CAVEATS IN MANAGENT OF DIABETES

Moderator – Professor Tint Swe Latt

Panelists –

- Professor Ko Ko
- Professor Moe Wint Aung
- A. Professor Thein Myint

Diagnostic dilemma

Diabetes in children and adolescent

Professor Ko Ko

Type 1 Diabetes

- ¾ of all cases of T1DM are dx'd in patients <18 yrs.
- Distinguishing between type 1 and type 2 can be challenging.
- Diabetes-associated autoantibodies and ketosis may be present in patients with features of type 2 such as obesity and acanthosis nigricans.
- Accurate diagnosis is critical.

American Diabetes Association Standards of Medical Care in Diabetes. Children and adolescents. *Diabetes Care* 2017; 40 (Suppl. 1): S105-S113

Attention to

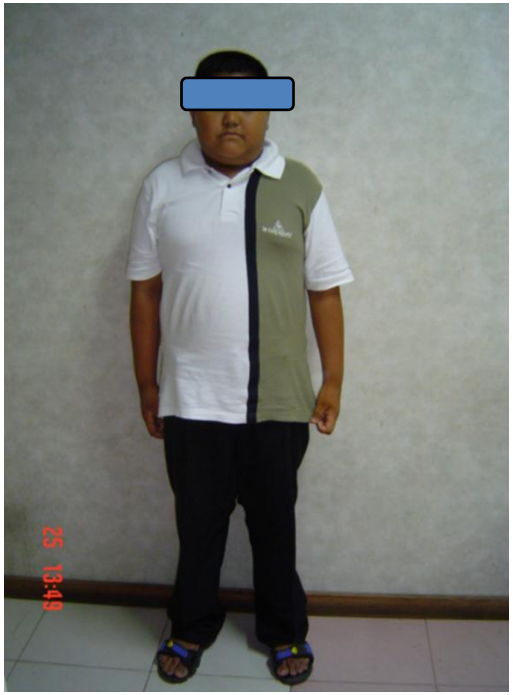
- Psychosocial issue(stress,depression,if need , Mental health professionals should be involved)
- Family involvement and encourage
- Assess for the presence of autoimmune conditions(thyroid,celiac disease) associated with type 1 diabetes soon after the diagnosis and if symptoms develop. E
- Screening for Hypertension(ACEIARB),Dyslipidemia(LDL<100)

retinopathy,nephropathy,neuropathy(after 5 years of diagnosis or >10 years)

- Discourage smoking in youth who do not smoke and encourage smoking cessation in those who do. B

Diagnosis
Type 1 or 2

- Testing for C-peptide levels
- Testing for antibodies
  - GAD-65
  - IA2
  - Insulin
  - Islet-cell
- Trial of oral agents



Type 1 vs Type 2

Comparison of type 1 and 2 diabetes		
Feature	**Type 1 diabetes**	**Type 2 diabetes**
Onset	Sudden	Gradual
Age at onset	Any age (mostly young)	Mostly in adults
Body habitus	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased
Concordance in identical twins	50%	90%
Prevalence	Less prevalent	More prevalent - 90 to 95% of U.S. diabetics

Criteria for Testing for T2DM in Children & Adolescents

- Overweight plus any 2 :
  - Family history of type 2 diabetes in 1st or 2nd degree relative
  - Race/ethnicity
  - Signs of insulin resistance or conditions associated with insulin resistance
  - Maternal history of diabetes or GDM
- Age of initiation 10 years or at onset of puberty
- Frequency: every 3 years
- Test with FPG, OGTT, or A1C

American Diabetes Association Standards of Medical Care in Diabetes.
Classification and diagnosis of diabetes. Diabetes Care 2017; 40 (Suppl. 1): S11-S24

Recommendations: Monogenic Diabetes Syndromes

- All children diagnosed with diabetes in the first 6 months of life should have genetic testing for neonatal diabetes. A
- Children and adults, diagnosed in early adulthood, who have diabetes not characteristic of T1D or T2D that occurs in successive generations should have genetic testing for MODY. A

American Diabetes Association Standards of Medical Care in Diabetes. Classification and diagnosis of diabetes. Diabetes Care 2017; 40 (Suppl. 1): S11-S24

Definitions: T1D, 'LADA', T2D

May Seem Precise BUT…, Overlapping Phenotypes

In particular :

'LADA'- Ambiguous classification

- Later age; SPIDDM, 'Slowly progressive T1D
  - 'Slower' destruction of β-cells than T1D
- Antibody positive T2D = 'T1.5D'
  - 'Faster' destruction of β-cells than in T2D
- T-cell abnormal SPIDDM
  - Antibody negative
- Insulin commonly considered the 'go to' drug, even in patients with LADA with retained β-cell function

Distinct Etiologies and Characteristics

	T1D	'LADA'	T2D	MODY
Typical Age of Onset	All Ages	Usually Age >30	Adults	Usually Age <25
% of all Diabetes	10%	10%	75%	5%
Typical BMI	Mostly Normal or Thin	Mostly Normal or Overweight	Mostly Overweight or Obese	Mostly normal
Ethnicity	All	All	All	All
Progression to insulin Dependence	Fast (Days/Week)	Latent (Months/Years)	Slow (Years)	Depends on MODY type
Insulin Resistance	Mostly no; ~10% ,yes	Some	Yes	Depends on MODY type
Presence of Autoantibodies	Yes (ICA, IA2, GAD65, IAA)	Yes (mostly GAD65), Some not	Some	No
T cell Reponses to islet proteins	Yes	Yes	No	No
Insulin/ C-peptides Level at diagnosis	Undectable or extermely low	Low	Normal to High	Normal
Ketoacidosis	Yes	Yes, many not all	Rare	Rare
Insulin Secretion	Low/null	Varies	Varies	Varies
Islet Inflammation	Chronic Inflammation	Chronic Inflammation	Chronic Inflammation	None
HLA Link	High	Low	None	None
TCF7L2 Link	None	In some pop'n, stronger link than T2D	?5%	None
Other Genes Involved	*PTPN22; INS; CTLA4; CCR5; FOXP3;CLEC16a HNF1A; IL2RA; IL6; ITPR3; OAS1; SUMO4*	*PTPN22; INS*	*PPARG; JAZF1; KCNJ11; NOTCH2; WFS1; IGF2BP2; FTO; SLC30A8; HHEX*	*HNF4A; GCK; HNF1A; IPF1; HNF1B; NEUROD1*
Early Treatment	Insulin required, diet & exercise helpful	Non-Insulin or insulin, diet & exercise helpful	Non-Insulin, diet & increased activity	Gene Specific
Late Treatment	Insulin, diet, exercise	Insulin, pills, diet, exercise	Insulin, pills, diet, exercise	Gene Specific

Type 1 Diabetes: Glycemic Control

Blood glucose goal range		A1C	Rationale
Before meals	Bedtime/ overnight		
90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<7.5%	A lower goal (<7.0%) is reasonable if it can be achieved without excessive hypos

1. **Goals should be individualized; lower goals may be reasonable.**
2. **Modify BG goals in youth w/ frequent hypos or hypoglycemia unawareness.**
3. **Measure postprandial BG if discrepancy between preprandial BG and A1C & to assess glycemia in basal–bolus regimens.**

American Diabetes Association Standards of Medical Care in Diabetes. Children and adolescents. *Diabetes Care* 2017; 40 (Suppl. 1): S105-S113

Recommendations: Pharmacologic Therapy For Type 1 Diabetes

- Most people with T1DM should be treated with multiple daily injections of prandial insulin and basal insulin or continuous subcutaneous insulin infusion (CSII). A
- Most individuals with T1DM should use insulin analogs to reduce hypoglycemia risk. A
- Health care providers and families should begin to prepare youth in early to mid-adolescence and, at the latest, at least 1 year before the transition to adult health care. E

American Diabetes Association Standards of Medical Care in Diabetes.
Approaches to glycemic treatment. Diabetes Care 2017; 40 (Suppl. 1): S64-S74

