochrane.html#c1> (free full text)

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#### SUMMARY

**Clinical Scenario.** A 54-year-old woman with type 2 diabetes comes into your office. She has no evidence of diabetic nephropathy and needs medication for hypertension.

**Clinical Question.** Is one class of antihypertensive agents superior to others for the prevention of diabetic nephropathy?

**Evidence-Based Answer.** Angiotensin-converting enzyme (ACE) inhibitors are the only antihypertensive agents with proven effectiveness for the primary prevention of diabetic nephropathy (defined as an albumin excretion of less than 30 mg per day on three serial measurements) caused by type 1 or type 2 diabetes. However, ACE inhibitors have not been shown to decrease all-cause mortality in patients with diabetes. Based on limited data, ACE inhibitors have not been shown to reduce end-stage renal disease significantly when compared with placebo.

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### Reading 7 - HbA1C monitoring

Reynolds TM, Smellie WS, Twomey PJ. Glycated haemoglobin (HbA1c) monitoring. BMJ. 2006 Sep 16;333(7568):586-8.

URL: <http://www.bmj.com/cgi/content/full/333/7568/586> (payment required for full text)

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#### SUMMARY

This article describes two common scenarios involving the use of glycated haemoglobin (HbA1c) that may be seen in primary care and considers their potential clinical implications in monitoring patients with diabetes. HbA1c has become established as the monitoring test of choice to assess medium term diabetic control and as a key parameter on which to base changes in management of patients. Common situations exist, however, in which the HbA1c can be misleading. As the average lifespan of a red blood cell is approximately 120 days, in situations in which red cell lifespan is reduced HbA1c may not accurately reflect diabetic control. With increasing emphasis on achieving lower HbA1c values in patients with diabetes, clinicians need to be aware of these situations and understand the limitations of the test methods used.

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### Reading 8 - Vascular complications - prevention and early detection

Marshall SM, Flyvbjerg A. Prevention and early detection of vascular complications of diabetes. BMJ. 2006 Sep 2;333(7566):475-80.

URL: <http://www.bmj.com/cgi/content/full/333/7566/475> (payment is required for full text)

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#### SUMMARY

Diabetes reduces life expectancy by five to 10 years. Premature cardiovascular disease is the most common cause of morbidity and mortality, but the microvascular complications specific to diabetes are also contributory factors. Diabetes is the most common reason for renal replacement therapy worldwide, the most common cause of blindness in the under 65s, and the most common cause of non-traumatic amputation. With our current knowledge, most of these devastating events could be prevented or delayed, or their impact minimised. This review focuses on the prevention, early detection, and initial management of the vascular complications of diabetes in adults.

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## Reading 9 - Quality improvement strategies in type 2 diabetes mellitus

Shojania KG, Ranji SR, McDonald KM, Grimshaw JM, Sundaram V, Rushakoff RJ, Owens DK. Effects of quality improvement strategies for type 2 diabetes on glycaemic control: a meta-regression analysis. *JAMA*. 2006 Jul 26;296(4):427-40.

URL: <http://jama.ama-assn.org/cgi/content/full/296/4/427> (payment required for full text)

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### ABSTRACT

**CONTEXT:** There have been numerous reports of interventions designed to improve the care of patients with diabetes, but the effectiveness of such interventions is unclear.

**OBJECTIVE:** To assess the impact on glycaemic control of 11 distinct strategies for quality improvement (QI) in adults with type 2 diabetes.

**DATA SOURCES AND STUDY SELECTION:** MEDLINE (1966-April 2006) and the Cochrane Collaboration's Effective Practice and Organisation of Care Group database, which covers multiple bibliographic databases. Eligible studies included randomized or quasi-randomized controlled trials and controlled before-after studies that evaluated a QI intervention targeting some aspect of clinician behavior or organizational change and reported changes in glycosylated hemoglobin (HbA1c) values.

**DATA EXTRACTION:** Postintervention difference in HbA1c values were estimated using a meta-regression model that included baseline glycaemic control and other key intervention and study features as predictors.

**DATA SYNTHESIS:** Fifty randomized controlled trials, 3 quasi-randomized trials, and 13 controlled before-after trials met all inclusion criteria. Across these 66 trials, interventions reduced HbA1c values by a mean of 0.42% (95% confidence interval [CI], 0.29%-0.54%) over a median of 13 months of follow-up. Trials with fewer patients than the median for all included trials reported significantly greater effects than did larger trials (0.61% vs 0.27%,  $P = .004$ ), strongly suggesting publication bias. Trials with mean baseline HbA1c values of 8.0% or greater also reported significantly larger effects (0.54% vs 0.20%,  $P = .005$ ). Adjusting for these effects, 2 of the 11 categories of QI strategies were associated with reductions in HbA1c values of at least 0.50%: team changes (0.67%; 95% CI, 0.43%-0.91%;  $n = 26$  trials) and case management (0.52%; 95% CI, 0.31%-0.73%;  $n = 26$  trials); these also represented the only 2 strategies conferring significant incremental reductions in HbA1c values. Interventions involving team changes reduced values by 0.33% more (95% CI, 0.12%-0.54%;  $P = .004$ ) than those without this strategy, and those involving case management reduced values by 0.22% more (95% CI, 0.00%-0.44%;  $P = .04$ ) than those without case management. Interventions in which nurse or pharmacist case managers could make medication adjustments without awaiting physician authorization reduced values by 0.80% (95% CI, 0.51%-1.10%), vs only 0.32% (95% CI, 0.14%-0.49%) for all other interventions ( $P = .002$ ).

**CONCLUSIONS:** Most QI strategies produced small to modest improvements in glycaemic control. Team changes and case management showed more robust improvements, especially for interventions in which case managers could adjust medications without awaiting physician approval. Estimates of the effectiveness of other specific QI strategies may have been limited by difficulty in classifying complex interventions, insufficient numbers of studies, and publication bias.