

Key Points and Patient Care Disclaimer

Diabetes is an important condition in the elderly. According to the American Diabetes Association at least 20% of patients over the age of 65 have diabetes and the number is expected to grow. The prevalence of diagnosed cases rises with age and peaks at 10% in this population. Because there are no long-term studies in this population that demonstrate the benefits of tight glycemic control, and older patients with diabetes are at a greater risk for common geriatric syndromes such as polypharmacy, depression, cognitive impairment, urinary incontinence, injurious falls, and persistent pain, the care of these patients is complicated and controversial.

Hypoglycemia (BG <50 mg/dl) avoidance is important in the elderly. Mechanisms which increase the potential for hypoglycemia in this age group are decreased hepatic oxidative enzyme activity which may interfere with sulfonylurea metabolism, a decline in renal function, chronic liver disease, and poor nutrition or fasting. In addition, hypoglycemic unawareness poses a problem. Elderly patients may also develop hypoglycemia during periods of low activity such as golfing or grocery shopping presumably due to age related decline in beta-adrenoceptor function. Because disruption of health and quality of life is likely with hypoglycemia in the elderly patients, steps should be taken to minimize that risk.

As a general principle, uncomplicated geriatric patients may adhere to the therapy and goals of their younger counterparts. However, in patients with advanced diabetes complications, life-limiting comorbid illness or cognitive or functional impairment, it is important to "start low and go slow" and it is reasonable to set less intensive goals. As a general principle, FBG of <150 mg/dl is an acceptable endpoint, as is an HbA1c of 7.0-8.0 in frail elderly, those with a life expectancy of < 5 years, or those where the risks of tight control outweighs the benefits. Because of the heterogeneity of the geriatric population, care must be individualized to the presenting patient and the benefits and risks of therapy must be weighed judiciously.

1. Brown AF, Mangione CM, Saliba D, Sarkisian CA: Guidelines for improving the care of the older person with diabetes mellitus. *J Am Geriatr Soc* 51:S265-S280, 2003. (Also reference for Table 4 on back)
2. Chelliah A, Burge MR: Hypoglycaemia in Elderly Patients with Diabetes Mellitus: Causes and Strategies for Prevention. *Therapy In Practice. Drugs & Aging.* 21(8):511-530, 2004.
3. American Diabetes Association: Standards of Medical Care in Diabetes 2007 *Diabetes Care* 30: S4-41S.

Specific Oral Drug Comments

Drug	Comment
Metformin	Avoid in renal impairment and CHF due to lactic acidosis risk. Efficacy may be diminished due to lack of beta cell function. Scr may be underestimated in frail patients. May contribute to suboptimal vitamin B12 absorption which is generally decreased in the elderly. Not recommended in patients over the age of 80 unless normal CrCl is documented.
Chlorpropamide	Do not use in the elderly. Increased risk for hypoglycemia and long duration of action.
Glyburide	Avoid due to rapid and prolonged hypoglycemia despite hypertonic glucose injections. Weight gain occurs. Higher incidence of hypoglycemia than glimepiride.
Glipizide	Best sulfonylurea to use in renal impairment. Use with caution with CYP inhibitors.
Glimepiride	Risk for hypoglycemia.
Repaglinide	No comments
Nateglinide	No changes in safety and efficacy in elderly
Acarbose	Flatulence and diarrhea may be problematic. Cannot use sucrose for hypoglycemia.
Miglitol	Flatulence and diarrhea may be problematic. Cannot use sucrose for hypoglycemia.
Rosiglitazone*	Avoid in class 3/4 heart failure. May exacerbate edema. Potential increased risk for fractures in females. (ADOPT trial)
Pioglitazone*	Avoid in class 3/4 heart failure. May exacerbate edema. Potential increased risk for fractures in females. Reduces incidence of nonfatal MI and stroke. Increases incidence of HF, weight gain, and edema. Various drug interactions complicate administration. Lipid profile benefits are documented with this drug.
Exenatide*	May be beneficial in obese patients. Polypharmacy may increase potential for nausea and vomiting.
Sitagliptin*	May be beneficial in functionally impaired patients and those unwilling to take injectable drugs. However, efficacy may be diminished in older patients with minimal or non-existent B-cell function. Exenatide may be preferred in obese patients. May be used in combination with metformin or a TZD.
Pramlintide	Intended practically for obese patients not adequately controlled on insulin alone. When used in combination with insulin, pramlintide further reduces HbA1c levels by 0.39—0.62%. In patients 65+ YO hemoglobin values and hypoglycemia frequencies were not different in elderly patients versus younger patients. The drug may cause severe hypoglycemia when used with insulin and should be avoided in patients with recurrent severe hypoglycemia or those unable to recognize hypoglycemia. The drug has not been studied in patients in renal failure, however, it did not show significant pharmacokinetic changes in CrCl 21-50 ml/min. Use with caution in patients with osteoporosis. Do not use in patients with gastroparesis or in patients requiring agents for gastrointestinal motility. <small>Gold Standard Multimedia. Clinical Pharmacology 1994-2006. V2.22.</small>