Changes in pathogenesis

Newer understandings of causes of DM and mechanisms of hyperglycemia

Precision Medicine

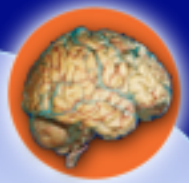
Ominous Octets to Egregious Eleven

Potential Causes of Insulin Resistance and Their Interplay

Weight Reduction Agents

Central IR

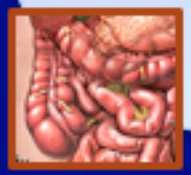
Loss of dopamine surge in SCN
increased appetite
Increased sympathetic tone



Bromocriptine-QR

Hyperinsulinemia

Biome IR



Pro-Biotics,
Pre-Biotics,
Antibiotics

Peripheral IR

TZD (Pio-) ,
Metformin

Inflammation IR

Anti-Inflammatories
Immune modulators

B. β-*Cell-Centric Construct: Egregious Eleven*

Targeted Treatments for Mediating Pathways of Hyperglycemia

1. Pancreatic β-cells
↓ β-Cell function
↓ β-Cell mass
Insulin
Incretins, Ranolazine
FINAL COMMON DENOMINATOR

2. ↓Incretin effect
Incretins

3. α-cell defect
↑ Glucagon
Incretins
Pramlintide

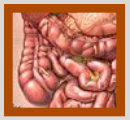
4. Adipose
TZDs
Metformin

5. Muscle
TZDs
Metformin

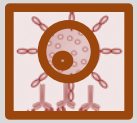
6. Liver
Metformin
TZDs

7. Brain
Incretins
Dopamine agonist-QR
Appetite Suppressants

8. Colon/Biome
Probiotics
Incretins
Metformin



9. Immune Dysregulation/ Inflammation
Incretins,
Anti-Inflammatories
Immune modulators



10. Stomach/ Small intestine
GLP-1 Agonists
Pramlintide
AGI

11. Kidney
SGLT2 inhibitors

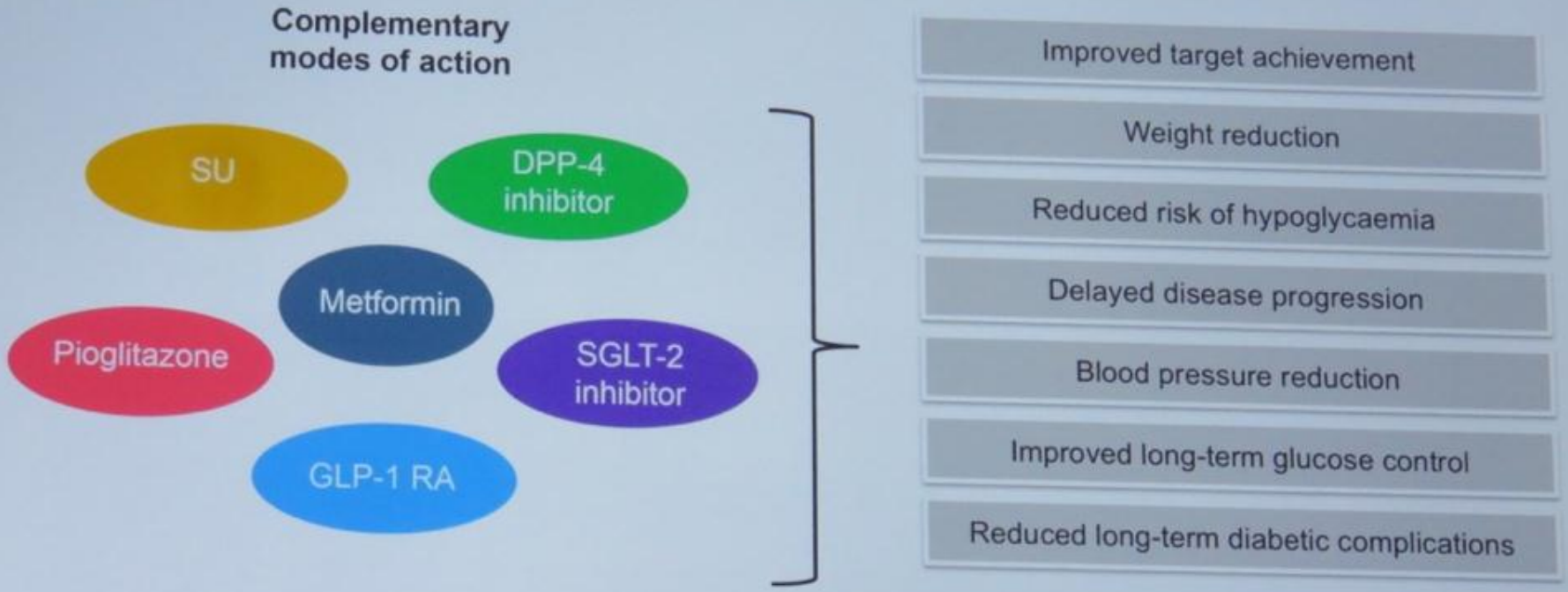
↓Amylin

HYPERGLYCEMIA

INSULIN RESISTANCE

Not competition betw. Classes; early combination

Combining treatments with complementary modes of action may demonstrate clinical benefits in the treatment of type 2 diabetes



Phung OJ, *et al. Diabetes Obes Metab* 2014;16:410–17.

Diabetes in elderly

Professor Moe Wint Aung

Diabetes and the Elderly

- Diabetes mellitus (DM) frequency is a growing problem worldwide, because of long life expectancy and life style modifications. In old age (≥60–65 years old), DM is becoming an alarming public health problem in developed and even in developing countries
- People with diabetes have higher incidence of all-cause dementia, Alzheimer's disease and vascular dementia than people with normal glucose tolerance

- Effects of hyperglycemia and hyperinsulinaemia are area of research
- Alzheimer disease seems to share the same risk factors as DM, which means insulin resistance due to lack of physical activity and eating disorders. Visual and physical handicaps, depression, and memory troubles are a barrier to care for DM treatment
- Cognitive dysfunction makes it difficult to perform complex self-care tasks, glucose monitoring and adjusting insulin dose,
- also hinders the ability to maintain the timing and content of diet

Recommendation

- Hypoglycemia should be avoided in older adults with diabetes. It should be assessed and managed by adjusting glycemic targets and pharmacologic interventions. C
- Healthy older adults with few coexisting chronic illness and intact cognitive function and good functional status. A1C <7.5(58mmol/mol). C
- Those with multiple coexisting chronic illness, cognitive impairment and poor functional status.A1C <8.0 to 8.5% (64-69mmol/mol) .C

- Treatment of hypertension to individualized target level 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. C.
- There is less evidence for lipid lowering therapy and aspirin therapy
- For patients receiving palliative care and end-of-life care, the focus should be to avoid symptoms and complications from glycemic management.

- In older adults at increased risk of hypoglycemia, medication classes with low risk of hypoglycemia are preferred. B
- Overtreatment of diabetes in older adults is common and should be avoided. B
- the fundamental rule is “go slowly and individualize” to avoid interaction with poly medicated elder persons and fatal iatrogenic hypoglycemias in those treated with sulfonylureas or insulin.

- Depression screening in the elderly population with diabetes is of great importance, as elderly patients with diabetes experience more isolation, less support, and more feeling of hopelessness
- The elderly with diabetes who are capable of activities of daily living without assistance, and who have no cognitive impairment should have A1C and blood sugar goals similar to that of a younger person.

