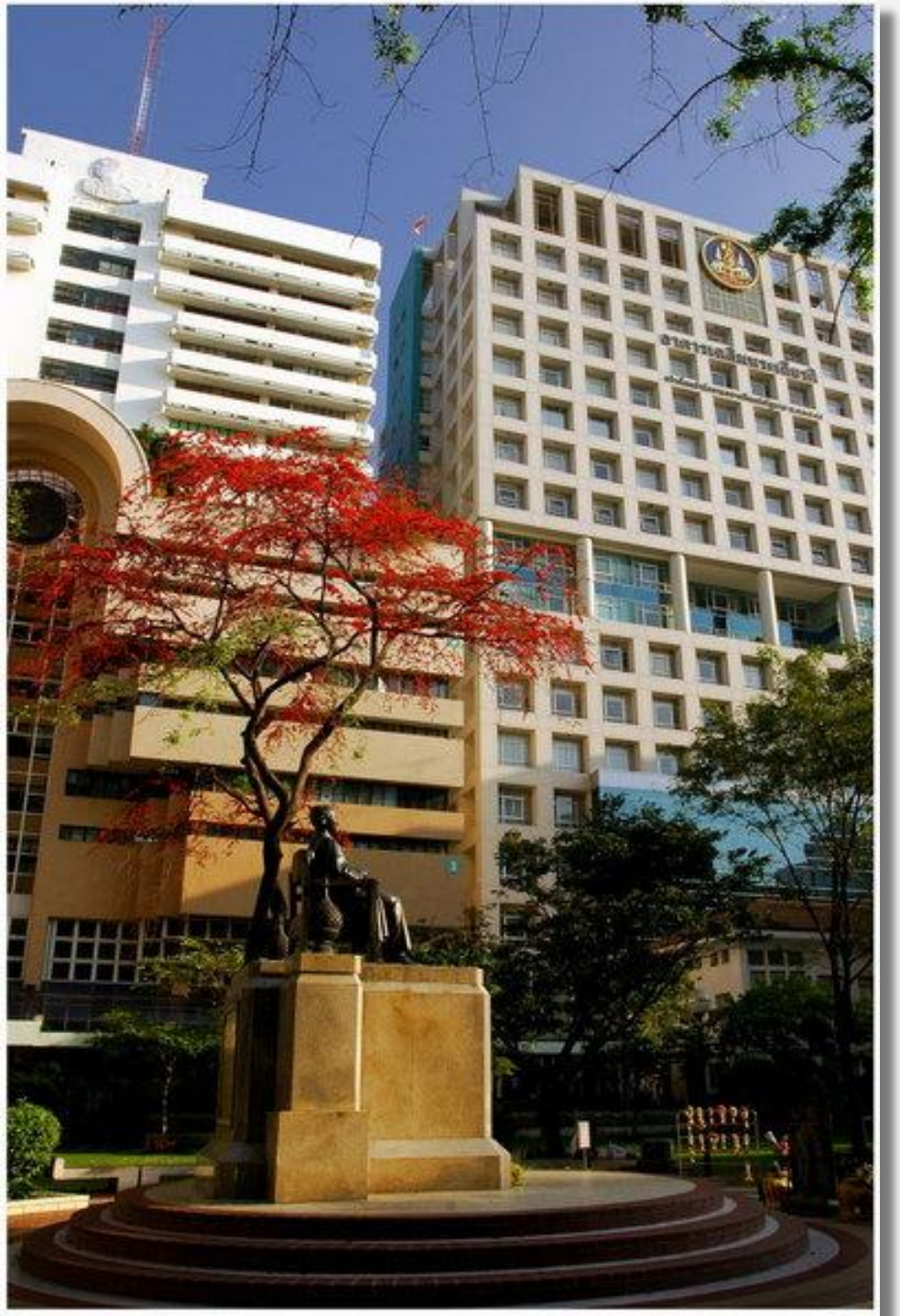
Update Diabetes Management

รศ.พญ.อภิรดี ศรีวิจิตรกมล
สาขาวิชาต่อมไร้ท่อและเมตะบอลิสม
ภาควิชาอายุรศาสตร์
คณะแพทยศาสตร์ศิริราชพยาบาล



