DIABETIC MEDICINE

PPG and FPG contributions to hyperglycaemia

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

1 It is well known that postprandial hyperglycaemia greatly increases the risk of cardiovascular disease (CVD), but elevated postprandial plasma glucose (PPG) levels, even within the non-diabetic range, also increase this CVD risk.

2 This study used 12-hour plasma glucose (PG) profiles to ascertain the effect of PPG and fasting or preprandial plasma glucose (FPG) on excess daytime hyperglycaemia and HbA_{1c} in 52 people with type 2 diabetes.

3 Twelve-hour PG profiles were determined in response to three serial and identical test meals; PPG values were determined for each meal. Excess hyperglycaemia (>5.5 mmol/L) and fasting hyperglycaemia (difference between excess hyperglycaemia and PPG exposure) were also determined.

4 Participants were assigned to groups according to their HbA_{1c} level (group 1, HbA_{1c} <7.3% [<56 mmol/mol], *n*=18; group 2, HbA_{1c} 7.3–8.0% [56–64 mmol/mol], *n*=17; group 3, HbA_{1c} >8.0% [>64 mmol/mol], *n*=17).

5 The relative contributions of PPG to excess hyperglycaemia decreased as HbA_{1c} levels increased (i.e. was lowest in group 3, who had the poorest glycaemic control).

6 The contribution of fasting hyperglycaemia increased with deteriorating glycaemic control.

7 The absolute contributions of PPG to increased HbA_{1c} levels were 1.4%, 1.6% and 1.3% for groups 1, 2 and 3, respectively, which did not reach statistical significance.

Peter R, Dunseath G, Luzio SD et al (2009) Relative and absolute contributions of postprandial and fasting plasma glucose to daytime hyperglycaemia and HbA1c in subjects with type 2 diabetes. *Diabetic Med* **26**: 974–80

Postprandial and fasting glucose contributions to hyperglycaemia: Where do you stand?

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Postprandial hyperglycaemia in people with type 2 diabetes continues to be a controversial subject. There has been much debate about (a) whether it is a specific risk factor for cardiovascular disease and (b) how much it contributes to overall hyperglycaemia as measured by HbA_{1c}. The position you take in the debate is likely to influence the sort of self-monitoring of blood glucose regimen you advocate and may influence the sort of blood glucose-lowering therapies you favour.

When short-acting secretagogues were launched nearly 10 years ago, publicity suggested that these agents, by dealing with post-meal "glucose spikes", might be able to reduce adverse cardiovascular events. These particular agents have not become widely used, and this suggestion of potential benefit of these agents lacks evidence at present. However, views on the importance of postprandial hyperglycaemia may affect insulin prescribing today. One prescriber may favour a particular sort of insulin and insulin regimen over another on the basis that one is perceived to better control postprandial hyperglycaemia than does another.

The article by Peter et al (2009; summarised alongside) provides data on the contribution of postprandial hyperglycaemia to overall hyperglycaemia as measured by HbA_{1c}. Reporting on 12-hour glucose profiles in 52 people with type 2 diabetes, in response to three serial identical test meals, this study suggests that in people with type 2 diabetes who have HbA_{1c} levels of ≥8% (≥64 mmol/mol), fasting glucose levels are the main driver of overall hyperglycaemia.

The authors also state that postprandial glucose is the main driver when HbA_{1c} levels are ≤7.3% (≤56 mmol/mol).

In practical terms, the results of this study mean that the glycaemic-lowering emphasis needs to be on controlling fasting glucose in people who have poor glycaemic control (with HbA_{1c} levels of ≥8% [≥64 mmol/mol]). So in a person with type 2 diabetes on oral blood glucose-lowering agents and 40 units of basal insulin who has an HbA_{1c} level of 8.3% (67 mmol/mol) the implication is that more units of basal insulin are needed, rather than a switch to a basal–bolus regimen.

DIABETES CARE

Dapagliflozin further decreases HbA_{1c} and lowers weight

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

1 This study examined the effect of dapagliflozin, which selectively inhibits glucose reabsorption, on lowering hyperglycaemia in people with poorly controlled type 2 diabetes.