Choice of therapy

- Metformin – first line agent for older people with DM, can safely used until GFR > or = 30ml/min
- Thiazolidinediones – not a good choice with risk of falls and fractures, contraindicated in CHF
- Insulin secretogauges – sulphonylureas aand others should be used with caution as risk of hypoglycemia, short acting ones are preferably used
- Incretin based therapies –oral DPP4 inhibitor has few side effects and minimal hypoglycemia, but cost may be barrier to some older patients
- SGLT2 inhibitors may be convenient for older adults but risk of genital fungal infections and UTI, euglycemic DKA, as well as long term experience is limited

Injectable therapy

- Multiple injections are complex and limited to the older adults who has reduced visual, motor and cognitive skills, even burden to the care givers
- Once daily basal injections may be useful of simplicity and low risk of hypoglucemia
- Well structured regime, timing and adjustment scheme should be educated to the care givers
- GLP1 agonists can cause nausea, vomiting and pancreatic side effects, so not a good choice for older adults with diabetes

SMBG

Dr Thein Myint

Method of assessment of glycaemic control

- SMBG – Self-monitoring of blood glucose
- CGM – Continuous glucose monitoring
- HbA1C

American Diabetes Association®
ADA 2018

SMBG – Self-monitoring of blood glucose

Recommendations

- **Patients with intensive insulin regimens**
  - prior to meals and snacks,
  - at bedtime,
  - **occasionally** postprandially,
  - prior to exercise and critical tasks such as driving
  - When suspect and after treating low blood glucose until they are normoglycemic
- **T2DM using oral agents and/or basal insulin**
  - No evidence for when and how SMBG

American Diabetes Association®

ADA 2018

SMBG – Self-monitoring of blood glucose

Less frequent insulin injections or non-insulin Rx

- **help guide**
  - treatment decisions and/or
  - self-management for patients
- **SMBG allows patients to**
  - evaluate their individual response to therapy and
  - assess whether glycemic targets are being achieved.
- **Integrating SMBG results into diabetes management can be a useful tool for**
  - guiding medical nutrition therapy and physical activity,
  - preventing hypoglycemia, and
  - adjusting medications (particularly prandial insulin doses)
- **Type 1 diabetes,**
  - greater SMBG frequency → lower A1C

American Diabetes Association®

ADA 2018

SMBG – Self-monitoring of blood glucose

Recommendations

Less frequent insulin injections or non-insulin Rx

- **When prescribing SMBG, ensure that**
  - patients receive ongoing instruction and
  - regular evaluation of
    - SMBG technique,
    - SMBG results, and
    - their ability to use SMBG data to adjust therapy

Which one first ?– FBS or 2HPP

Fix Fasting First

Why

- Safer
- Simpler

[Lowering FPG first will lower all PG values throughout the day and thus will also reduce PPG and may be sufficient.]

- Which one is important?

- FPG ------for microvascular complication
- 2HPP ----for macrovascular complication (mainly CVS)

Both are important

Therapeutic dilemma

Changes in 2018 Standard care

Professor Ko Ko

Changes in 2018 Standard care

- Post transplant DM
- Hypoglycemia
- Obesity Mx(Metabolic Surgery)
- Empagliflozin and Liraglutide to reduce cardiovascular risk

Classification of Hypoglycemia

Table 6.3—Classification of hypoglycemia (61)

Level	Glycemic criteria	Description
Glucose alert value (level 1)	≤70 mg/dL (3.9 mmol/L)	Sufficiently low for treatment with fast-acting carbohydrate and dose adjustment of glucose-lowering therapy
Clinically significant hypoglycemia (level 2)	<54 mg/dL (3.0 mmol/L)	Sufficiently low to indicate serious, clinically important hypoglycemia
Severe hypoglycemia (level 3)	No specific glucose threshold	Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

Recommendations: Assessment

- At each patient encounter, BMI should be calculated and documented in the medical record. B
  - Discuss with the patient
  - Asian American cutpoints:

Normal	**<23 BMI kg/m^2**
Overweight	**23.0 - 27.4 kg/m^2**
Obese	**27.5 - 37.4 kg/m^2**
Extremely obese	**≥37.5 kg/m^2**

American Diabetes Association Standards of Medical Care in Diabetes. Obesity management for the treatment of type 2 diabetes. Diabetes Care 2017; 40 (Suppl. 1): S57-S63

Overweight/Obesity Treatment

	Body Mass Index Category (kg/m^2)				
Treatment	23.0* or 25.0-26.9	27.0-29.9	27.5* or 30.0-34.9	35.0-39.9	≥40
Diet, physical activity & behavioral therapy	┼	┼	┼	┼	┼
Pharmacotherapy		┼	┼	┼	┼
Metabolic surgery			┼	┼	┼

* Asian-American individuals

┼ Treatment may be indicated for selected, motivated patients.

American Diabetes Association Standards of Medical Care in Diabetes. Obesity management for the treatment of type 2 diabetes. Diabetes Care 2017; 40 (Suppl. 1): S57-S63

Recommendations: Pharmacotherapy

- Consider impact on weight when choosing glucose-lowering meds for overweight or obese patients. E
- Minimize the medications for comorbid conditions that are associated with weight gain. E
- Weight loss meds may be effective adjuncts to diet, physical activity & behavioral counseling for select patients. A

American Diabetes Association Standards of Medical Care in Diabetes. Obesity management for the treatment of type 2 diabetes. Diabetes Care 2017; 40 (Suppl. 1): S57-S63

Recommendations: Pharmacotherapy

- If patient response to weight loss medications <5% after 3 months or there are safety or tolerability issues at any time, discontinue medication and consider alternative medications or treatment approaches. A

American Diabetes Association Standards of Medical Care in Diabetes. Obesity management for the treatment of type 2 diabetes. Diabetes Care 2017; 40 (Suppl. 1): S57-S63

Metabolic Surgery

- Evidence supports gastrointestinal operations as effective treatments for overweight T2DM patients.
- Randomized controlled trials with postoperative follow-up ranging from 1 to 5 years have documented sustained diabetes remission in 30–63% of patients, though erosion of remission occurs in 35-50% or more.
- With or without diabetes relapse, the majority of patients who undergo surgery maintain substantial improvement of glycemic control for at least 5 to 15 years

American Diabetes Association Standards of Medical Care in Diabetes. Obesity management for the treatment of type 2 diabetes. Diabetes Care 2017; 40 (Suppl. 1): S57-S63

Recommendations: Metabolic Surgery

- Metabolic surgery *should be recommended* to treat T2DM for all appropriate surgical candidates with BMIs ≥ 40 (37.5*) and those with BMIs 35.0-39.9 (32.5-37.4*) when hyperglycemia is inadequately controlled despite lifestyle & optimal medical therapy. A
- Metabolic surgery *should be considered* for the treatment of T2DM in adults with BMIs 30-34.9 (27.5-32.4*) when hyperglycemia is inadequately controlled despite optimal medical control by either oral or injectable medications (including insulin). B
- Metabolic surgery should be performed in high-volume centers with multidisciplinary teams that understand and are experienced in the management of diabetes and gastrointestinal surgery. C

American Diabetes Association Standards of Medical Care in Diabetes. Obesity management for the treatment of type 2 diabetes. Diabetes Care 2017; 40 (Suppl. 1): S57-S63

New Recommendation: Pharmacologic Therapy For T2DM

- In patients with long-standing suboptimally controlled type 2 diabetes and established atherosclerotic cardiovascular disease, empagliflozin or liraglutide should be considered as they have been shown to reduce cardiovascular and all-cause mortality when added to standard care. Ongoing studies are investigating the cardiovascular benefits of other agents in these drug classes. B

American Diabetes Association Standards of Medical Care in Diabetes. Approaches to glycemic treatment. Diabetes Care 2017; 40 (Suppl. 1): S64-S74

Therapeutic dilemma

Fasting hyperglycemia

Professor Moe Wint Aung

Therapeutic dilemma

- **Fasting hyperglycemia-** Possible causes:
- Dawn phenomena
- Somogyi effect
- insufficient insulin the night before,
- insufficient anti-diabetic medication dosages
- carbohydrate snack consumption at bedtime.

