Guidelines

For The Management Of

Type 2 Diabetes Mellitus

By

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Setting Clinical and Professional Excellence

Screening is the process of identifying those individuals who are at sufficiently high risk of a specific disorder to warrant further investigation or direct action

Diagnosis refers to confirmation of a disorder in people who have symptoms, or who have had a positive screening test.

Screening of the general population should be considered by their health care provider at *3-year intervals beginning at age 45*. The rationale for this interval is that false negatives will be repeated before substantial time elapses, and there is little likelihood of an individual developing any of the complications of diabetes to a significant degree within 3 years of a negative screening test result.

Screening should be considered at a *younger age or be carried out more frequently* in individuals with one or more of the following risk:
*Family history of diabetes (i.e., parents or siblings with diabetes).
*Overweight (BMI ≥25 kg/m^2).
*Habitual physical inactivity.
*Previously identified impaired fasting glucose IFG or impaired glucose tolerance IGT.
*Hypertension (≥140/90 mmHg in adults).
*HDL cholesterol ≤35 mg/dl and/or a triglyceride level ≥250 mg/dl.
*History of gestational diabetes mellitus GDM or delivery of a baby weighing >9 lbs.
*Polycystic ovary syndrome.

For younger age group: it is recommends that overweight youths
(*defined as BMI >85th percentile for age and sex, weight for height >85th percentile or weight >120% of ideal [50th percentile] for height*) with any two of the risk factors listed below be screened.
Screening should be done every 2 years starting at age 10 years or at the onset of puberty if it occurs at a younger age. Screening may be considered in other high-risk patients who display any of the following characteristics:
A. Have a family history of type 2 diabetes in first- and second-degree relatives.
B. Belong to a certain race/ethnic group (Native Americans, African-Americans, Hispanic Americans, and Asians/South Pacific Islanders).
C. Have signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome).

Patients presenting to health care providers with any of the following should receive ***diagnostic*** testing for diabetes:
*Symptoms of marked hyperglycemia: polyuria, polydipsia, weight loss, blurred vision.
*Those with potential complications of diabetes.
*Those with any other clinical presentation in which diabetes is included in the differential diagnosis.
Such diagnostic testing, however, does not constitute screening.

The fasting plasma glucose FPG is the recommended screening test. The OGTT may be necessary for the diagnosis of diabetes when the FPG is normal. The FPG is preferred over OGTT for screenings because it is faster and easier to perform, more convenient,

acceptable to patients, and less expensive.
1. FPG ≥126 mg/dl is an indication for retesting, which should be repeated on a different day to confirm a diagnosis.
2. If the FPG is <126 mg/dl and there is a high suspicion for diabetes, an OGTT should be performed.
3. A 2-h post-load value in the OGTT ≥200 mg/dl is a positive test for diabetes and should be confirmed on an alternate day.
Impaired fasting glucose IFG & Impaired glucose tolerance IGT are risk factors for future diabetes.

A Casual Plasma Glucose measurement is plasma glucose testing without regard to time of last meal & may be performed on individuals who have taken food or drink shortly before testing. A casual plasma glucose level ≥200 mg/dl needs further diagnostic tests.

Normoglycemia	IFG or IGT	Diabetes Mellitus
FPG <110mg/dl	**(IFG)** FPG ≥110 - <126 mg/dl	FPG ≥126 mg/dl
2.h PG <140 mg/dl	**(IGT)** OGTT with 2-h PG ≥140 - <200 mg/dl	2-h PG ≥200 mg/dl Symptoms of diabetes and casual plasma glucose concentration ≥200 mg/dl

Diabetes can be diagnosed on any of the following World Health Organization (WHO) criteria:
• Fasting plasma glucose (FPG) ≥ 126 mg/dl OR,
• 75 g oral glucose tolerance test (OGTT) with FPG ≥ 126 mg/dl and/or
2 hour plasma glucose ≥ 200 mg/dl OR,
• Glycated haemoglobin (HbA_1c) ≥ 6.5% OR,
• Random plasma glucose ≥ 200 mg/dl in the presence of classical diabetes symptoms

*Where a random plasma glucose level ≥ 100 mg/dl and < 200 mg/dl is detected, a FPG should be measured, or an OGTT performed, or an HbA_1c measured.
*People who screen negative should be re-tested after 3-5 years. These people should also be offered lifestyle advice to minimize their risk of developing diabetes.