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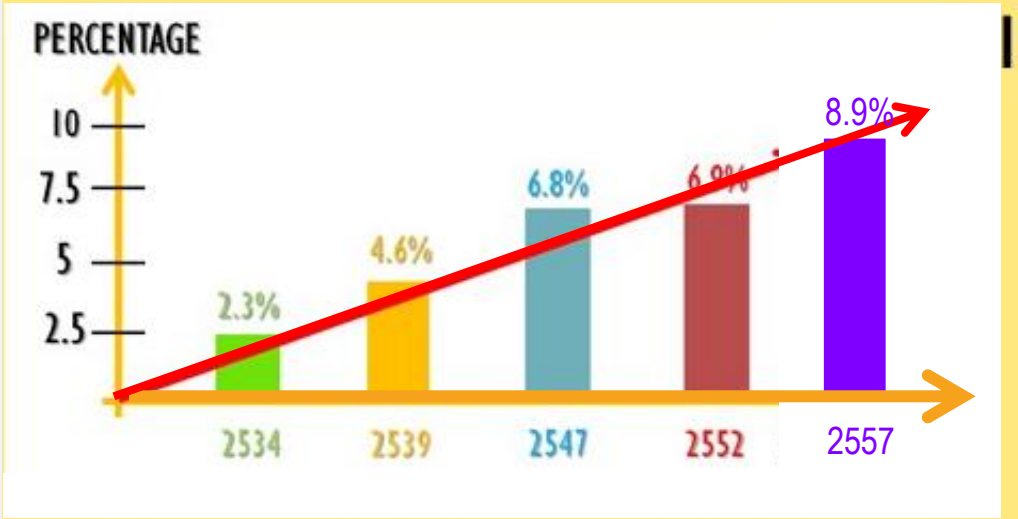
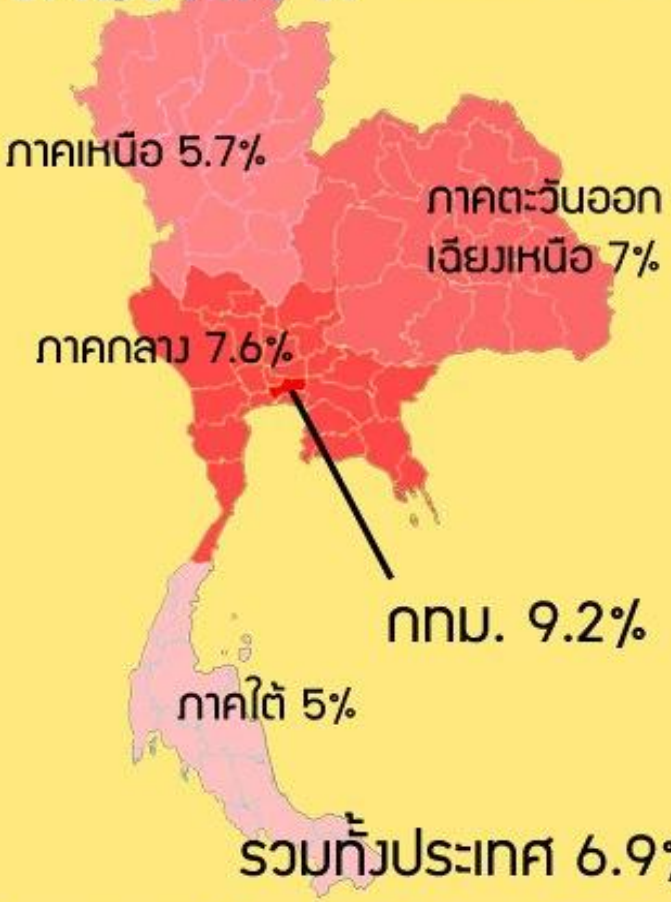
เบาหวาน .. ใครว่าไกลตัว ?



เมื่อแบ่งตามภาค ..

เมื่อวานป้าทานอะไร?