- **Fasting hyperglycemia** is a phenomenon that has been occurred due to dysregulation of the normal circadian hormonal patterns resulting in increased hepatic glucose output
- generally can be attributed to inadequate or inappropriate hepatic insulinization or the **dawn phenomenon** (fasting hyperglycemia occurring in the absence of antecedent hypoglycemia). Less commonly, the **Somogyi effect** (marked fasting hyperglycemia following antecedent hypoglycemia)

Dawn Phenomenom

- Is a term to describe early morning hyperglycemia or an increase in amount of insulin needed to maintain normoglycemia, occurring in the absence of antecedent hypoglycemia or waning insulin level
- dawn phenomenon occurs when endogenous insulin secretion decreases
- In the early morning hours, hormones (growth hormone, cortisol, and catecholamines) cause the liver to release large amounts of sugar into the bloodstream. The most likely pathogenic mechanism is growth hormone –mediated impairment of insulin sensitivity at the liver and muscles.
- Approximately 54% of T1DM and 55% of T2DM patients experience the dawn phenomenom

Somogyi Effect

- **The somogyi effect** is caused by night time hypoglycemia, which leads to a rebound hyperglycemia in the early morning hours
- The Somogyi effect is a result of having extra insulin the body before bedtime, either from not having a bedtime snack, or from having your long-acting insulin not at the proper dose. The Somogyi effect occurs mainly with type 1 diabetics

How can you tell the difference?

- The Somogyi effect can occur any time you or your child has extra insulin in the body. To sort out whether an early morning high blood sugar level is caused by the dawn phenomenon or Somogyi effect, check blood sugar levels at bedtime, around 2 a.m. to 3 a.m., and at your normal wake-up time for several nights. A continuous glucose monitor could also be used throughout the night.
- If the blood sugar level is low at 2 a.m. to 3 a.m., suspect the Somogyi effect.
- If the blood sugar level is normal or high at 2 a.m. to 3 a.m., it's likely the dawn phenomenon.

Therapy

- Increase in the bed time doses of hypoglycemic agents with night time peak action may correct early morning hyperglycemia but associated with undesirable nocturnal hypoglycemia
- Using peakless basl insulin or continuous subcutaneous insulin infusion therapy can facilitate the prevention of early morning hyperglycemia

Therapeutic dilemma

Post prandial hyperglycemia

Professor Moe Wint Aung

Therapeutic dilemma

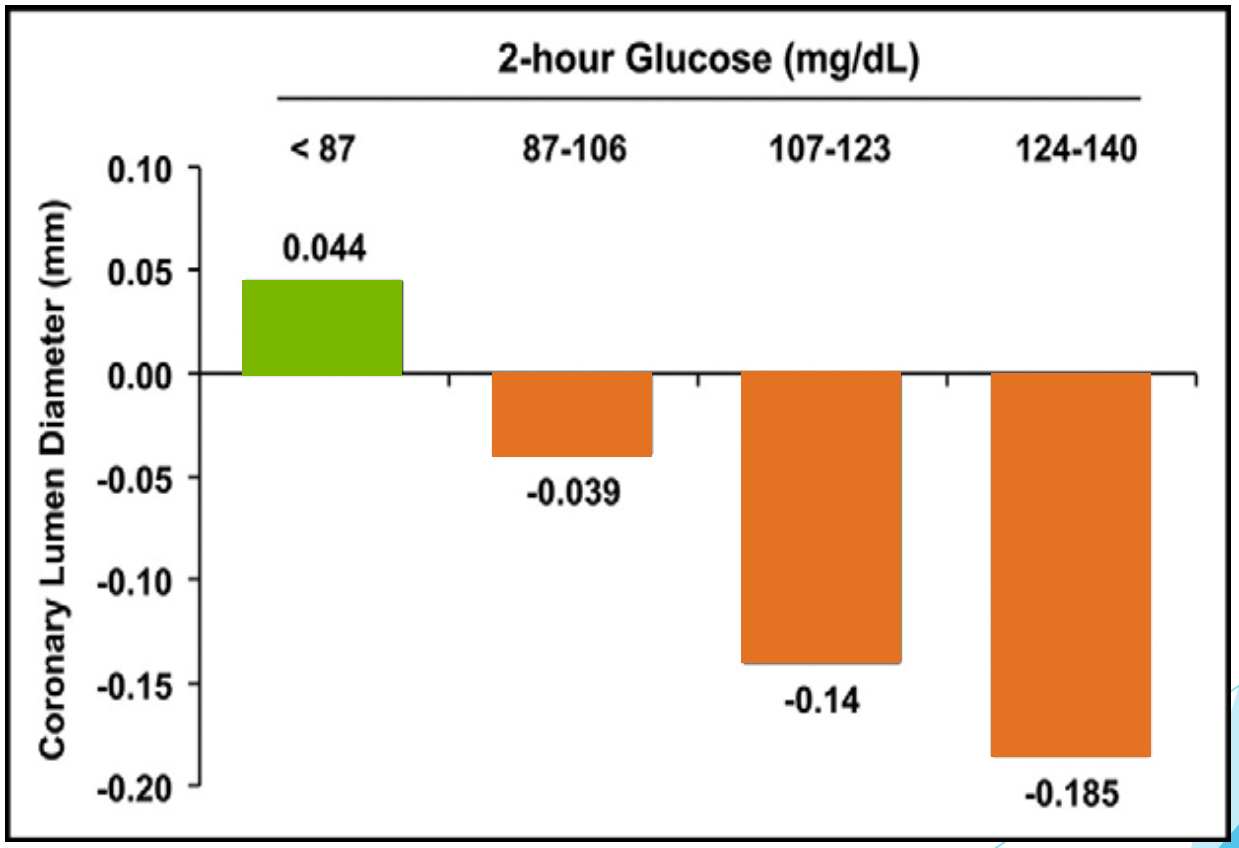
- **Post prandial hyperglycemia**
  - What is its significance?
  - What are the possible causes?
  - Approach to the postprandial hyperglycemia

What is the significance

- postprandial state is a contributing factor to the development of atherosclerosis. In diabetes, the postprandial phase is characterized by a rapid and large increase in blood glucose levels, and the possibility that the postprandial “hyperglycemic spikes” may be relevant to the onset of cardiovascular complications