Glucose control levels
1.Measure HbA_1c every 2 - 6 months depending on level, stability of blood glucose control and changes in therapy.
2. Advise people with diabetes that maintaining an HbA_1c below 7.0% minimizes the risk of developing complications.

3. A lower HbA_1c target may be considered if it is easily and safely achieved.
4. A higher HbA_1c target may be considered for people with co-morbidities or when previous attempts to optimize control have been associated with unacceptable hypoglycemia.
5. Treatment should be reviewed and modified if HbA_1c level is above the agreed target on two consecutive occasions.
6. Advise those in whom target HbA_1c levels cannot be reached that any improvement is beneficial.
7. Aim to have the following target during treatment:

HbA_1c	< 7.0%
Fasting/pre-meal capillary plasma glucose	115 mg/dl
Post meal capillary plasma glucose	160 mg/dl

8. HbA_1c can be falsely low or high in certain patients if it is affected by abnormal haemoglobin turnover, the presence of variant haemoglobins, co-existing illnesses such as haematological disorders, renal or liver disease, or the effect of some drugs.
A high reticulocyte count leading to increased red cell turnover (polycythaemia rubra vera) can decrease HbA_1c while iron deficiency increases HbA_1c.
9. Continuous ambulatory blood glucose monitoring is recommended in conjunction with intensive insulin regimen to improve glycaemic control in selected people with type 1 diabetes. However, there is no good evidence-base for its routine use in people with type 2 diabetes
10. Self monitoring blood glucose SMBG on an ongoing basis should be available to those people with diabetes using insulin.
SMBG should be considered for people using oral glucose lowering medications as an optional component of self-management, and in association with HbA_1c testing:
• To provide information on and help to avoid hypoglycemia.
• To assess changes in blood glucose control due to medications and lifestyle changes.
• To monitor the effects of foods on postprandial glycaemia.
• To monitor changes in blood glucose levels during intercurrent illness**.**

Glucose control therapy

1. Begin oral glucose lowering medications when lifestyle interventions alone are unable to maintain blood glucose control at target levels
2. Consider each initiation or dose increase of an oral glucose lowering medications as a trial, monitoring the response in 3 months.
3. Consider cost and benefit: risk ratio when choosing medication.
4. Consider discontinuing ineffective therapies.

First-line therapy

1. Begin with metformin unless there is evidence of renal impairment or other contraindication.
2. Titrate the dose over early weeks to minimize discontinuation of metformin due to gastrointestinal intolerance.

3. Monitor renal function and use metformin with caution if estimated glomerular filtration rate (eGFR) < 45 ml/min/1.73 m^2.
4. Other options include a sulfonylurea for rapid response where glucose levels are high, or a-gIucosidase inhibitors; these agents can also be used initially where metformin cannot.
5. In some circumstances dual therapy may be indicated initially if it is considered unlikely that single agent therapy will achieve glucose targets.

Second-line therapy
When glucose control targets are not being achieved, add a sulfonylurea.
Other options include adding metformin if not used first-line, an a-glucosidase inhibitor, a dipeptidyl peptidase 4 (DPP-4) inhibitor or a thiazolidinedione.
A rapid-acting insulin secretagogue is an alternative option to sulfonylureas.

Third-line therapy
When glucose control targets are no longer being achieved, start insulin or add a third oral agent.
If starting insulin, add basal insulin or use premix insulin.
If adding a third oral agent options include an a-glucosidase inhibitor, a DPP-4 inhibitor or a thiazolidinedione.
Another option is to add a glucagon-like peptide-1 receptor agonist (GLP-1 RA).

Fourth-line therapy
Begin insulin therapy when optimized oral blood glucose lowering medications (and/or GLP-1 RA) and lifestyle interventions are unable to maintain target glucose control.
Intensify insulin therapy if already using insulin.

