DIABETES MANAGEMENT: AN INSIGHT

Introduction

- Diabetes is fast gaining the status of a potential epidemic in India
- >62 million diabetic individuals currently diagnosed with the disease.
- In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus
- It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India,

Anjana RM et al. Lancet Diabetes Endocrinol. 2017 Aug;5(8):585-596

Burden

- India currently faces an uncertain future in relation to the potential burden imposed by Diabetes.
- Many influences affect the prevalence of disease throughout a country
- Identification of those factors is necessary to facilitate change when facing health challenge
- The aetiology of diabetes in India is multifactorial

Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.
Kalra S et al Indian J Endocrinol Metab. 2015 Sep-Oct; 19(5): 577–596

Overcoming Diabetes Burden

- To reduce the disease burden that diabetes creates in India, appropriate government interventions and combined efforts from all the stakeholders of the society are required.

- Clinicians may be targeted to facilitate the implementation of
  - screening and early detection programmes,
  - diabetes prevention,
  - self-management counselling, and
  - therapeutic management of diabetes

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Overcoming Diabetes Burden

- Continuing education programmes for general practitioners may provide
  - The “clinical inertia” required to initiate programme adherence,
  - May be a major step in achieving target glycaemic levels and the prevention of disease complications.

Aggressive clinical measures in terms of early screening combined with optimal doses of oral hypoglycaemic agents and appropriate lifestyle modification could also have long-term positive effects in disease management.

Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.
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CASE STUDY OF A PATIENT WITH NEWLY DIAGNOSED, ASYMPTOMATIC HYPERGLYCEMIA

Case -1: A Patient with Newly Diagnosed, Asymptomatic Hyperglycemia

- 31-year-old man was found to have a fasting plasma glucose of 150 mg/dL at a routine medical examination.
- He was asymptomatic.
- His past medical history was unremarkable.
- There was no family history of diabetes.
- He worked as an air traffic controller, which was the reason for his routine medical examination.

Lab Investigations: *Case 1: Continued*

- His laboratory results revealed the following:
  - Weight 80.30 kg
  - Height 177.0 cm
  - BMI 25.6 kg/m^2
  - Pulse : regular
  - Blood pressure 140/80 mmHg
  - HbA1c: 8.4%
  - Urinalysis, including albuminuria, was negative.

Examination and Investigation: Case 1 Contd..

- The feet were in good condition with no evidence of sensory neuropathy.
- The ankle jerks were preserved. The pedal pulses were palpable.
- There were no carotid bruits.
- Physical examination was otherwise unhelpful.

Case 1: Diagnosis

- A screen for islet cell antibodies revealed a high titer of IA-2 antibodies with negative GAD and insulin antibodies, confirming this as type 1 diabetes.

- This has been called late autoimmune diabetes in adults (LADA), although in reality, it is simply slowly evolving type 1 diabetes that, therefore, usually presents in adults.

Case – 1 : Management

- Initial therapy was a diet and exercise regimen, metformin, and gliclazide targeting a normal BMI and HbA1c in the absence of hypoglycemia.
- Twenty-one months later, the BMI was 23.7 kg/m^2 and the HbA1c 5.8%.
- He has not experienced any hypoglycemia.

CASE STUDY OF DIZZINESS, LIGHTHEADEDNESS, AND SYNCOPE IN A PATIENT WITH TYPE 2 DIABETES

Case 2: Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- 57-year-old man with type 2 diabetes (T2D) for 7 years and peripheral neuropathy was referred in 2012 for evaluation of episodic "hypoglycemic" symptoms

  (lightheadedness, dizziness, shakiness, sweating, headaches, tremors, and pallor), unrelated to position or meals, resulting in one episode of syncope and a fall.

- The episodes resolved with ingestion of glucose tablets or meals.

Case 2 : History

- Past medical history was significant for panic disorder, posttraumatic stress disorder, fibromyalgia, hypertension, sleep apnea, and hyperlipidemia.
- Current medications for T2D were metformin 1,000 mg twice daily and pioglitazone,30 mg daily.
- Discontinuation of these medications did not reduce the occurrence of these episodes.
- Diet included three meals and two snacks daily, sometimes consisting of high calories and carbohydrates.

Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- Physical examination showed the following:
  - BMI 30 kg/m2
  - Blood pressure 145/80 mmHg supine
  - 120/90 mmHg standing
- He was unable to stand >3 min because of lightheadedness and sweating.
- Blood pressure decreased by 25 mmHg during bedside tilt.
- Electrocardiogram, corrected Q and T waves (QTc) was 498 mm, and monofilament sensation wasdecre ased.

Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- Fasting and premeal self-monitored blood glucose (SMBG) ranged from 120 to 180 mg/dL (6.6–10 mmol/L),
- postmeal SMBG ranged from 160 to 210 mg/dL (8.8–11.6 mmol/L).
- This patient's symptoms of lightheadedness, shaking, sweating, and tremors and relief of symptoms with meals and glucose tablets suggested hypoglycemia.
- Both the SMBG and BG, however, did not display values <70 mg/dL (3.9 mmol/L).

Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- In September 2012, hemoglobin A1c (HbA1c) was 6.8%.
- A continuous glucose monitoring (CGM) study was performed

Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- CGM study showed sensor glucose values between 72 and 208 mg/dL with postmeal glycemic surges.
- The patient experienced symptoms at BG 140–150 mg/dL.
- Because the symptoms persisted, were inconsistent with meals, and no BG <70 mg/dL, we considered other causes for presyncope, flushing, and tremors

Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- Other laboratory tests ruled out carcinoid syndrome, pheochromocytomoa, thyroid dysfunction, cardiac disease, cerebrovascular disease, seizure disorder, and hypogonadism.
- Because of persistent early satiety and bloating sensation, a gastric emptying study was done. Results confirmed delayed emptying in all times (1 h = 26%, 2 h = 49%, 3 h = 71% emptying of stomach).
- Gastroparesis, NOH, and the prolonged QT interval of 498 mm were consistent with DAN.

Case 2: Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- The patient had stopped taking his pioglitazone because of his fear of hypoglycemia.
- He was started on sitagliptin 50 mg daily (HbA1c 7%).
- He continued to complain of these episodes.
- In April 2014, the patient's SMBG showed fluctuating values between 120 and 220 mg/dL with continued "hypoglycemic symptoms" at BG of 150 mg/dL.
- Therefore, Voglibose 0.2 mg with breakfast was started. We also recommended dietary management with low-carbohydrate, high-protein regular meals and snacks.

Case 2: Dizziness, Lightheadedness, and Syncope in a Patient with Type 2 Diabetes

- In May 2014, he was started on glargine 5 units at bedtime in addition to
- Voglibose 0.2 mg three times a day with meals, metformin 1,000 mg twice daily, and sitaglipitin 50 mg.
- CGM study in 2014 showed an average BG 219 mg/dL (12.1 mmol/L; range = 142–333 mg/dL, 7.8–18.5 mmol/L).
- Symptoms documented during the CGM study did not correlate with low BG readings. HbA1C remained between 6.2 and 7.1%.
- Three years later, the patient returned to the endocrine clinic for reevaluation.
- He reported that whenever he did not follow the diet and forgot to
- Take Voglibose, he developed the “hypoglycemic symptoms,” regardless of any other diabetes medication changes.

CASE STUDY OF ELDERLY PATIENT WITH LONG STANDING DIABETES

Mr. AH

- Mr. AH is a 70-year-old man who was diagnosed with T2DM 10 years ago. He was initially treated with lifestyle management and metformin.
- 3 years later, his doctors advised him to add long acting basal insulin analogue to metformin, reached to 40U/day .
- Other current medical conditions include: hypertension, hypothyroidism, and mild osteoporosis without fracture history.
- Current medications; Metformin 1000 mg bid, long acting basal insulin analogue 40U/day , Candesartan 16 mg qd, Alendronate 70 mg once weekly, Levothyroxine 100 mg qd.
- Physical exam: BMI 26 kg/m2, BP 140/80 mmHg, otherwise unremarkable.
- His current FPG 140 mg/dL and HbA1c 8.5%. Kidney and liver functions are normal.

Does his age should be a concern and why ?

What Kind of Care should this patient receive specifically ?

Q1. Based on the patient's age, physical examination, history, and laboratory values, what is an appropriate glycemic target for him?

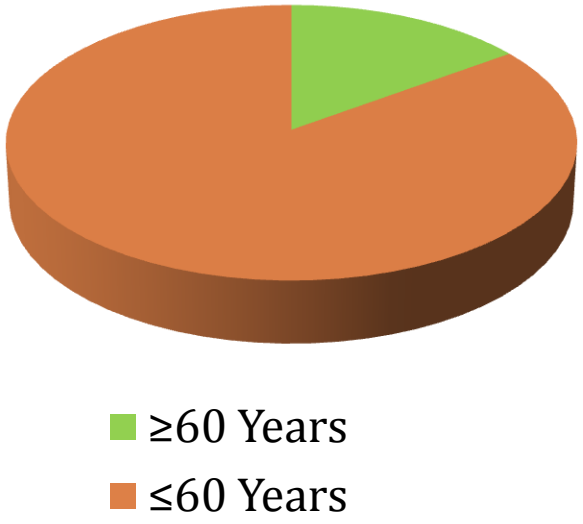
A. 9.0%
B. 8.0%
C. 7.0%
D. 6.5%
E. 7-8%

Q2. Do you think increasing insulin dose is the best choice for Mr. A.H.?

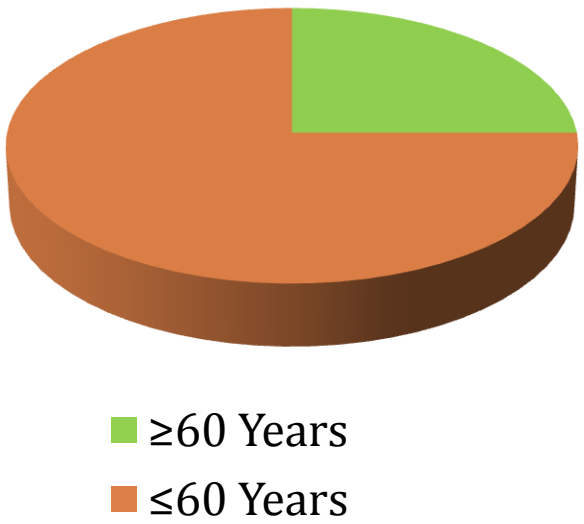
A. Yes
B. No

Increasing in the proportions of older persons (60 years or older)