Postprandial Hyperglycemia and Coronary Artery Disease

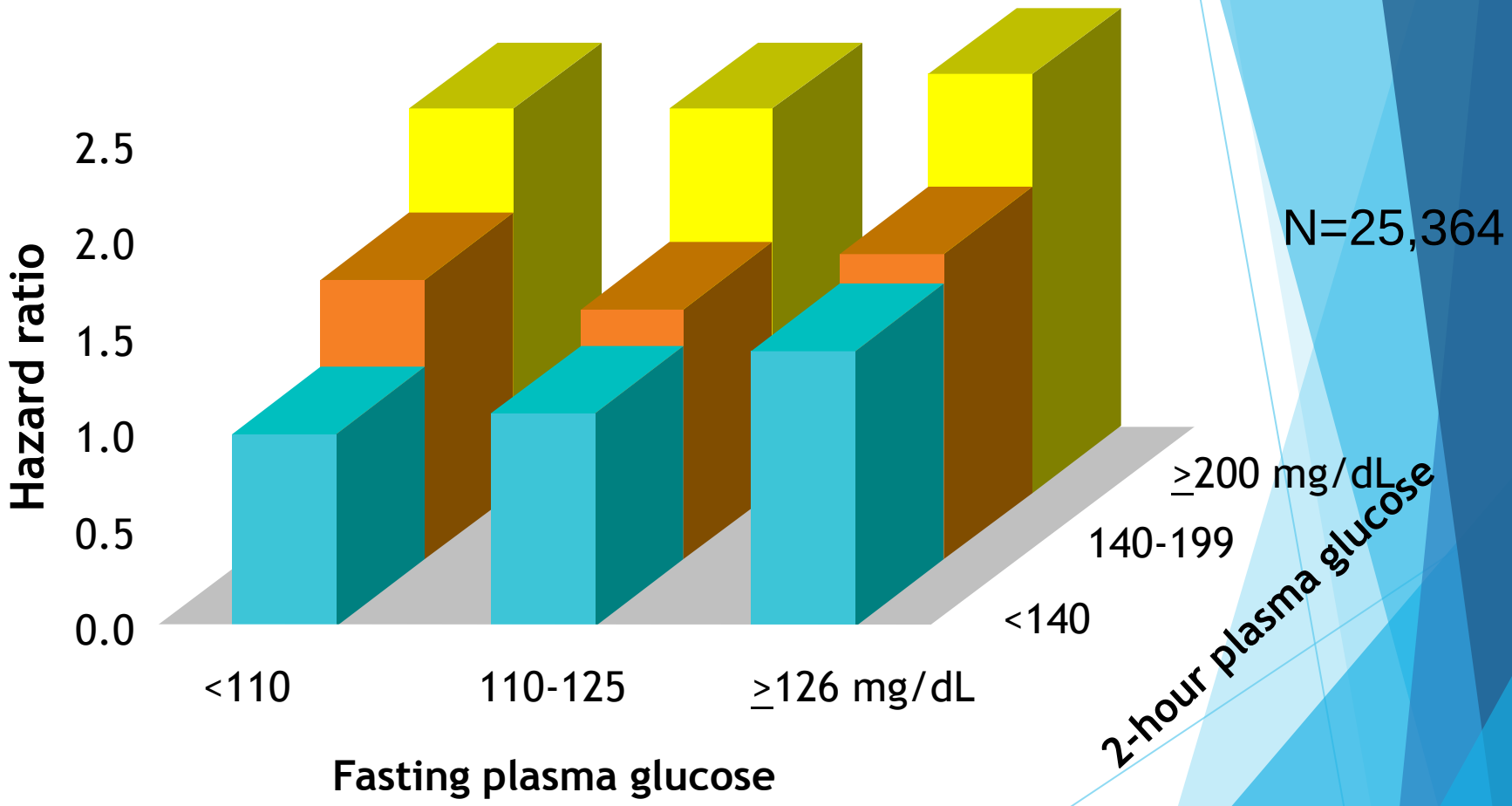
Reduction in Coronary Lumen Diameter with each PPG increase



Mellen PB et al. *Poster Presentation at American Heart Association.* 2006

- Isolated post prandial hyperglycaemia (PPHG) has been shown to double the risk for cardiovascular mortality. It also makes a significant contribution to overall glycaemia reflected in the HbA1c level. The harmful effects of PPHG are increased cardiovascular mortality, association with microvascular complications, cognitive decline and cancers. (Santosh Kumar Singh, *Indian J Endocrinol Metab* : 2012 Dec; 16(Suppl 2): S245–S247)

Postprandial Hyperglycemia and Relative Risk of Death (regardless of FPG)



Adjusted for age, center, sex ; 7 year followup study
DECODE Study Group. *Lancet* 1999;354:617-621

PPHG

- Contributes more to HbA1C than FPG when HbA1C is lower than 8.5%

Harmful effects

- Endothelial dysfunction
- Increase inflammatory markers
- Increase oxidative stress
- Increase protein glycosylation
- Coagulation affected

Therapy

- A variety of both non – pharmacologic and pharmacologic therapies should be considered to target PPG.
- Diets with a low glycemic load are beneficial in improving post-meal glycemia.
- Therapies which are available for PPHG include Alpha glucosidase inhibitor, Glinides, short-acting SU (Glipizide), and rapidly acting human insulins/ insulin analogues and biphasic (pre-mixed) insulins/insulin analogues, DPP4 Inhibitors, and GLP -1 derivatives.

- DPPIV inhibitors has been reported to effectively reduce PPG fluctuations and block the AGE – RAGE axis.
- Rizzo *et al*. reported that reductions in oxidative stress and markers of inflammation were greater in T2DM patients taking Vildagliptin than those taking Sitagliptin

- alpha-Glucosidase inhibitors like acarbose and miglitol attenuate the rate of absorption of sucrose by acting on the luminal enzymes. Adverse effects of these agents are predominantly gastrointestinal.
- Newer insulin secretagogues have been developed which attempt to mimic the physiological release of insulin and thus ameliorate PPHG. These include third generation sulfonylureas like glimepiride and nonsulfonylurea secretagogues like repaglinide and nateglinide.
- Rapid-acting insulin analogs, the amino acid sequences of which have been altered such that they have a faster onset of action, less hypoglycemic affect

Difficult to control Glycaemia

Professor Ko Ko

Therapeutic dilemma

- When the HbA1c does not come down to the target?
  - Clinical inertia/adherence problem
  - What are the check points for poorly control diabetes?

If RBS control is difficult(HbA1c is not going down

- Always ask about other medications
  - Steroids
  - Thiazide
  - Beta-blockers
- Always check diets
- Always check sepsis and stress
  - Skin – carbuncle, abscess, gan
  - Foot – ulcer
  - Lungs – TB, Pneumonia
  - Renal – UTI, pylonephritis
  - Stroke/MI