Insulin therapy
The natural history of type 2 diabetes is of progression of islet β-cell failure.
Ultimately insulin remains the only glucose-lowering therapy which can maintain blood glucose control despite such progression.
1. Do not unduly delay the commencement of insulin.
2. Maintain lifestyle measures including diet modification, increase in physical activity, and weight reduction in the overweight and smoking cessation
3. Consider every initiation or dose increase of insulin as a trial, monitoring the response.
4. Explain to the person with diabetes from the time of diagnosis that insulin is one of the options available to manage their diabetes, and that it may turn out to be the best, and eventually necessary, way of maintaining glucose control, especially in the longer term.
5. Provide education and appropriate self-monitoring.
6. Explain that starting doses of insulin are low, for safety reasons, but that eventual dose requirement is expected to be 30-100 units/day.
7. Continue metformin. Other oral agents may also be continued.
8. Begin with:
• A basal insulin once daily such as neutral protamine Hagedorn (NPH) insulin, insulin glargine or insulin determir.

• Once or twice daily premix insulin (biphasic insulin).
9. Initiate insulin using a self-titration regimen (dose increases of two units every 3 days) or with biweekly or more frequent contact with a health-care professional.
10. Aim for pre-meal glucose levels of < 115 mg/dl.
11. Monitor glucose control for deterioration and increase dose to maintain target levels or consider transfer to a basal plus mealtime insulin regimen.
12. During periods of regular change in food consumption (e.g. Ramadan), the dose of glucose lowering therapies will usually need to be adjusted, especially insulin. The total amount of insulin should not be reduced but redistributed according to the amount and timing of carbohydrate intake.

Blood pressure control

1. Measure blood pressure at every routine clinic visit.
2. Initiate a trial of lifestyle modification with appropriate education aiming to reduce energy intake, salt intake, smoking cessation & alcohol intake and inactivity.
3. Consider secondary causes of raised blood pressure if there is evidence of renal disease, electrolyte disturbance or other specific features.
4. Consider blood pressure lowering treatment if blood pressure is consistently above 130/80 mmHg.
5. In diabetes not complicated by raised albumin excretion rate any agent can be used as first line therapy except for a-adrenergic blockers, with consideration of costs, and actively titrating dose according to response.
• Angiotensin converting enzyme-inhibitors (ACE-inhibitors) and angiotensin-II receptor blockers (ARBs) may offer some advantages over other agents in some situations, but do not use the two together
• Calcium channel blockers (CCBs) should be avoided in congestive heart failure.
• Use β-adrenergic blockers in people with angina; β-adrenergic blockers and ACE inhibitors in people with coronary artery disease; ACE-inhibitors or diuretics in those with heart failure; ACE-inhibitor plus low dose thiazide or thiazide-like diuretic (indapamide or chlorthalidone), or ACE-inhibitor plus CCB in people with cerebrovascular disease.
Care should be taken with combined thiazide and β-adrenergic blockers because of risk of deterioration in metabolic control.
6. Add further medications from a different class if targets are not reached on maximal doses of current medications, reviewing for adverse effects and likely adherence problems as tablet numbers increase.
The preferred combinations are:
• ACE-inhibitor plus CCB.
• ACE-inhibitor plus low dose thiazide or thiazidelike diuretic (indapamide or chlorthalidone).
7. Accept that blood pressure target may not be achievable with three or more anti-hypertensive medications in some people.

