Guidelines for Optimal Management of Type 2 Diabetes

The Hong Kong Diabetes Advisory Panel

Optimal disease management of type 2 diabetes leads to immediate and long-term improvements in patients' quality of life. However, the size of the evidence base and the inherent complexity of diabetes care mean that some patients remain sub-optimally managed. International and national guidelines are available, but these can be conflicting, repetitive, or overwhelming for busy clinicians. Therefore, the International Diabetes Federation (IDF) Clinical Guidelines Task Force has developed global guidelines using evidence-based reviews, recommendations and key meta-analyses.[1] A local adaptation of these guidelines is summarised in this publication.

Screening programmes to detect diabetes early

It is estimated that 30–90% of people with type 2 diabetes worldwide remain undiagnosed. Although the benefits of screening programmes remain unproven, targeted screening in subjects at high risk of the disease is recommended, since early detection can prevent the complications associated with delayed presentation.

"Targeted screening in high-risk subjects is recommended for early detection"

The IDF guidelines suggest that as the primary method of detection, asymptomatic individuals with fasting plasma glucose (FPG) levels of between 100 mg/dL (≥5.6 mmol/L) and 126 mg/dL (>7.0 mmol/L), should undergo a 75-gram oral glucose tolerance test (OGTT). Asymptomatic individuals who exhibit random plasma glucose levels of >140 mg/dL (>7.8 mmol/L) and <200 mg/dL (<11.0 mmol/L) should undergo either a 75-gram OGTT or FPG test. Diabetes is diagnosed if FPG levels of ≥126 mg/dL (≥7 mmol/L) are detected on two separate occasions (Table 1).[1]

Table 1. WHO definition of diabetes, impaired fasting glycaemia (IFG), impaired glucose tolerance (IGT) and normal glucose tolerance (NGT)

		Fasting plasma glucose (mmol/L)		
		<6.0	≥6.0–6.9	≥7
2-hour plasma glucose post 75-gram OGTT (mmol/L)	<7.8	NGT	IFC	Diabetes
	≥7.8–11.1	Isolated IGT	IFG+IGT	Diabetes
	≥11.1	Diabetes	Diabetes	Diabetes

Note: The American Diabetes Association defines NGT and IFG as FPG levels of <5.6 mmol/L (100 mg/dL) and ≥5.6–6.9 mmol/L (≥100–125 mg/dL), respectively.

Managing diabetes

Lifestyle management

Modifying an unhealthy lifestyle can help control blood glucose, and lipid levels as well as blood pressure abnormalities without the need for pharmacotherapy. Thus, good advice on nutrition and physical activity is essential to diabetes self-management training programmes.

IDF guidelines on lifestyle recommendations

- Advise patients that diet and exercise modifications can control many of the adverse risk factors associated with type 2 diabetes
- Provide access to a dietician for initial consultations
- Provide ongoing counselling and yearly assessments
- Provide individualised dietary advice to match patients' needs, preferences and culture
- Advise patients to reduce consumption of foods with high amounts of sugar, fat and salt
- Advise patients to stop smoking and avoid excessive alcohol intake
- Integrate drug therapy, where needed
- Advise patients of the need for consistent carbohydrate intake via regular meals
- Offer education on carbohydrate content of food, where necessary, especially for patients on fixed insulin regimens
- Provide advice on the use of foods in the prevention and management of hypoglycaemia
- Encourage the gradual introduction of physical activity, increasing in duration and frequency of activity up to 30–45 minutes a day, for 3–5 days per week
- Provide guidelines for adjusting medications (insulin) and/or adjusting carbohydrate content for physical activity as appropriate
- Advise obese patients that it may be appropriate to consider weight loss medications as adjunct therapy

Diabetes-related complications

Diabetes causes major morbidities including visual loss, foot ulceration, renal disease and nerve damage. Guidelines for reducing these complications have been published by the IDF (Table 5).

Table 5. IDF guidelines to reduce diabetes-related complications

Kidney disease

- Annual checks for proteinuria (microalbuminuria) in morning urine
- Measure serum creatinine annually, and calculate eGFR
- If morning urine protein:creatinine or albumin:creatinine ratio is high, repeat testing over the following 6 months
- Intensive control of risk factors including blood pressure and glucose levels, and use of renin–angiotensin system inhibitors is recommended
- Refer if eGFR <60 mL/min/1.73 m^2 in the presence of other surgically amenable causes such as obstruction

Foot ulcerations

- Assess patients' feet (skin, sensation and pulses) annually
- Discuss and agree on a foot care plan, and provide necessary foot care education
- Classify and manage patients according to risk categories:
  - low risk: no loss of sensation or sign of peripheral arterial disease
  - high risk: diminished sensation, peripheral arterial disease, history of ulceration
  - foot ulceration or active infection