Maximum dose of 3 drugs
Not control for 3 months
Drugs failure
Time for insulin

Compliance of drugs

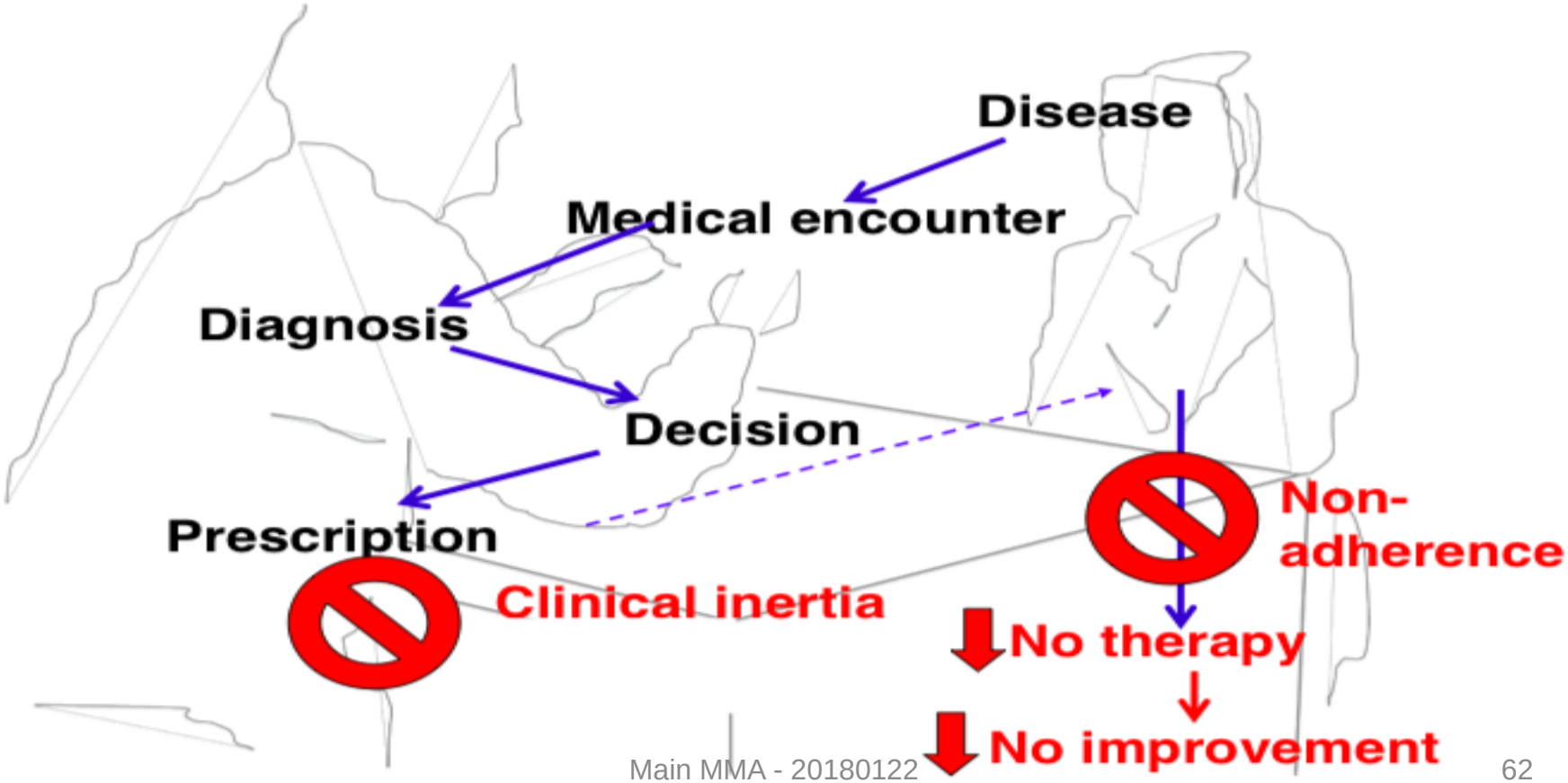
Clinical inertia

clinical inertia', defined as 'failure of healthcare providers to initiate or intensify therapy when indicated)

Two obstacles to efficient care

Physician's clinical inertia and patient's non adherence

Two barriers to care



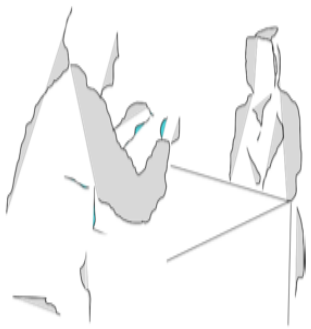
Clinical inertia

The goals for management are well defined,
effective therapies are widely available,
and practice guidelines for each of these diseases
have been disseminated extensively.
Despite such advances, health care providers
often do not initiate or intensify therapy appropriately
during visits of patients with these problems.
We define such behavior as *clinical inertia* —
recognition of the problem, but failure to act. »

Phillips LS et al., Clinical inertia, *Ann Intern Med* 2001 ; 135 : 825-834.

HOMOLOGY

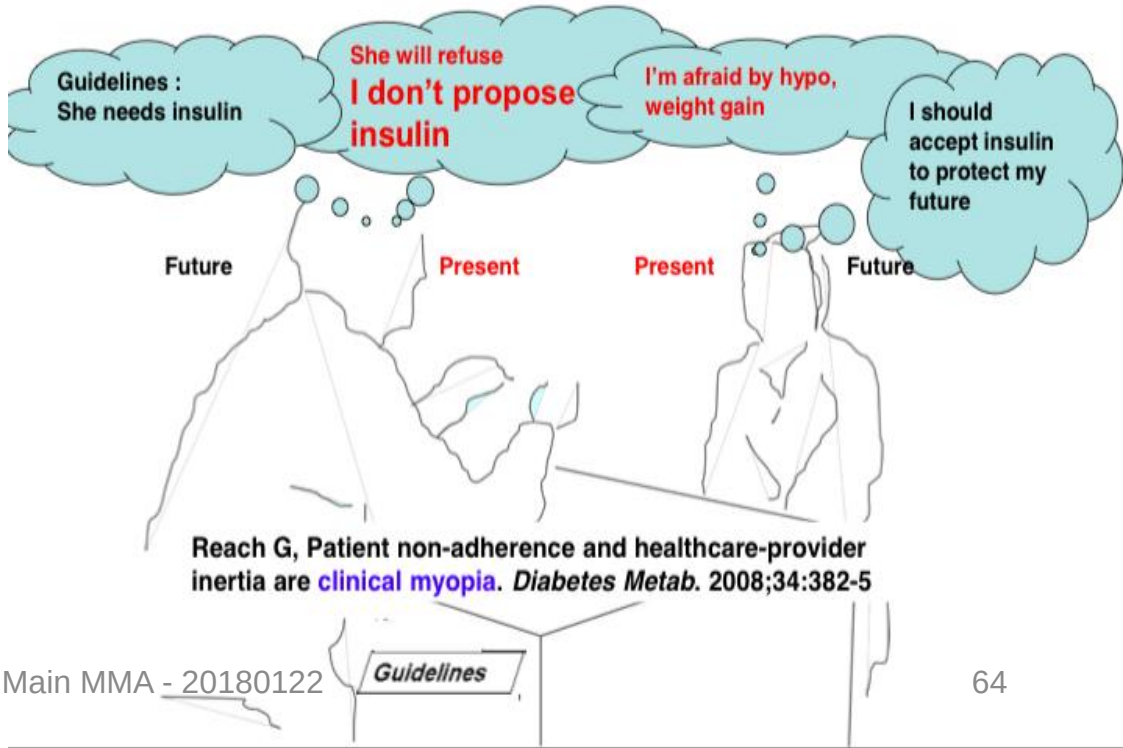
Psychological insulin resistance
The same reasons



Doctor	Patient
Patients don't want it	Adherence painful and difficult
Difficult, extra time	Fear of weight gain and hypos
Patients need referrals	"End of the road", diabetes worse
Hypos, weight gain	Employment, dependency
Won't work, costly	

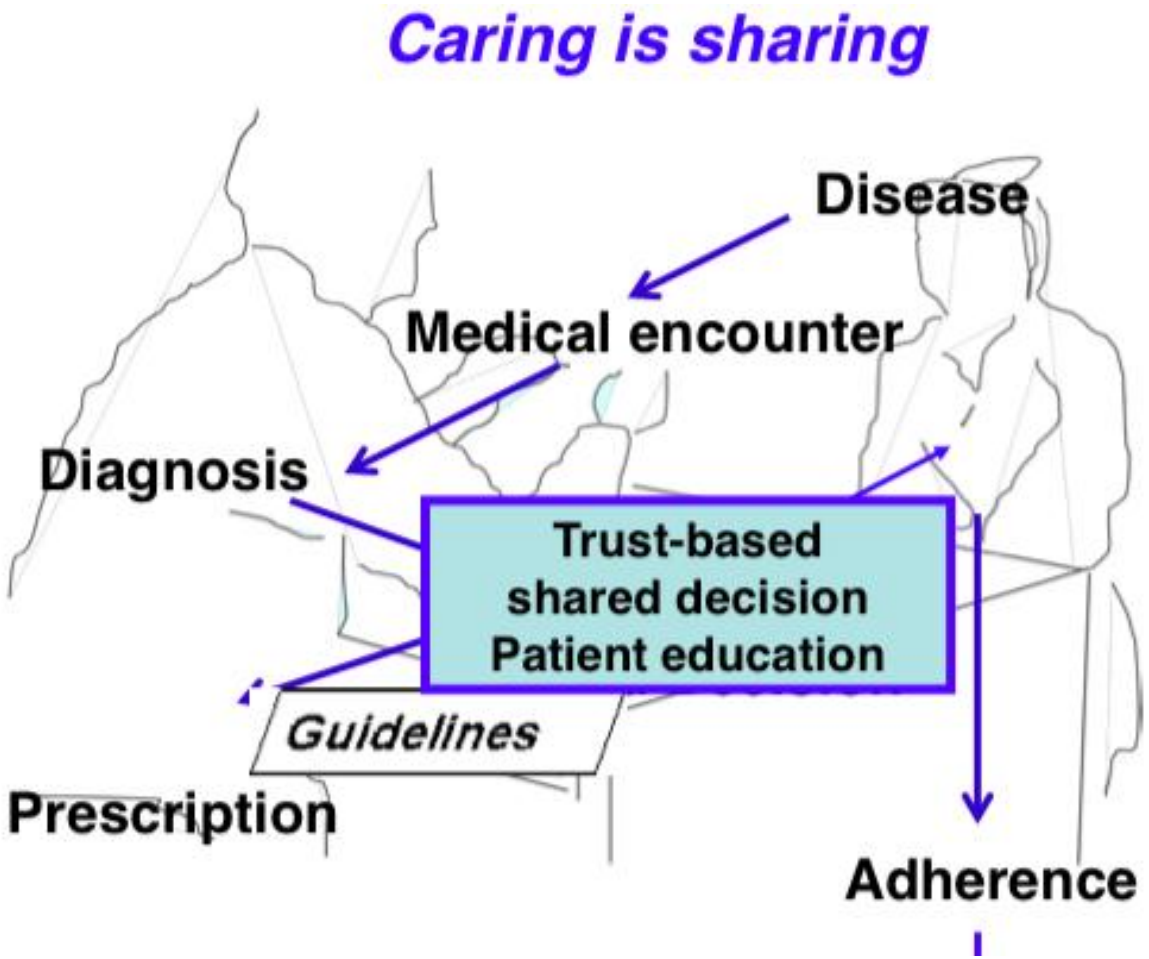
Phillips P, Type 2 Diabetes – Failure, blame and guilt in the adoption of insulin therapy. *Rev Diabet Stud* 2005; 2: 35–39