2013



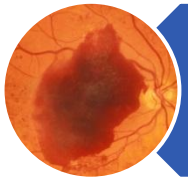
2050



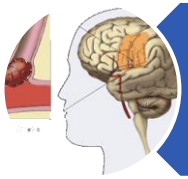
These changes present significant challenges to welfare, pension, and healthcare systems in both developing and developed nations

Diabetes-related complications are common in the elderly

- Diabetes-related complications are the major causes of morbidity, disability and mortality in older patients with type 2 diabetes:



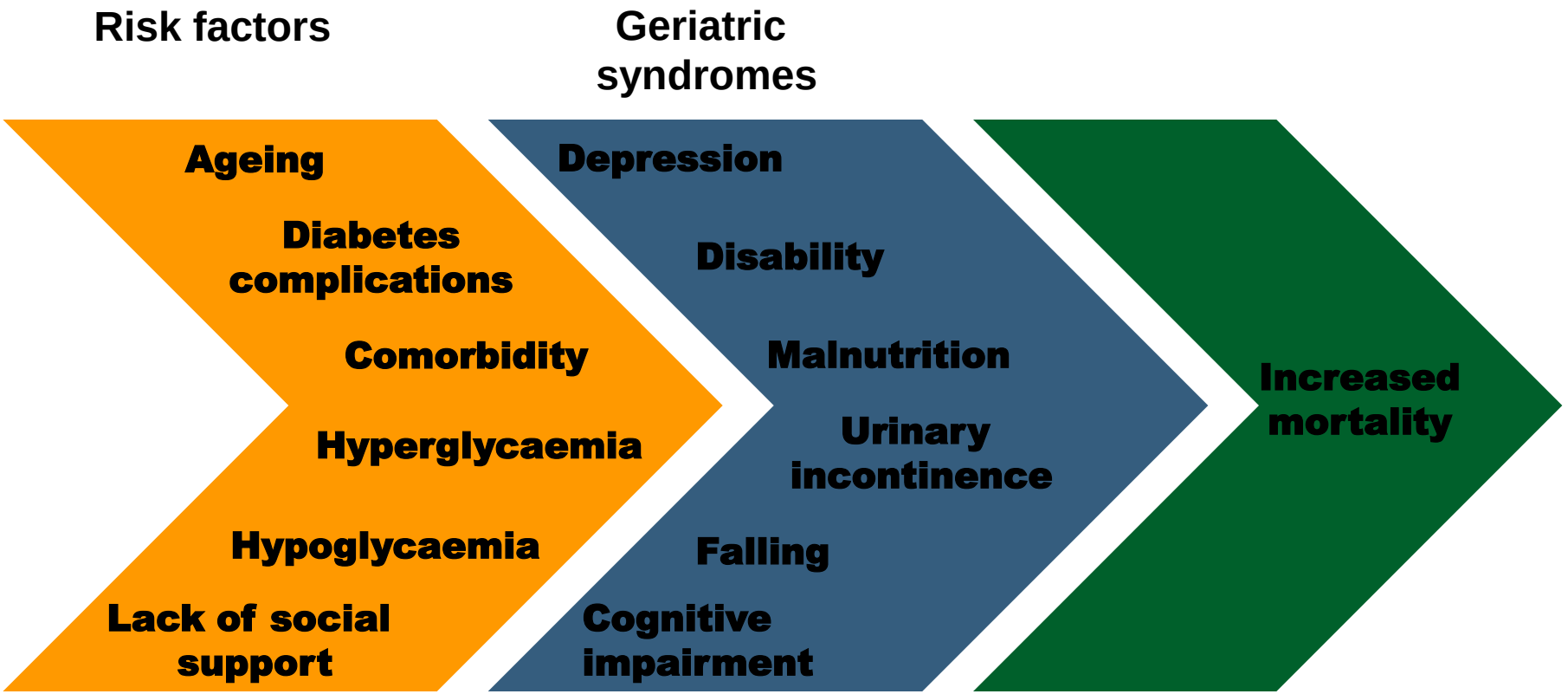
Microvascular: Neuropathy,Retinopathy,Nephropathy



Macrovascular: Cardiovascular disease, Stroke

- There is now overwhelming evidence that the level and duration of glycemia influences the development of diabetes-related complications