Cardiovascular risk protection

1. Assess cardiovascular risk factors at diagnosis and at least annually thereafter including:
• Current or previous CVD.
• Age and BMI (abdominal adiposity).
• Conventional CVD risk factors including smoking, blood pressure, serum lipids and family history of premature CVD.
• Renal damage (particularly albuminuria).
• Atrial fibrillation (for stroke).
2. High risk individuals should be actively treated to reduce CVD risk with lifestyle modification and pharmacotherapy. Anti-platelet therapy is not routinely recommended in high risk individuals who have not had a CVD event.
3. Treat high risk individuals with statins unless contraindicated or considered clinically inappropriate.
4. Consider the addition of fenofibrate where serum triglycerides are > 2.3 mmol/l (> 200 mg/dl) and high density lipoprotein (HDL) cholesterol is low, especially when retinopathy is present. Combination of gemfibrizol with a statin is not recommended.
5. Consider other medications for dyslipidaemia (bile acid binding resins, ezetimibe, sustained release nicotinic acid, concentrated omega-3 fatty acids) in those failing to reach lipid lowering targets or intolerant of conventional medications.
6. Lipid targets are as follows:
LDL cholesterol < 2.0 mmol/l (< 80 mg/dl),
LDL cholesterol should be < 1.8 mmol/l (< 70 mg/dl) in established CVD
HDL cholesterol > 1.0 mmol/l (> 39 mg/dl),
Non- HDL cholesterol < 2.5 mmol/l (< 97 mg/dl)
Triglyceride < 2.3 mmol/l (< 200 mg/dl)
7. Refer early for further investigation and consideration of revascularisation those with problematic or symptomatic peripheral arterial disease, those with problems from coronary artery disease, and those with evidence of carotid disease.
8. Serum levels of ultrasensitive C-reactive protein may be helpful to assess risk beyond LDL cholesterol. Serum levels of ultrasensitive C-reactive protein > 2 mg/l may call for more aggressive statin treatment.
9. Anti-platelet agents to consider might include clopidogrel substituted for aspirin, in particular for those with multiple CVD events/problems, peripheral arterial disease, or previous coronary bypass grafting.
10. There is general agreement that the following people with type 2 diabetes are at high CVD risk:
• Previous cardiovascular event.
• Micro and macroalbuminuria.
• Markedly elevated single risk factors.
For people with established CVD the benefit of long-term aspirin for reducing the risk of MI, stroke and vascular death is well established. However guidelines generally do not support the routine use of aspirin (or other antiplatetet agents) in CVD prevention in

people who have not had a CVD event. Dual anti-platelet therapy (clopidogrel and aspirin) is also not recommended for primary prevention of CVD.

Kidney damage

1. Kidney function should be assessed at diagnosis and annually by:
• Urine test for albuminuria.
• Measurement of serum creatinine and calculation of eGFR.
2. Urinary albumin:creatinine ratio (ACR) measurement in an early morning first void spot specimen is the preferred method for assessment of albuminuria/ proteinuria where a first void specimen is not possible or practical, a random spot urine specimen is acceptable.
3. If ACR is raised (microalbuminuria ACR > 2.5 mg/ mmol in men, > 3.5 mg/mmol in women), repeat ACR twice over the following 4 months.
Microalbuminuria is confirmed if ACR is elevated in two out of three tests, in the absence of infection or overt proteinuria.
If both repeat tests are not raised, check again annually.
An ACR > 30 mg/mmol indicates macroalbuminuria.
4. Chronic kidney disease is diagnosed on the basis of a raised urine albumin/protein or a reduced eGFR (< 60 ml/min/1.73 m2) calculated from the *MDRD formula online*:

Serum creatinine _____ (mg/dL)

Age _____

African American □Yes □ No

Gender □ Male □ Female

GFR value _____ mL/min/1.73 m^2

This equation should only be used for patients 18 and older and for chronic renal disease

5. Individuals with chronic kidney disease should be managed as follows:
• Use ACE-inhibitors or ARBs in individuals with micro- or macroalbuminuria, titrated to maximum tolerated dose.
• Intensify management of blood pressure (target ≤ 130/80 mmHg) using blood pressure lowering medications and dietary modification
• Intensify management of blood glucose
• Monitor ACR, eGFR and serum potassium.
• Advise limiting protein intake to 1 g/kg daily if proteinuric.
• Intensify other renal and cardiovascular protection measures
6. Agree referral criteria for specialist renal care
Referral criteria might include eGFR < 30 ml/ min/1.73 m^2, progressive deterioration of kidney function, persistent proteinuria, and biochemical or fluid retention problems.

Eye screening

1. Ensure that examination of the eyes of people with type 2 diabetes is performed around the time of diagnosis and then routinely every 1-2 years as part of a formal recall process:
• Measure and document visual acuity, corrected with glasses or pinhole.
• Assess retinopathy
2. The following frequency of screening is suggested:
• 1-2 years if no retinopathy.
• 12 months if minimal unchanged retinopathy.
• 3 - 6 months if worsening since last examination.
• More often during pregnancy.
3. The following situations require referral to ophthalmologist:
• *The same day*:
** Sudden loss of vision. ** Evidence of retinal detachment.
• *Within 1 week*:
** Evidence of pre-retinal and/or vitreous haemorrhage.
** New vessel formation or rubeosis iridis.
• *Within 1-2 months*:
** Advanced retinal lesions (4:2:1 rule).
- Microaneurysms or retinal haemorrhages in 4 quadrants.
- Venous beading in 2 quadrants.
- IRMAs in 1 quadrant (Intraretinal microvascular abnormalities).