Common mechanism
Clinical myopia



Reach G, Patient non-adherence and healthcare-provider inertia are clinical myopia. *Diabetes Metab.* 2008;34:382-5

Solution


Caring is sharing
Disease
Medical encounter
Diagnosis
Trust-based
shared decision
Patient education
Guidelines
Prescription
Adherence

Hypertension in Diabetes

Dr Thein Myint

Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Recommendation 5

- In the population age **≥18 years with diabetes**, initiate pharmacologic treatment at
  - SBP ≥ 140 mmHg or
  - DBP ≥ 90 mmHg and
- treat to a
  - goal SBP ≤ 140 mmHg and
  - goal DBP ≤ 90 mmHg

(E)

Diabetes Mellitus

COR	LOE	Recommendations for Treatment of Hypertension in Patients With DM
I	SBP: B-R[SR] DBP: C-EO	In adults with DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of less than 130/80 mm Hg.
I	A[SR]	In adults with DM and hypertension, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective.
IIb	B-NR	In adults with DM and hypertension, ACE inhibitors or ARBs may be considered in the presence of albuminuria.

SR indicates systematic review.

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MANAGEMENT OF BLOOD PRESSURE

Screening & Dx	Measure BP at every visit, confirm ↑BP with multiple readings including that on separate day
Monitoring	Should monitor BP at home
Goals	DM + HTN → **<140/90 mmHg** DM + HTN + high risk of CVD → **<130/80 or <120/80 mmHg** (if they can be achieved without undue treatment burden) DM + HTN + Pregnancy → **<120–160/ 80–105 mmHg** **(in 2016 ADA -** BP targets - 110-129/65-79 mmHg)

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ADA 2018

MANAGEMENT OF BLOOD PRESSURE

Lifestyle intervention	▪ Indication → **>120/80** ▪ Weight ↓ → if overweight or obese ▪ DASH (Dietary Approaches to Stop Hypertension) ▪ ↑ physical activity
Pharmacologic intetrventions	▪ Indication → **≥140/90** ▪ **≥160/100** → initiate with 2 drugs or single-pill combination
Drug choices	▪ ACEI, ARB, thiazide-like diuretics, dihydropyridine CCB ▪ Generally – multiple drug therapy is required ▪ **NOT recommend** – ACEI + ARB or ACEI + ARB + direct Renin Inhibitor ▪ DM + HTN + **UACR ≥300 mg/g or 30-299 mg/g** → ACEI or ARB ▪ **Resistant Hypertension –** mineralocorticoid receptor antagonist therapy
Monitoring	▪ With ACEI/ ARB/ diuretics → Serum creatinine, K^+, eGFR ▪ At least annually

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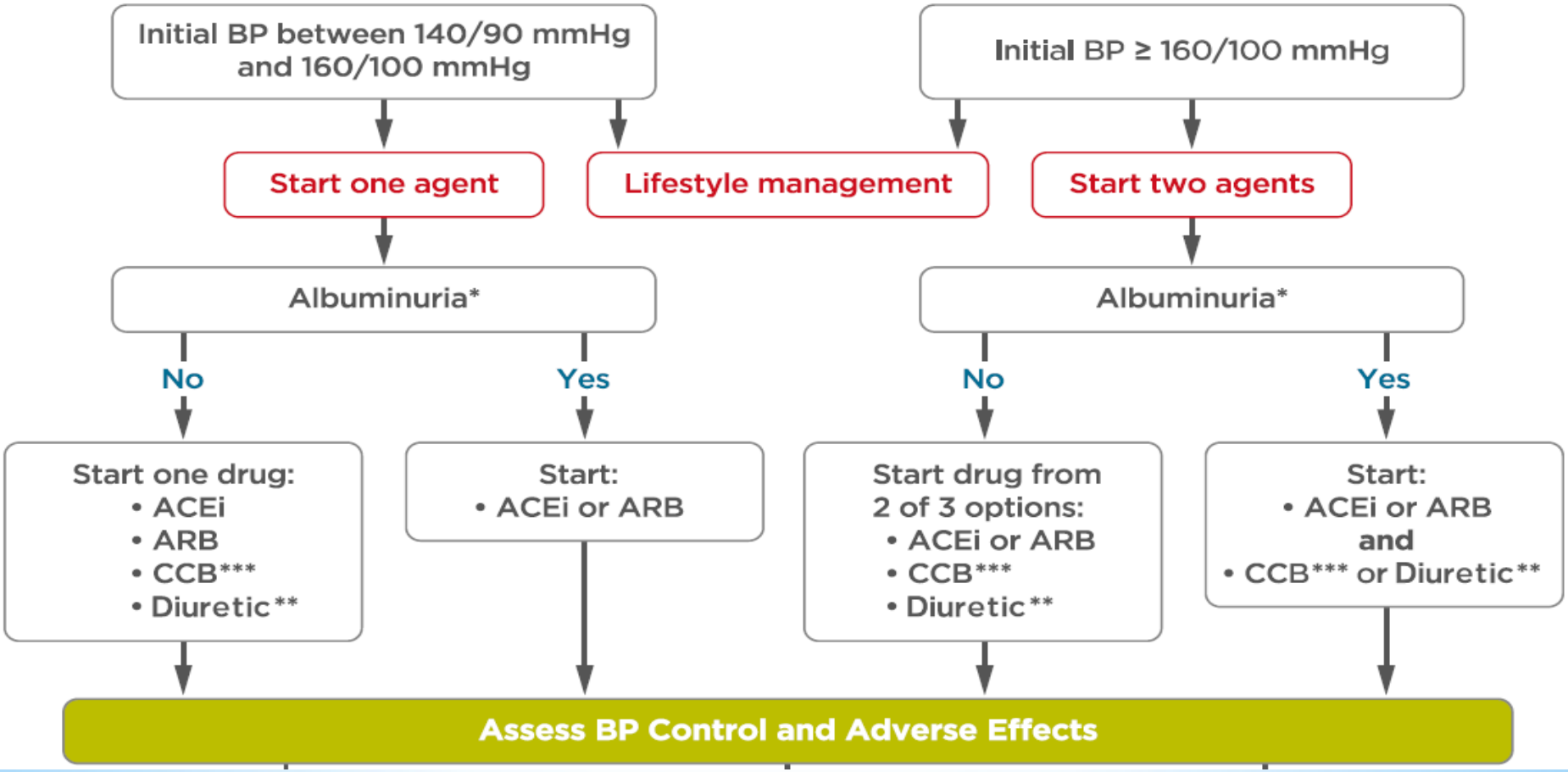
MANAGEMENT OF BLOOD PRESSURE