Hypoglycemic Risk

Drug	Hypoglycemia	Requires Insulin for Efficacy
Metformin	Yes (with insulin)	Yes
Glyburide	Yes	No
Glipizide	Yes	No
Glimepiride	Yes	No
Repaglinide	Yes (less)	No
Nateglinide	Yes (less)	No
Acarbose	No	Yes
Miglitol	No	Yes
Rosiglitazone	Yes (with insulin)	Yes
Pioglitazone	Yes (with insulin)	Yes
Exenatide	No	No
Sitagliptin	No	No

Insulin Therapy—Clinical Pearls

Insulin therapy may be safely initiated in many geriatric patients. The clinician should evaluate the physical and intellectual capacity of the patient to draw up and give appropriate doses of insulin, to monitor blood glucose, and to recognize and treat hypoglycemia. Treatment should be uncomplicated and the use of prefilled pens should be encouraged. Lower doses may be recommended in patients with a GFR < 50 ml/min due to increased insulin sensitivity.

Insulin glargine once daily in the morning in combination with oral therapy is simple and provides good benefits. For obese patients, exenatide may provide the added benefit of weight loss with similar HbA1c benefits as glargine.

Tighter control can be achieved with mealtime rapid-acting insulin analogs given based on carbohydrate counting, a sliding scale, or body weight calculation.

For patients who can count carbohydrates, the clinician may initiate 1 unit of insulin for every 10-15 grams of carbohydrates. For those unable to count carbs, the clinician may use a sliding scale where 2 units of quick-acting insulin is used for every 50 mg/dl above 150 mg/dl 1 hour after a meal. Finally, a weight based approach of 0.1 unit/kg may be used, however, is discouraged because this may overestimate insulin need.

Pre-mixed insulin analogs provide the advantage of less hypoglycemia and better postprandial control with similar HbA1c results but are primarily useful in patients with regular meals and unvarying calorie intake.

Drug Use Precautions*

Drug	Renal Impairment Avoidance	Contraindications**
Metformin	eGFR <30 Avoid if Clcr < 60-70 ml/min Caution 80+ YO Dialyzable 170 ml/min	SCr >1.5 mg/dl Males SCr >1.4 mg/dl Females CHF requiring medications per manufacturer. This extends to hypoxia, dehydration and sepsis.
Glyburide	Clcr <50 ml/min	DKA
Glipizide	Clcr <10 ml/min	Severe hepatic disease
Glimepiride	Clcr <22 ml/min (initiate at 1 mg)	DKA
Repaglinide	Clcr 20-40 ml/min (initiate 0.5 mg with meals)	DKA
Nateglinide	No adjustment	DKA
Miglitol	Scr >2 mg/dL	Intestinal disorders, DKA
Acarbose	Clcr <25 ml/min (6 times AUC increase)	Intestinal disorders, DKA
Rosiglitazone	No adjustment. Watch hepatic failure.	Transaminases >2.5 times the upper limit of normal. NYHA Class 3/4 HF
Pioglitazone	No adjustment. Watch hepatic failure.	Transaminases >2.5 times the upper limit of normal. NYHA Class 3/4 HF
Exenatide	Clcr <30 ml/min	DKA
Sitagliptin	Clcr 30-50: 50 mg daily Clcr <30: 25 mg daily ESRD w/ dialysis: 25 mg daily	None

*Precautions are not exhaustive. Lexi-comp Drug Information Handbook 14th Ed.