** Unexplained deterioration of visual acuity.
** Macular oedema.
** Unexplained retinal findings.
** Cataract.
** Inability to visualise fundus.
4. Advise that good control of blood glucose, blood pressure and blood lipids can help to reduce the risk of eye damage developing or worsening.
5. Advise that diabetic retinopathy is not a contraindication for use of aspirin if this is indicated for prevention of CVD.
6. Advise that tests of intra-ocular pressure should be made periodically.

Foot care

1. Assess feet of people with diabetes as part of an annual review for lesions which require active treatment and for risk factors for ulcer and amputation:
a. History of previous foot ulceration or amputation, symptoms of peripheral arterial disease, physical or visual difficulty in self-foot care.
b. Foot deformity (hammer or clawed toes, bone prominences); visual evidence of neuropathy (dry skin, dilated veins) or incipient ischaemia; callus; nail deformity or damage; footwear.
c. Detection of neuropathy by 10 g monofilament (or 128 Hz tuning fork); a biothesiometer is an option for quantitative assessment (cut-off point for ulcer risk > 25 volts); non-traumatic pinprick.
d. Palpation of foot pulses (dorsalis pedis and posterior tibial).

2. Discuss the reasons for foot review with each person with diabetes as part of the foot care educational process.
3. People with foot ulceration or infection require the following management:
Refer to multidisciplinary foot-care team within 24 hours for:
a. Appropriate wound management, dressings and debridement as indicated.
b. Infections should be assessed & consideration of systemic antibiotic therapy (often longer term) for extensive cellulitis or bone infection as indicated; generic penicillins, macrolides, clindamycin and/or metronidazole as indicated as first-line medications, with ciprofloxacin or coamoxicllin as examples of second-line medications.
c. Probing to bone, radiology and scans, magnetic resonance imaging, and biopsy where indicated for suspected osteomyelitis.
d. Reduce weight bearing, relief of pressure (walking with crutches, rest) and optimal pressure distribution (casting if indicated and not contraindicated)
e. Investigation and treatment for vascular insufficiency.
f. Optimal blood glucose control.
7. Amputation should not be considered unless:
a. A detailed vascular evaluation has been performed by the vascular staff.
b. Ischemic rest pain cannot be managed by analgesia or revascularization.
c. A life-threatening foot infection cannot be treated by other measures.
d. A non-healing ulcer is accompanied by a higher burden of disease than would result from amputation.

Nerve Damage

1. Diagnose sensorimotor nerve damage by history and examination (monofilament with or without temperature, non-traumatic pin-prick, vibration [tuning fork], ankle reflexes), and/or simple quantitative testing (e.g. biothesiometer vibration perception).
2. Evaluate creatinine/ urea, serum B12, thyroid function tests and medication/ alcohol consumption history to exclude other causes.
3. Manage by stabilizing blood glucose control and treatment with tricyclic antidepressants if simple analgesia is not successful.
If a one month trial of tricyclic therapy is not successful, further treatment options include pregabalin/gabapentin and duloxetine, then tramadol and oxycodone.
4. Diagnose erectile dysfunction by history (including medication history), exclusion of endocrine conditions (measure prolactin and testosterone), and try a phosphodiesterase type-5 (PDE5) inhibitor (where not contraindicated by nitrate therapy).
Consider other approaches such as intra-urethral or intracavernosal drugs and sexual and relationship counselling, where PDE5 inhibitors fail or cannot be used.
5. Diagnose gastroparesis by history, trial of a prokinetic drug (metoclopramide, domperidone) and if troublesome by gastric emptying studies.
6. Diagnose cardiovascular autonomic neuropathy by resting heart rate (> 100 bpm) and heart rate response to provocation tests (lying-standing, Valsalva, deep breathing), orthostatic reduction in blood pressure (a fall in SBP > 20 mmHg on standing without an appropriate heart rate response).

Older people

1. Diagnosis of diabetes in older people should be in accordance with WHO criteria which apply to all age groups

2 .An agreements should be done between the clinician and the patient about treatment aims and goals of care designed to optimize **patient empowerment**.