The management of T2DM in the elderly is challenging

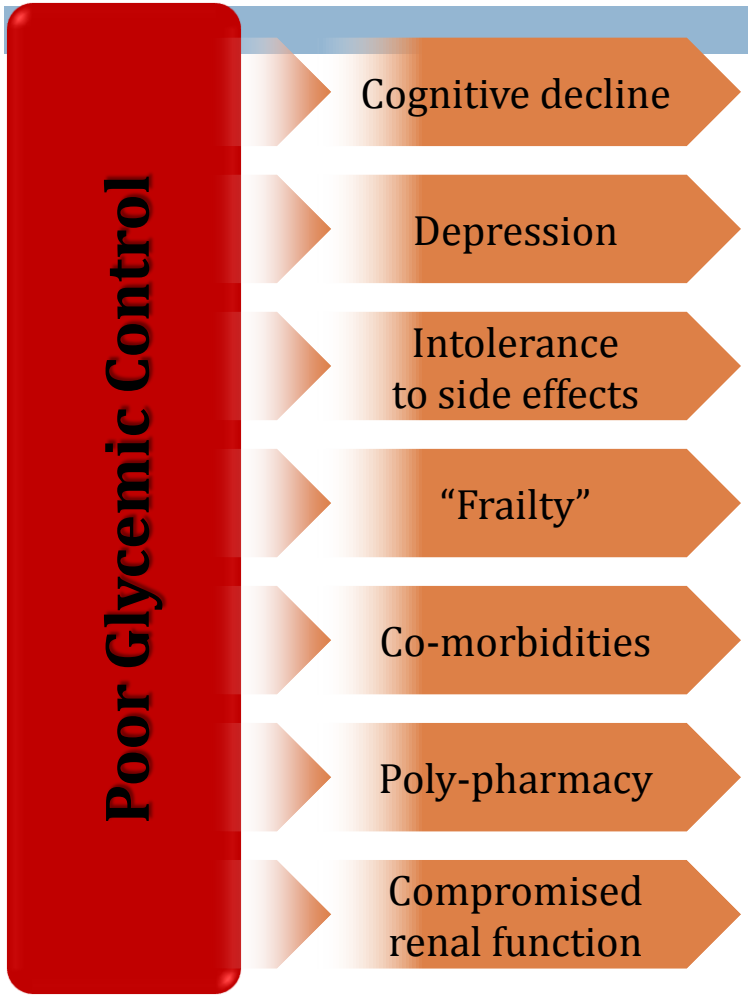


Ageing, diabetic microvascular and macrovascular complications, hyperglycaemia, hypoglycaemia, multiple morbidity and lack of social support are risk factors for the geriatric syndromes

T2DM=type 2 diabetes mellitus.

Araki A, Ito H. *Geriatr Gerontol Int.* 2009; 9: 105–114.

The achievement of good glycemic control in the elderly is challenging



1. Gregg et al. Arch Intern med 2000 ; 160 : 174-80; 2. Ott et al. Diabetologia 1999 ; 53 : 1937-42
3. Rockwood et al. Drugs Aging 2000 ; 17 : 295-302; 4. Wolff et al. Arch Intern med 2002 ; 162 : 2269-76
5. Shorr et al. Arch Intern med 1997 ; 157 : 1681-6

Hypoglycaemia is a major challenge in the treatment of diabetes in the elderly

I. Patient risk factors

- Advanced age
- Recent hospitalization
- Intercurrent illness
- Chronic liver, renal or cardiovascular disease
- Endocrine deficiency (thyroid, adrenal, pituitary)
- Loss of normal counter-regulation
- Hypoglycaemic unawareness

II. Lifestyle risk factors

- Poor nutrition or fasting
- Prolonged physical exercise
- Alcohol (ethanol)

III. Drug risk factors

- Use of SU and / or insulin
- Drug interactions with SUs

Mortality and CV risk associated with different insulin secretagogues compared with metformin in type 2 diabetes

- All subjects initiating single-agent insulin secretagogues or metformin between 1997- 2006 were followed for up to 9 years (median 3.3 years).
- A total of 1,07,806 subjects were included, of whom 9607 had previous MI.

Sulfonylurea	No prior MI	Prior MI
Glimepiride	1.27 (1.18-1.36)	1.30 (1.08-1.57)
Glibenclamide	1.13 (1.02-1.25)	1.34 (1.03-1.75)
Glipizide	1.16 (1.03-1.30)	1.58 (1.19-2.09)
Tolbutamide	1.12 (0.99-1.26)	1.46 (1.06-2.01)
Gliclazide	1.05 (0.91-1.21)	0.85 (0.61-1.17)
Repaglinide	1.00 (0.78-1.29)	1.15 (0.68-1.98)

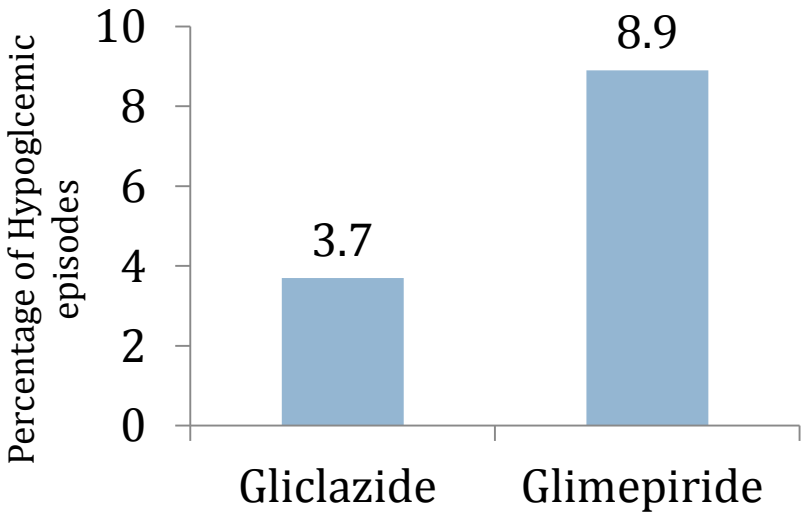
among st all SUs

Schramm TK et al. Eur Heart J. 2011 Aug;32(15):1900-8

GUIDE study: double-blind comparison of once-daily gliclazide MR and glimepiride in type 2 diabetes