Eye disease

- Examine eyes (visual acuity and fundoscopy) at time of diagnosis and annually thereafter
- Discuss reasons for eye examination
- Exclude history of glaucoma seek patient's consent to use tropicamide eyedrops to dilate pupils before examination (direct fundoscopy or retinal photography)
- Classify patients based on findings of the eye examinations, as requiring:
  - routine annual review
  - earlier review
  - referral to ophthalmologist
- The following situations require referral to a specialist:
  - sudden loss of vision, or evidence of retinal detachment
  - evidence of pre-retinal and/or vitreous haemorrhage
  - new vessel formation or rubeosis iridis
- Advise patients on the importance of managing blood glucose, and blood pressure to reduce risk of new onset or progression of eye disease
- Advise on periodical intra-ocular pressure tests

Nerve damage

Diagnose:

- sensorimotor nerve damage by history and examination, and/or quantitative tests (e.g. graduated tuning fork, monofilament) and exclude causes such as B12 deficiency or alcoholism
- erectile dysfunction by history, exclusion of endocrine conditions, and trial of a phosphodiesterase type 5 (PDE5) inhibitor as appropriate
- gastroparesis by history and by gastric emptying studies if symptomatic, followed by a prokinetic drug trial
- cardiovascular autonomic neuropathy by examining resting heart rate and other provocation tests such as postural hypotension testing as appropriate

References:

1. International Diabetes Federation. Global guideline for type 2 diabetes. At: http:www.idf.org (Nov 2008).
2. Jellinger PS *et* al. Road maps to achieve glycemic control in type 2 diabetes mellitus: ACE/AACE Diabetes Roadmap Taskforce. *Endocrine Practice* 2007;13:261–268.

About the Hong Kong Diabetes Advisory Panel (HKDAP)

The HKDAP was established in May 2007 with a mission to prevent diabetes and promote improvements in diabetes care through education and awareness campaigns, for people with diabetes as well as healthcare professionals and the general public.

Members of the HKDAP are experts from Hong Kong in the field of endocrinology: Professor Juliana Chan and Dr Francis CC Chow (Department of Medicine & Therapeutics, Prince of Wales Hospital), Professor Kathryn Tan (Department of Medicine, Queen Mary Hospital) and Dr Vincent TF Yeung (Department of Medicine & Geriatrics, Our Lady of Maryknoll Hospital); family medicine: Professor Cindy Lam (Family Medicine Unit, The University of Hong Kong); nephrology: Dr Felix Fu-Keung Li (private practitioner) and cardiology: Dr Victor WT Yan (private practitioner).

In addition to the HKDAP members, the following experts in diabetes serve as Honorary Consultants to the Panel: Professor Ignatius Kum-po Cheng (private practitioner), Professor Rosie Young (Department of Medicine, The University of Hong Kong) and Dr Clive Cockram (Department of Medicine & Therapeutics, Prince of Wales Hospital).

Editorial assistance provided by International Medical Press (Hong Kong) Limited and made possible through an unrestricted educational grant from Merck, Sharp and Dohme (Asia) Ltd. The views expressed do not necessarily reflect those of the publisher or sponsor. Consult full prescribing information before issuing prescriptions for any products mentioned in this publication.

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Blood glucose control

The importance of blood glucose control for preventing diabetes-associated complications, particularly vascular disease, is well established; however the optimal glycaemic target remains an ongoing debate. Existing IDF guidelines suggest patients should aim to maintain a Diabetes Control and Complications Trial (DCCT)-aligned HbA_{1c} of <6.5%. More recent studies, however, support a DCCT-aligned HbA_{1c} of <7%; where capillary blood levels pre-meal and 1 to 2 hours post-meal are <110 mg/dL (<6.1 mmol/L), and <145 mg/dL (<8.0 mmol/L), respectively. Patients who fail to maintain a level of <7% should be advised that any improvement in HbA_{1c} is beneficial to diabetes management.