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



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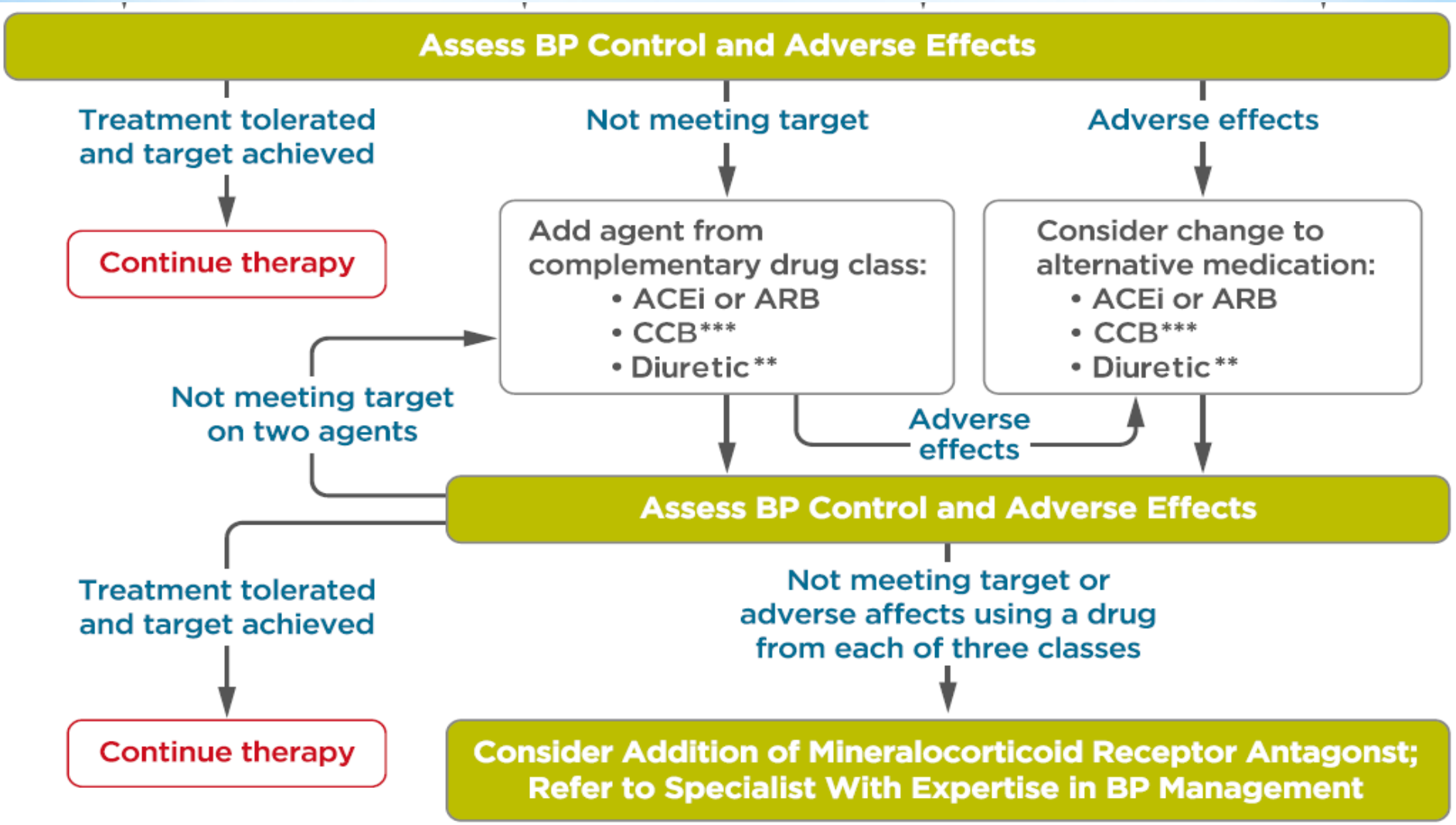
MANAGEMENT OF BLOOD PRESSURE



Lipid in Diabetes

Dr Thein Myint

American Diabetes Association

ADA 2018

MANAGEMENT OF LIPID

Lipid profile -

not taking statins or other lipid-lowering therapy - at

- the time of diabetes diagnosis,
- an initial medical evaluation, and
- every 5 years thereafter if under the age of 40 years,
- or more frequently if indicated. E

If statins or other lipid-lowering therapy recommended - at

- initiation
- 4–12 weeks after initiation or
- A change in dose, and
- annually thereafter

(as it may help to monitor the response to therapy and inform adherence)

MANAGEMENT OF LIPID

Lifestyle modifications

- Weight ↓ (if indicated)
- ↓ intake - saturated fat, *trans* fat, cholesterol;
- ↑ intake - dietary n-3 fatty acids, viscous fiber, and plant stanols/sterols
- ↑ physical activity

Intensify lifestyle therapy and optimize glycemic control for patients with

- **↑ triglyceride** (≥150 mg/dL [1.7 mmol/L]) and/or
- **↓ HDL** (<40 mg/dL [1.0 mmol/L] for men,
  <50 mg/dL [1.3 mmol/L] for women).

MANAGEMENT OF LIPID

Statin Treatment

- DM + ASCVD → high-intensity statin + lifestyle
- DM + < 40 yrs + ASCVD risk → moderate-intensity statin + lifestyle
- DM + 40–75 yrs and >75 yrs + NO ASCVD → moderate-intensity statin + lifestyle
- DM + ASCVD → if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, → consider adding additional LDL lowering therapy (such as ezetimibe or PCSK9 inhibitor) after evaluating the potential for further atherosclerotic cardiovascular disease risk reduction, drug-specific adverse effects, and patient preferences.
- (Ezetimibe may be preferred due to lower cost)
- Statin therapy is contraindicated in pregnancy

MANAGEMENT OF LIPID

Other combination therapy

- fasting TG ≥ 500 mg/dL (5.7 mmol/L)
  - evaluate for secondary causes of hypertriglyceridemia and
  - consider medical therapy to reduce the risk of pancreatitis.

- **Combination therapy** →generally **not** recommended.
  - Statin + fibrate
  - Statin + niacin (↑ risk of stroke and additional side effects)

ASCVD Risk Categories and Treatment Goals

Risk category	Risk factors/10-year risk	Treatment goals		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in individuals after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in individuals with DM, stage 3 or 4 CKD, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% – DM or stage 3 or 4 CKD with 1 or more risk factor(s) – HeFH	<70	<100	<80
High risk	– ≥2 risk factors and 10-year risk 10%-20% – DM or stage 3 or 4 CKD with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

Abbreviations: ACS, acute coronary syndrome; apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus; HeFH, heterozygous familial hypercholesterolemia; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NR, not recommended.

Barter PJ, et al. *J Intern Med*. 2006;259:247-258; Boekholdt SM, et al. *J Am Coll Cardiol*. 2014;64(5):485-494; Brunzell JD, et al. *Diabetes Care*. 2008;31:811-822; Cannon CP, et al. *N Engl J Med.* 2015;372(25):2387-2397; Grundy SM, et al. *Circulation.* 2004;110:227-239; Heart Protection Study Collaborative Group. *Lancet*. 2002;360:7-22; Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice*. 2017;23(4):479-497; Lloyd-Jones DM, et al. *Am J Cardiol*. 2004;94:20-24; McClelland RL, et al. *J Am Coll Cardiol*. 2015;66(15):1643-1653; NHLBI. NIH Publication No. 02-5215. 2002; Ridker PM, *J Am Coll Cardiol*. 2005;45:1644-1648; Ridker PM, et al. *JAMA*. 2007;297(6):611-619; Sever PS, et al. *Lancet*. 2003;361:1149-1158; Shepherd J, et al. *Lancet*. 2002;360:1623-1630; Smith SC Jr, et al. *Circulation*. 2006;113:2363-2372; Stevens RJ, et al. *Clin Sci*. 2001;101(6):671-679; Stone NJ. *Am J Med*. 1996;101:4A40S-48S; Weiner DE, et al. *J Am Soc Nephrol.* 2004;15(5):1307-1315.

Thank You

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