- The European GUIDE study is the first large-scale head-to-head comparison of two sulphonylureas designed for once-daily administration.
- The safety of gliclazide MR was significantly better, demonstrating approximately 50% fewer confirmed hypoglycaemic episodes in comparison with glimepiride

Fig. 1: Incidence of Hypoglycemia



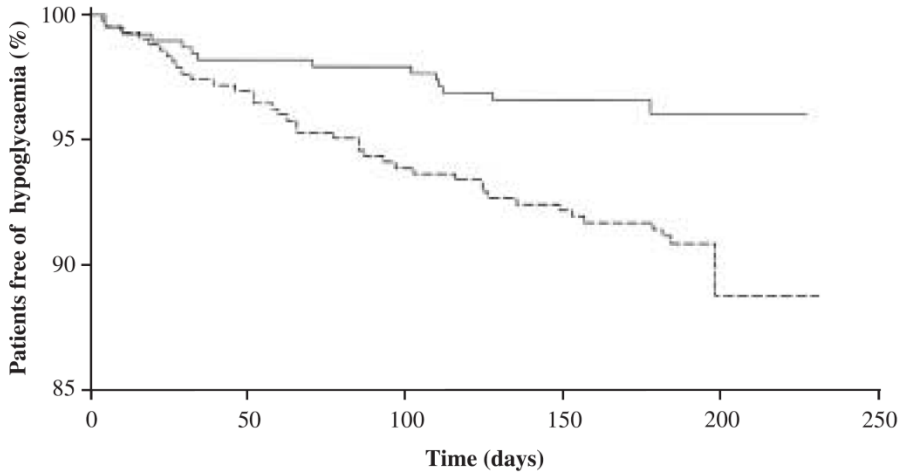


Figure 2 Kaplan–Meier curves for time to appearance of the first hypoglycaemia with blood glucose level < 3 mmol L^{-1}. —: gliclazide MR; - -: glimepiride. Wilcoxon test, $P = 0{\cdot}004$.

Schernthaner G et al. Eur J Clin Invest 2004Aug;34(8):535-4

GUIDE (GlUcose control in type 2 diabetes: Diamicron MR vs. glimEpiride)

Sulfonylureas in the management of type 2 diabetes mellitus in South Asia – A consensus statement

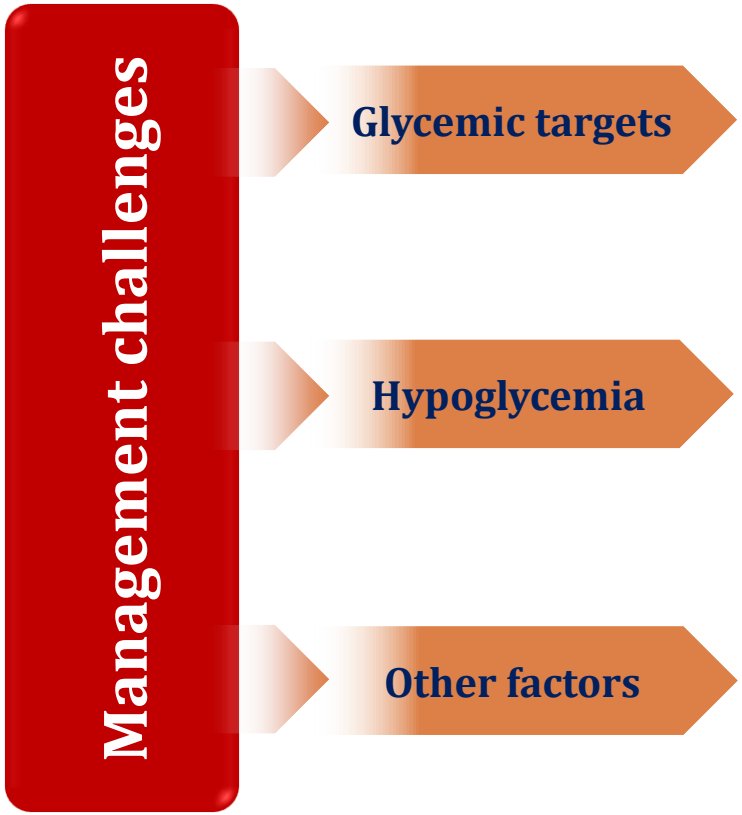
An initiative of South Asian Federation of Endocrine Societies (SAFES)

Preferred Sulfonylureas

- B1. Modern SUs (Glimepiride and Gliclazide MR) should be preferred over conventional SUs in view of the reduced mortality (all-cause and CV mortality), better CV outcomes (composite of acute myocardial infarction, stroke, and CV mortality), and renal protection (Grade A; EL 1).
- B2. Modern SUs (Glimepiride and Gliclazide MR) should be preferred over conventional SUs in T2DM patients at increased risk of hypoglycemia (Grade A; EL 1).
- B3. Modern SUs (Glimepiride and Gliclazide MR) should be the preferred choice of SU in overweight/obese T2DM patients (Grade A; EL 1).
- B4. Modern SUs (Glimepiride and Gliclazide MR) should be preferred over conventional SUs in patients at increased risk of cardiovascular disease (CVD) or with CVD (Grade A; EL 2).