3. Glucose-lowering interventions should aim to achieve an HbA_1c of 7.0-7.5%.

A higher target may be appropriate in the presence of modifying factors such as vulnerability to hypoglycaemia, presence of co-morbidities, cognitive and mood status, and limited life expectancy.

Care should be taken in commencing blood glucose lowering medications unless FPG is consistently 108mg/dL or higher.

As a precaution to reduce the risk of hypoglycemia, particular care should be taken to avoid FPG < 108mg/dL on treatment.

4. At initial assessment, all older people with diabetes should have:

• Basic assessment of walking and activities of daily living abilities including the use of walking aids and special footwear, and a history taken enquiring about falls.

• History taken of any recent memory problems.

• Nutritional evaluation using a recognized assessment tool

• Cardiovascular risk assessment and review/ discussion of modifiable risk factors including smoking cessation.

5. **Structured patient educational** should be accessible to all older people and take into account culture, language, nutritional preferences, ethnicity, level of disability, geographical factors and needs of carers.

6. Provide continuing care and support including:

• Promoting self-management including SMBG if indicated

• Annual Review including weight and height, BMI, blood pressure, falls risk assessment, assessment for foot and eye problems, eGFR and urine albumin and lipid profile.

7. Regularly review those on oral agents taking into consideration the often increased risk of hypoglycaemia, renal dysfunction, polypharmacy and difficulties in adherence to treatment.

8. In general, advanced age is not a barrier to the use of any glucose-, blood pressure- or lipid-lowering agent used in the treatment of adults with type 2 diabetes.

*Metformin can be considered as first-line glucose lowering therapy and as an adjunct to insulin therapy in those requiring insulin.

*Sulfonylurea is suitable as second-line therapy but is best avoided in those at higher risk of hypoglycaemia

*Where risk of hypoglycaemia is moderate and an insulin secretagogue is being considered, an agent with a lower hypoglycaemic potential should be used.

*A DPP-4 inhibitor may be considered as second-line therapy.

*A GLP-1 RA may be considered in obese non-frail older subjects as third-line therapy with metformin and a sulfonylurea.

*Insulin treatment should not be delayed but offered as an option when clinical features are appropriate.

A basal insulin regimen may be safer in terms of hypoglycaemia risk than a pre-mixed insulin regimen.

9. Blood pressure lowering treatment should be commenced when blood pressure is consistently 140/90 mmHg or higher in people aged 70 to 80 years and if consistently 150/90 or higher in people aged over 80 years.
Aim for a target clinic blood pressure below 140/90 mmHg in people aged 70 - 80 years.
Aim for a target clinic blood pressure below 150/90 mmHg in people aged over 80 years.Caution should be exercised in implementing aggressive blood pressure lowering therapy in older people.

In-patient care

Management during in-patient procedures

1. Evaluate blood glucose control and metabolic and vascular complications (in particular renal and cardiac status) prior to planned procedures; provide advice on the management of diabetes on the day or days prior to the procedure.
2. Ensure the provision and use of an agreed protocol for in-patient procedures and surgical operations.
3. Aim to maintain premeal blood glucose < 140mg/dl and random blood glucose <180 mg/dl, provided these targets can be safely achieved.
3. IV insulin delivery where needed, would generally be given as a glucose/insulin/potassium infusion.
4. Ensure awareness of special risks to people with diabetes during hospital procedures, including risks from:
• Neuropathy (heel ulceration, cardiac arrest).
• Intra-ocular bleeding from new vessels (vascular and other surgery requiring anticoagulation).
• Medication (risks of acute renal failure causing lactic acidosis in people on metformin, for example with radiological contrast media).

Critical care situations

1. Provide access to intensive care units (ICU) for life threatening illness, including blood glucose control usually with IV insulin therapy.
2. Provide protocol-driven care to ensure detection and immediate control of hyperglycaemia for anyone with a presumed acute coronary event or stroke, normally using IV insulin therapy with transfer to subcutaneous insulin therapy once stable and eating.
3. Once insulin therapy is started, a glucose range of 140-180 mg/dl is recommended for the majority of critically ill patients while avoiding hypoglycaeamia.
4. Emergency rooms must have clearly visible standing orders stating all critically ill patients must have their blood glucose checked.

References

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Treatment algorithm for people with type 2 diabetes