2 Seventy-one people with type 2 diabetes who had poor glycaemic control on insulin in combination with oral antidiabetes agents (OADs) were randomised to placebo (*n*=23), dapagliflozin 10 mg (*n*=24) or dapagliflozin 20 mg (*n*=24) in addition to their OADs and 50% of their insulin dose.

3 HbA_{1c}, fasting plasma glucose (FPG) and total body weight were measured at baseline and at 12 weeks.

4 From baseline to 12 weeks, 65.2% of people receiving dapagliflozin (10 mg and 20 mg) showed a ≥0.5% decrease in HbA_{1c} level compared with 15.8% of people in the placebo group; the effect on FPG was dose-dependent.

5 Dapagliflozin lowered weight more than placebo, with an additional weight loss of about 2.5 kg.

Wilding JPH, Norwood P, T'joen C et al (2009) A study of dapagliflozin in patients with type 2 diabetes receiving high doses of insulin plus insulin sensitisers. *Diabetes Care* **32**: 1656–62

"Men with type 2 diabetes had a slightly higher excess mortality risk than women with type 2 diabetes."

BMC PUBLIC HEALTH

Excess mortality is higher in men with type 2 diabetes

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

1 To examine age-specific and sex-specific all-cause mortality patterns, 1323 people with type 2 diabetes were followed up for 16 years from diagnosis.

2 Compared with the general population, men and women with type 2 diabetes had a 1.5- to 2.5-fold increased mortality risk depending on age.

3 This excess risk was highest in the younger participants and decreased with increasing age in both sexes.

4 The authors concluded that men with type 2 diabetes had a slightly higher excess mortality risk than women with the condition.

Hansen LJ, Olivarius NdF, Siersma V (2009) 16-year excess all-cause mortality of newly diagnosed type 2 diabetic patients: a cohort study. *BMC Public Health* **9**: 400

ARCHIVES OF INTERNAL MEDICINE

Culturally tailored care reduces emergency visits

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

1 Although people of African–American descent are at increased risk of diabetes, little research has examined culturally tailored interventions to improve diabetes care in this group.

2 The study comprised 488 African Americans with type 2 diabetes randomised to receive either normal intervention (n=253) or intensive, culturally tailored care (n=235) provided by a nurse case manager (NCM) and a community health worker (CHW) team.

3 Data were collected at baseline and at 2 years, including HbA_{1c}, visits to accident and emergency departments and hospital admissions.

4 The authors found that those receiving intensive, culturally tailored care were 23% less likely to go to hospital as an emergency case.

5 Those who received the most attention from the NCM/CHW team showed further improved HbA_{1c} levels.

Gary TL, Batts-Turner M, Yeh H-C et al (2009) The effects of a nurse case manager and a community health worker team on diabetic control, emergency department visits and hospitalisations among urban African Americans with type 2 diabetes mellitus. *Arch Intern Med* **169**: 1788–94

DIABETIC MEDICINE

Triple oral therapy reduces progression to insulin treatment

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

1 The management of type 2 diabetes often comprises metformin combined with a sulphonylurea.

2 PROactive (Prospective Pioglitazone Clinical Trial in Macrovascular Events) examined the effect of metformin-sulphonylurea-pioglitazone triple therapy on glycaemic control in people with type 2 diabetes.

3 Of 1314 people on metformin-sulphonylurea combination therapy, 654 were additionally given pioglitazone (660 were additionally given placebo).

4 Triple therapy significantly improved and sustained glycaemic control compared with the placebo group.

5 The addition of pioglitazone significantly reduced progression to insulin therapy.

Scheen AJ, Tan MH, Betteridge DJ et al (2009) Long-term glycaemic control with metformin-sulphonylurea-pioglitazone triple therapy in PROactive (PROactive 17). *Diabet Med* **26**: 1033–9

DIABETIC MEDICINE

LM25 reduces HbA_{1c} levels in older people with T2D

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

1 This study compared the efficacy and safety profile of two starter insulin regimens, insulin lispro mix 25 (LM25) and insulin glargine, in a cohort (aged ≥65 years) with type 2 diabetes who had enrolled in the DURABLE trial.

2 Of this older population, 258 people were assigned to twice-daily LM25 and 222 were assigned to once-daily insulin glargine in addition to their pre-study oral glucose-lowering agents; glycaemic assessments were made during the 24-week initiation.