Kalra S et al. Indian J Endocr Metab 2015;19:577-96.

So, Management challenges can lead to cautious prescriptions in the elderly



ADA 2017 recommendations in Older Adults

Recommendations

- Consider the assessment of medical, mental, functional, and social geriatric domains in older adults to provide a framework to determine targets and therapeutic approaches for diabetes management. C
- Screening for geriatric syndromes may be appropriate in older adults experiencing limitations in their basic and instrumental activities of daily living, as they may affect diabetes self-management and be related to health-related quality of life. C
- Annual screening for early detection of mild cognitive impairment or dementia is indicated for adults 65 years of age or older. B
- Older adults (≥65 years of age) with diabetes should be considered a high-priority population for depression screening and treatment. B
- Hypoglycemia should be avoided in older adults with diabetes. It should be assessed and managed by adjusting glycemic targets and pharmacologic interventions. B
- Older adults who are cognitively and functionally intact and have significant life expectancy may receive diabetes care with goals similar to those developed for younger adults. C
- Glycemic goals for some older adults might reasonably be relaxed using individual criteria, but hyperglycemia leading to symptoms or risk of acute hyperglycemic complications should be avoided in all patients. C

ADA 2017 recommendations in Older Adults

- Screening for diabetes complications should be individualized in older adults. Particular attention should be paid to complications that would lead to functional impairment. C
- Treatment of hypertension to individualized target levels is indicated in most older adults. C
- Treatment of other cardiovascular risk factors should be individualized in older adults considering the time frame of benefit. Lipid-lowering therapy and aspirin therapy may benefit those with life expectancies at least equal to the time frame of primary prevention or secondary intervention trials. E
- When palliative care is needed in older adults with diabetes, strict blood pressure control may not be necessary, and withdrawal of therapy may be appropriate. Similarly, the intensity of lipid management can be relaxed, and withdrawal of lipid-lowering therapy may be appropriate. E
- Consider diabetes education for the staff of long-term care facilities to improve the management of older adults with diabetes. E
- Patients with diabetes residing in long-term care facilities need careful assessment to establish glycemic goals and to make appropriate choices of glucose-lowering agents based on their clinical and functional status. E
- Overall comfort, prevention of distressing symptoms, and preservation of quality of life and dignity are primary goals for diabetes management at the end of life. E

ADA 2017 recommendations in Older Adults

Table 11.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

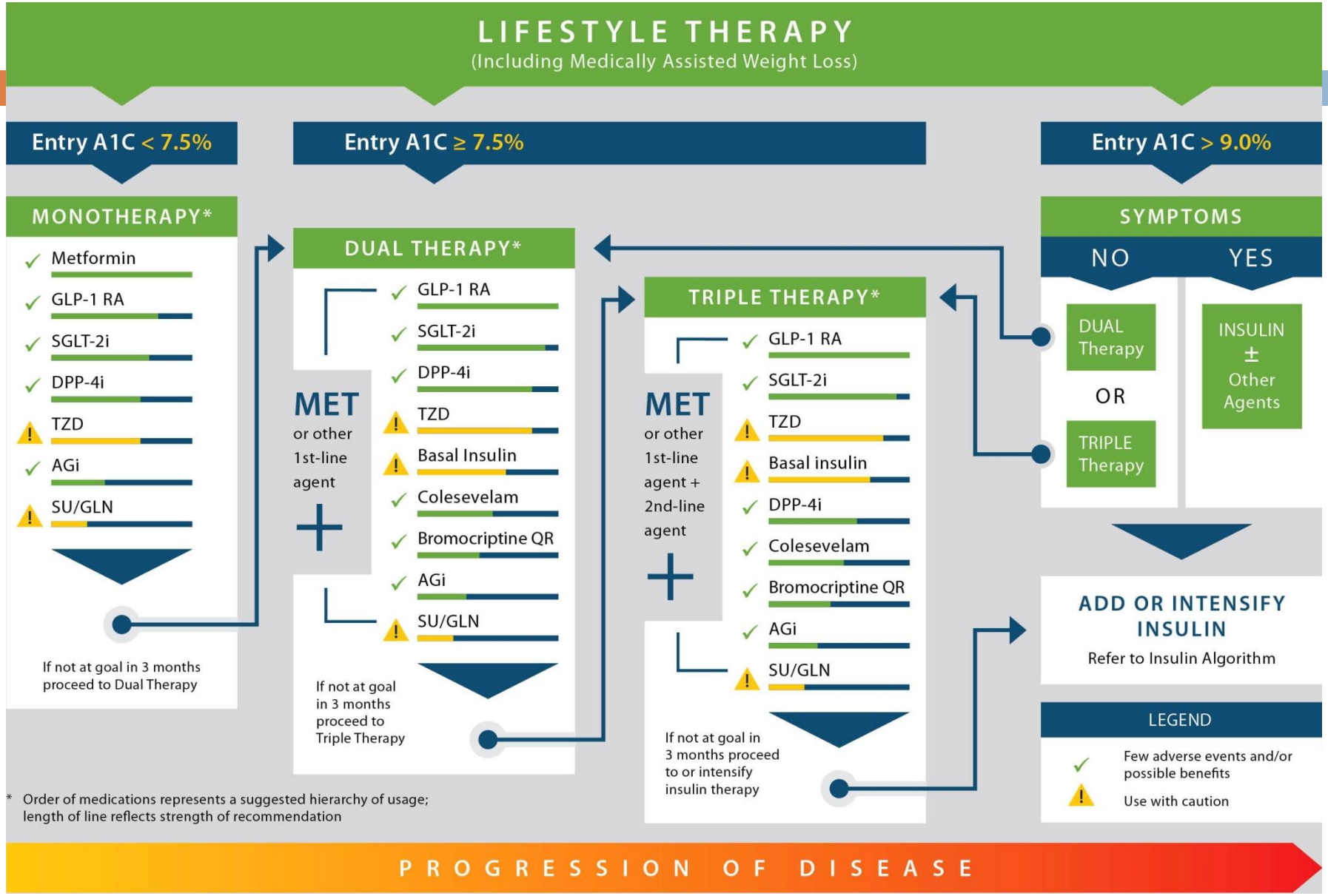
Patient characteristics/health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Bl
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)	90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<1
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<1
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<1

This represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The patient every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualizat preferences may change over time. ADL, activities of daily living. ‡A lower A1C goal may be set for an individual if achievable without recurrent or severe hypo chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, d incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By "multiple," we mean at least three, but many patients may have five chronic illness, such as stage 3–4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metas impairment of functional status and significantly reduce life expectancy. †A1C of 8.5% (69 mmol/mol) equates to an estimated average glucose of ~200 mg/ 8.5% (69 mmol/mol) are not recommended as they may expose patients to more frequent higher glucose values and the acute risks from glycosuria, dehydr and poor wound healing.

Diabetes Care 2017;40(Suppl. 1):S99–S104

DIABETES MANAGEMENT

GLYCEMIC CONTROL ALGORITHM



Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.

PRINCIPLES OF AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

1.	Lifestyle therapy, including medically supervised weight loss, is key to managing type 2 diabetes.
2.	The A1C target must be individualized.
3.	Glycemic control targets include fasting and postprandial glucoses.
4.	The choice of therapies must be individualized on basis of patient characteristics, impact of net cost to patient, formulary restrictions, personal preferences, etc.
5.	Minimizing risk of hypoglycemia is a priority.
6.	Minimizing risk of weight gain is a priority.
7.	Initial acquisition cost of medications is only a part of the total cost of care which includes monitoring requirements, risk of hypoglycemia, weight gain, safety, etc.
8.	This algorithm stratifies choice of therapies based on initial A1C.
9.	Combination therapy is usually required and should involve agents with complementary actions.
10.	Comprehensive management includes lipid and blood pressure therapies and related comorbidities.
11.	Therapy must be evaluated frequently until stable (e.g., every 3 months) and then less often.
12.	The therapeutic regimen should be as simple as possible to optimize adherence.
13.	This algorithm includes every FDA-approved class of medications for diabetes.

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Oral Hypoglycemic Agents for T2D

Class	Primary Mechanism of Action	Agent(s)	Available as
α-Glucosidase inhibitors	• Delay carbohydrate absorption from intestine	Acarbose Miglitol	Precose or generic Glyset
Amylin analogue	• Decrease glucagon secretion • Slow gastric emptying • Increase satiety	Pramlintide	Symlin
Biguanide	• Decrease HGP • Increase glucose uptake in muscle	Metformin	Glucophage or generic
Bile acid sequestrant	• Decrease HGP? • Increase incretin levels?	Colesevelam	WelChol
DPP-4 inhibitors	• Increase glucose-dependent insulin secretion • Decrease glucagon secretion	Alogliptin Linagliptin Saxagliptin Sitagliptin	Nesina Tradjenta Onglyza Januvia
Dopamine-2 agonist	• Activates dopaminergic receptors	Bromocriptine	Cycloset
Glinides	• Increase insulin secretion	Nateglinide Repaglinide	Starlix or generic Prandin

DPP-4 = dipeptidyl peptidase; HGP = hepatic glucose production.

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Oral Hypoglycemic Agents for T2D

Class	Primary Mechanism of Action	Agent(s)	Available as
GLP-1 receptor agonists	• Increase glucose-dependent insulin secretion • Decrease glucagon secretion • Slow gastric emptying • Increase satiety	Albiglutide Dulaglutide Exenatide Exenatide XR Liraglutide	Tanzeum Trulicity Byetta Bydureon Victoza
SGLT2 inhibitors	• Increase urinary excretion of glucose	Canagliflozin Dapagliflozin Empagliflozin	Invokana Farxiga Jardiance
Sulfonylureas	• Increase insulin secretion	Glimepiride Glipizide Glyburide	Amaryl or generic Glucotrol or generic Diaβeta, Glynase, Micronase, or generic
Thiazolidinediones	• Increase glucose uptake in muscle and fat • Decrease HGP	Pioglitazone Rosiglitazone	Actos Avandia

GLP-1 = glucagon-like peptide; HGP = hepatic glucose production; SGLT2 = sodium glucose cotransporter 2.

Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.