**Hypersensitivity to drug is an implied contraindication. This information does not substitute clinical judgment.

Glucose Regulation

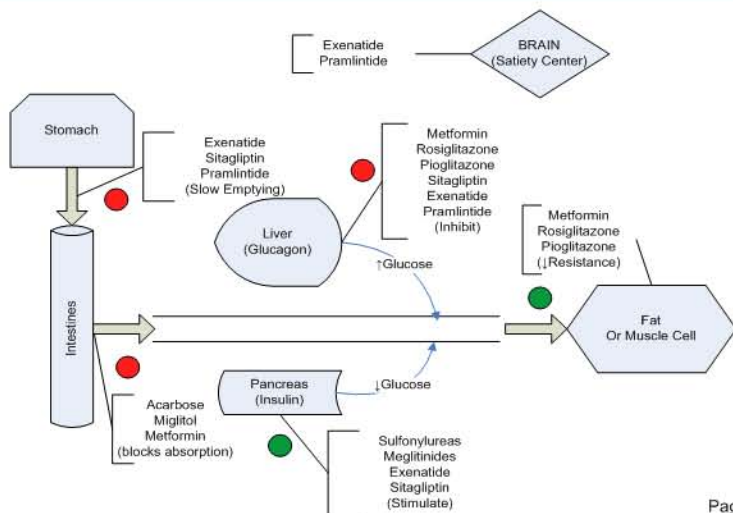


Table 4 Guidelines for improving the care of older persons with DM

Care should be simple and inexpensive. Older persons with diabetes are likely to benefit from cardiovascular risk reduction; therefore, monitor and treat hypertension and dyslipidemias. For many older persons, treatment of hypertension may require more than one medication to achieve adequate control. Treatment should be gradual if possible and persons should be monitored for drug interactions and side effects. Monitor and treat hyperglycemia, with a target of 7%, but less stringent therapy may be appropriate once patient preferences, diabetes severity, life expectancy, and functional status have been considered. Encourage diabetes education and make patients and their families aware that it is a covered benefit under Medicare. Dilated eye examinations should be performed every 2 years at a minimum and more when additional risks for diabetic eye disease or evidence of age-related eye disease. Maintain an updated medication list and evaluate the patient regularly for adverse medication effects. Older persons with diabetes should be screened for depression, and if depression is identified, therapy should be offered and response to therapy monitored. Persons should also be screened annually for cognitive impairment, urinary incontinence, injurious falls, and persistent pain because these conditions are prevalent among older persons with diabetes.

Hepatic Substrates*

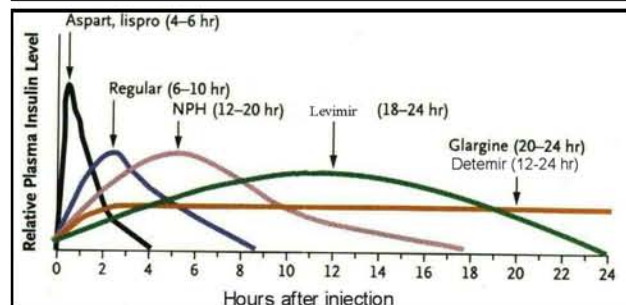
Substrate	Major CYP Enzyme
Glipizide	2C8/9
Glimepiride	2C9
Repaglinide	2C8, 3A4
Nateglinide	2C9, 3A4
Rosiglitazone	2C8
Pioglitazone	2C8

*Only major enzymes listed. Induction and inhibition omitted. Data per Lexi-comp Drug Information Handbook 14th Ed.

Metabolic Syndrome Goals*

A1c	<7.0%
Pre-prandial glucose	90-130 mg/dl
Post-prandial glucose	<180 mg/dl
Blood Pressure	<130/80 mmHg
Lipids	
LDL	<100 mg/dl
Triglycerides	<150 mg/dl
HDL	>40 mg/dl

*ADA. Diabetes Care. 2007;30:s4-41



Adapted from NEJM, 352;2