3 Although baseline HbA_{1c} was similar for both groups, at 24 weeks the older people in the LM25 group had a lower HbA_{1c} level (7.0±0.9% vs. 7.3±0.9%, P<0.001), a greater reduction in HbA_{1c} (–1.7±1.2% vs. –1.5±1.1%, P<0.001) and more people achieving the target HbA_{1c} level of <7.0% (55.6 vs. 41.0%, P=0.005) than those in the insulin glargine group.

4 At 24 weeks, the older people in the LM25 group were on more insulin (mean dose of 0.40±0.19 units/kg/day vs. 0.33±0.19 units/kg/day), had a higher rate of overall hypoglycaemia (40.8±47.6 vs. 31.1±48.5 episodes/person/year), with more incidence of severe hypoglycaemia, and had gained more weight (3.6±3.6 kg vs. 1.8±3.2 kg) than those in the insulin glargine group.

5 Although older people receiving LM25 twice-daily showed a reduced HbA_{1c} level at 24 weeks, the authors concluded that clinicians must be cautious with the starting insulin dose to minimise hypoglycaemic events in this population.

Wolffenbuttel BHR, Klaff LJ, Bhushan R et al (2009) Initiating insulin therapy in elderly patients with type 2 diabetes: efficacy and safety of lispro mix 25 vs basal insulin combined with oral glucose-lowering agents. *Diabet Med* **26**: 1147–55

DIABETES CARE

Saxagliptin boosts metformin therapy and improves HbA_{1c}

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

1 The use of saxagliptin in combination with metformin was assessed in people with T2D poorly controlled on metformin.

2 Participants were randomised to receive saxagliptin (2.5 mg, *n*=192; 5 mg, *n*=191; or 10 mg, *n*=181) or placebo (*n*=179) in addition to metformin (1500–2500 mg) for 24 weeks.

3 HbA_{1c}, fasting plasma glucose (FPG) and postprandial glucose (PPG) area under the curve (AUC) were taken at baseline and 24 weeks.

4 Compared with placebo, saxagliptin (2.5, 5 and 10 mg) in addition to metformin reduced HbA_{1c} (–0.59, –0.69 and –0.58%, respectively; +0.13% for placebo), FPG (–14.31, –22.03 and –20.50 mg/dL, respectively; +1.24 mg/dL for placebo) and PPG AUC (–8891, –9586 and –8137 mg•min/dL, respectively; –3291 mg•min/dL for placebo) at 24 weeks.

5 The authors concluded that addition of saxagliptin (2.5, 5 and 10 mg) to metformin enabled more than twice as many people to achieve an HbA_{1c} level <7.0% (<53 mmol/mol) compared with placebo (37, 44 and 44% respectively vs. 17%; *P*<0.0001).

DeFronzo RA, Hissa MN, Garber AJ et al (2009) The efficacy and safety of saxagliptin when added to metformin therapy in patients with inadequately controlled type 2 diabetes with metformin alone. *Diabetes Care* **32**: 1649–55

NEW ENGLAND JOURNAL OF MEDICINE

Prandial and basal insulin improve type 2 control

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

1 There is limited evidence to support the addition of specific insulin regimens to oral antidiabetes therapy in people with type 2 diabetes.

2 This 3-year, open-label, multicenter trial comprised 708 people with type 2 diabetes who were poorly controlled on metformin and sulphonylurea therapy.

3 Study participants were randomised to additionally receive biphasic insulin aspart (*n*=235), prandial insulin aspart (*n*=239) or basal insulin detemir (*n*=234). Outcome measures were HbA_{1c} levels, the proportion of participants with an HbA_{1c} level ≤6.5% (48 mmol/mol), rate of hypoglycemia, and weight gain.

4 After 3 years, the mean reduction in HbA_{1c} level from baseline was 1.3% (biphasic group), 1.4% (prandial group) and 1.2% (basal group); 31.9% (biphasic group), 44.7% (prandial group) and 43.2% (basal group) achieved an HbA_{1c} level of ≤6.5% (<48 mmol/mol).

5 The overall rate of hypoglycaemia was found to be highest in the prandial group (5.7/person/year) and lowest in the basal group (1.7/person/year).

Holman RR, Farmer AJ, Davies MJ et al (2009) Three-year efficacy of complex insulin regimens in type 2 diabetes. *N Engl J Med* **361**: 1736–47