PROFILE OF ANTIDIABETIC MEDICATIONS

	MET	GLP-1 RA	SGLT-2i	DPP-4i	AGi	TZD (moderate dose)	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL/ GU	Contra-indicated CKD Stage 3B,4,5	Exenatide Not Indicated CrCl < 30	Not Effective with eGFR < 45 / Genital Mycotic Infections	Dose Adjustment Necessary (Except Linagliptin)	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF	Neutral	Neutral	Possible Benefit	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral
CARDIAC ASCVD	Benefit					Neutral	?		Safe		
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Fracture Risk	Neutral	Neutral	Neutral	Neutral	Neutral

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

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Effects of Agents Available for T2D

	Met	GLP1RA	SGLT2I	DPP4I	TZD	AGI	Coles	BCR-QR	SU/ Glinide	Insulin	Pram
FPG lowering	Mod	Mild to mod*	Mod	Mild	Mod	Neutral	Mild	Neutral	SU: mod Glinide: mild	Mod to marked (basal insulin or premixed)	Mild
PPG lowering	Mild	Mod to marked	Mild	Mod	Mild	Mod	Mild	Mild	Mod	Mod to marked (short/ rapid-acting insulin or premixed)	Mod to marked

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; DPP4I = dipeptidyl peptidase 4 inhibitors; FPG = fasting plasma glucose; GLP1RA = glucagon-like peptide 1 receptor agonists; Met = metformin; Mod = moderate; PPG = postprandial glucose; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Mild: albiglutide and exenatide; moderate: dulaglutide, exenatide extended release, and liraglutide.

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Effects of Agents Available for T2D

	Met	GLP1RA	SGLT2I	DPP4I	TZD	AGI	Coles	BCR-QR	SU/ Glinide	Insulin	Pram
NAFLD benefit	Mild	Mild	Neutral	Neutral	Mod	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
Hypo-glycemia	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	SU: mod to severe Glinide: mild to mod	Mod to severe*	Neutral
Weight	Slight loss	Loss	Loss	Neutral	Gain	Neutral	Neutral	Neutral	Gain	Gain	Loss

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; DPP4I = dipeptidyl peptidase 4 inhibitors; GLP1RA = glucagon-like peptide 1 receptor agonists; Met = metformin; Mod = moderate; NAFLD, nonalcoholic fatty liver disease; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Especially with short/ rapid-acting or premixed.

Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.

Effects of Agents Available for T2D

	Met	GLP1RA	SGLT2I	DPP4I	TZD	AGI	Coles	BCR-QR	SU/ Glinide	Insulin	Pram
Renal impair-ment/ GU	Contra-indicated in stage 3B, 4, 5 CKD	Exenatide contra-indicated CrCl <30 mg/mL	GU infection risk	Dose adjust-ment (except lina-gliptin)	May worsen fluid retention	Neutral	Neutral	Neutral	Increased hypo-glycemia risk	Increased risks of hypo-glycemia and fluid retention	Neutral
GI adverse effects	Mod	Mod*	Neutral	Neutral*	Neutral	Mod	Mild	Mod	Neutral	Neutral	Mod
CHF	Neutral	Neutral	Neutral	Neutral†	Mod	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Possible benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Safe	?	Neutral	Neutral
Bone	Neutral	Neutral	Bone loss	Neutral	Mod bone loss	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; CHF = congestive heart failure; CVD = cardiovascular disease; DPP4I = dipeptidyl peptidase 4 inhibitors; GI = gastrointestinal; GLP1RA = glucagon-like peptide 1 receptor agonists; GU = genitourinary; Met = metformin; Mod = moderate; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Caution in labeling about pancreatitis.
†Caution: possibly increased CHF hospitalization risk seen in CV safety trial.

Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.

Monotherapy, Dual Therapy, and Triple Therapy for T2D

Monotherapy*	Dual therapy* Metformin (or other first-line agent) plus	Triple therapy* First- and second-line agent plus
Metformin	GLP1RA	GLP1RA
GLP1RA	SGLT2I	SGLT2I
SGLT2I	DPP4I	TZD†
DPP4I	TZD†	Basal insulin†
AGI	Basal insulin†	DPP4I
TZD†	Colesevelam	Colesevelam
SU/glinide†	BCR-QR	BCR-QR
	AGI	AGI
	SU/glinide†	SU/glinide†

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; DPP4I = dipeptidyl peptidase 4 inhibitors; GLP1RA = glucagon-like peptide 1 receptor agonists; Met = metformin; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Intensify therapy whenever A1C exceeds individualized target. Boldface denotes little or no risk of hypoglycemia or weight gain, few adverse events, and/or the possibility of benefits beyond glucose-lowering.

† Use with caution.

Garber AJ, et al Endocr Pract. 2017 Feb;23(2):207-238.

Conclusion

- Preventing diabetes is of enormous value for any nation particularly in the developing world because of the high cost of treating diabetes and its complication.
- Management of Diabetes in India faces multiple challenges, such as low levels of awareness, paucity of trained medical and paramedical staff and unaffordability of medications and services
- The need of the hour is to develop pragmatic, cost effective strategies for primary prevention to extend the benefits to the population at large.
- Novel interventions using readily available resources and technology promise to revolutionise the care of patients with diabetes in India.

Thank You