"Unless contraindicated, patients with type 2 diabetes should be encouraged to maintain a DCCT-aligned HbA_{1c} of <7% to minimise the risk of developing complications"

Role of oral blood glucose-lowering drugs

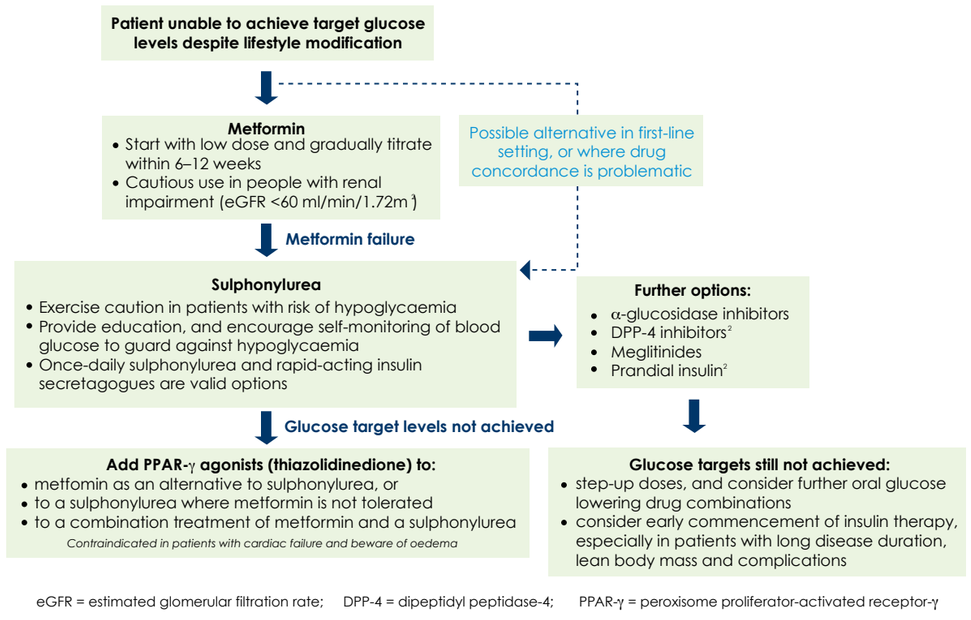
Lifestyle modifications provide effective glycaemic control in only a minority of patients with type 2 diabetes. Pharmacotherapy, such as oral blood glucose-lowering drugs and insulin injection (alone or in combination with oral agents) are often required to control hyperglycaemia. The IDF guidelines for the use of oral blood glucose-lowering drugs are summarised in Figure 1.

Different classes of oral blood glucose-lowering drugs in the treatment armamentarium, including their starting and maximum dosages, are shown in Table 2.

Table 2. Different classes of oral blood glucose-lowering drugs in the treatment armamentarium

Agent	Initial onset (i) or peak (p)	Half-life	Starting dose	Maximum dose
Biguanides				
Metformin	Within days (i) 2 weeks (p)	~ 6 hrs	10–16 years of age: 500 mg bd	2,000 mg/day
			≥17 years of age: 500 mg bd	2,550 mg/day
Sulphonylureas				
Glibenclamide	30 mins (i) 2–3 hrs (p)	~ 24 hrs	2.5–5 mg/day	20 mg/day
Gliclazide	4–5 hrs (p)	~ 10 hrs	40–80 mg/day	320 mg/day
Glipizide	30 mins (i)	2–4 hrs	2.5–5 mg/day	40 mg/day
Glimepiride	2–3 hrs (p)	5–9 hrs	1–2 mg/day	6 mg/day
PPAR-γ agonists (thiazolidinedione)				
Pioglitazone	Several weeks (p)	3–7 hrs	15–30 mg/day	45 mg/day
Rosiglitazone	Delayed 12 weeks (p)	3–4 hrs	4 mg/day	8 mg/day
DPP-4 inhibitors				
Sitagliptin	~ 1 hr (p)	~ 12 hrs	100 mg/day	N/A
α-glucosidase inhibitors				
Acarbose	1 hr (p)	~ 2 hrs	25 or 50 mg tds	≤60 kg: 50 mg tds >60 kg: 100 mg tds
Meglitinides				
Nateglinide	1 hr (p)	1.5 hrs	60–120 mg/meal	360 mg/day
Repaglinide	1 hr (p)	~ 1 hr	0.5–4 mg/meal	16 mg/day

Figure 1. Guidelines on the use of oral blood glucose-lowering drugs to achieve glycaemic control.
Adapted from IDF guidelines[1] and the recent 2007 Road Map to Achieve Glycaemic Goals[2]

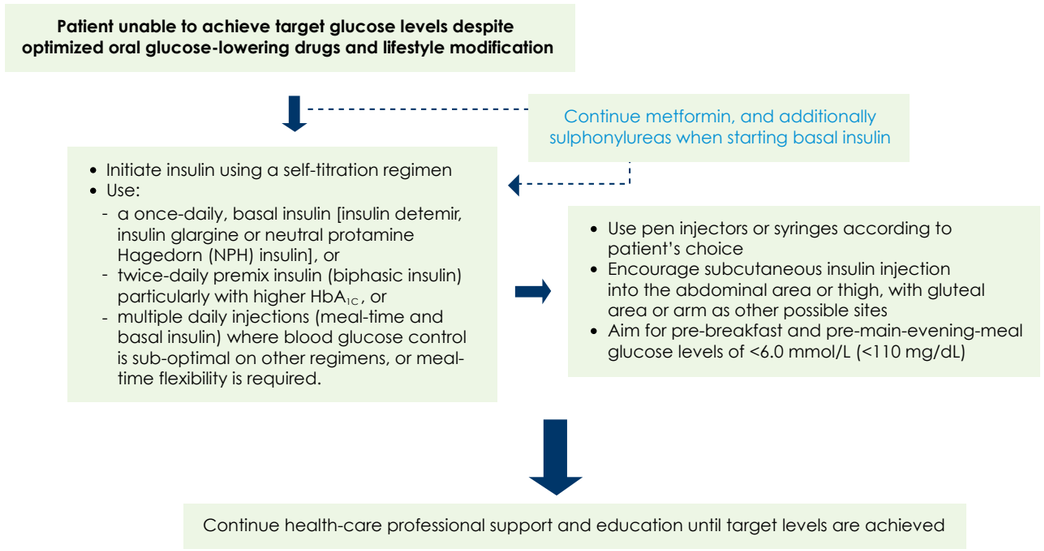


eGFR = estimated glomerular filtration rate; DPP-4 = dipeptidyl peptidase-4; PPAR-γ = peroxisome proliferator-activated receptor-γ

Role of insulin therapy

Insulin therapy should be commenced when DCCT-aligned HbA_{1c} exceeds 7.5% persistently, despite treatment with maximal doses of combined oral therapy and reinforcement of lifestyle and self-management modifications. The starting dosage and titration of insulin should be individualised to the patient. IDF guidelines on the use of insulin therapy in patients with type 2 diabetes, and available insulin preparations are shown in Figure 2 and Table 3, respectively.

Figure 2. IDF guidelines on the use of insulin therapy therapy in type 2 diabetes



"Insulin therapy should be commenced when DCCT-aligned HbA_{1c} persistently exceeds 7.5% despite maximal dosage of combined oral agents and reinforcement of appropriate lifestyle and self-management modifications"

Table 3. Insulin preparations on the market

Contents	Onset	Peak	Duration	Brand Names
Short- and rapid-acting				
Insulin aspart	10–20 mins	1–3 hrs	3–5 hrs	NOVORAPID
Insulin lispro	~15 mins	0.5–1.5 hrs	3–5 hrs	HUMALOG
Regular insulin (soluble, neutral)	0.5 hr	1–3 hrs	8 hrs	ACTRAPID HM
	0.5 hr	2–4 hrs	6–8 hrs	HUMULIN R
Intermediate-acting				
NPH insulin (isophane insulin)	1–2 hrs	6–12 hrs	18–24 hrs	HUMULIN N
	1.5 hrs	4–12 hrs	24 hrs	PROTAPHANE HM
Long-acting				
Insulin glargine	2–5 hrs	Peakless	24 hrs	LANTUS
Insulin detemir	3–4 hrs	6–8 hrs	~24 hr	LEVEMIR
Premixed				
70% NPH insulin and 30% regular insulin	0.5 hr	1–5 hrs	24 hrs	HUMULIN 70/30
30% insulin aspart and 70% protaminated insulin aspart	10–20 mins	1–4 hrs	24 hrs	NOVOMIX 30
30% regular insulin and 70% NPH insulin	0.5 hr	2–8 hrs	24 hrs	MIXTARD 30 HM

Cardiovascular risk protection

Heart disease and stroke account for more than 65% of deaths in patients with type 2 diabetes. Effective disease management can substantially reduce the risk of cardiovascular disease. In addition to making lifestyle and self-management modifications, at-risk patients should be encouraged to undergo regular monitoring to facilitate control of identified factors.

The use of blood pressure-lowering, lipid-modifying and anti-platelet therapies to treat patients with type 2 diabetes should be individualised to prevent cardiovascular complications (Table 4).

Table 4. IDF guidelines for reducing cardiovascular risk in patients with type 2 diabetes

Strategies for reducing cardiovascular risk
• Assess cardiovascular risk at diagnosis and at least annually thereafter
• Advise patient to stop smoking
• Provide aspirin (75–100 mg daily) in patients with, or who are at high risk of, cardiovascular disease
• Actively manage blood lipid profile:
– statin at standard dose for all patients >40 years old
– statin at standard dose for all patients >20 years old with, or who are at high risk of microalbuminuria
– consider use of other lipid-lowering drugs for patients who do not reach target levels or are intolerant to statins
• Refer high-risk or symptomatic patients to cardiologist for assessment