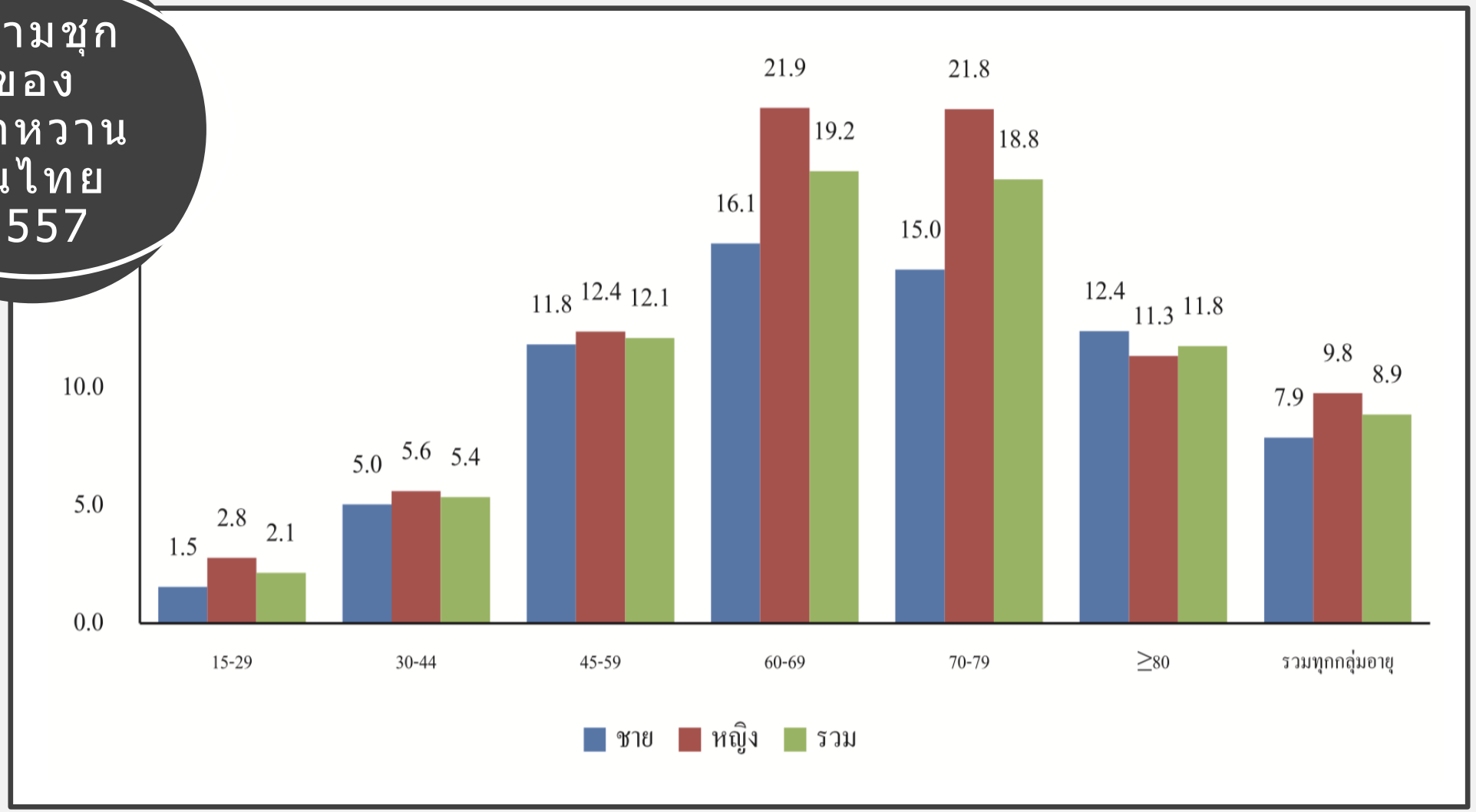
ความชุกของโรค เพิ่มขึ้นทุกปี ..
ปีนี้ 2555 .. ไม่รู้จะเท่าไหร่ !?

รวมทั้งประเทศ 6.9%

ข้อมูลจากการสำรวจครั้งที่ 4 พ.ศ. 2551-2

อ้างอิง:
สำนักงานสำรวจสุขภาพประชาชนไทย. รายงานการสำรวจสุขภาพประชาชนไทยครั้งที่ 1-4. พ.ศ. 2534-52.

ความชุกของเบาหวานในไทย 2557



PREVALENCE OF CARDIOVASCULAR DISEASE IN MIDDLE-AGED PEOPLE WITH DIABETES

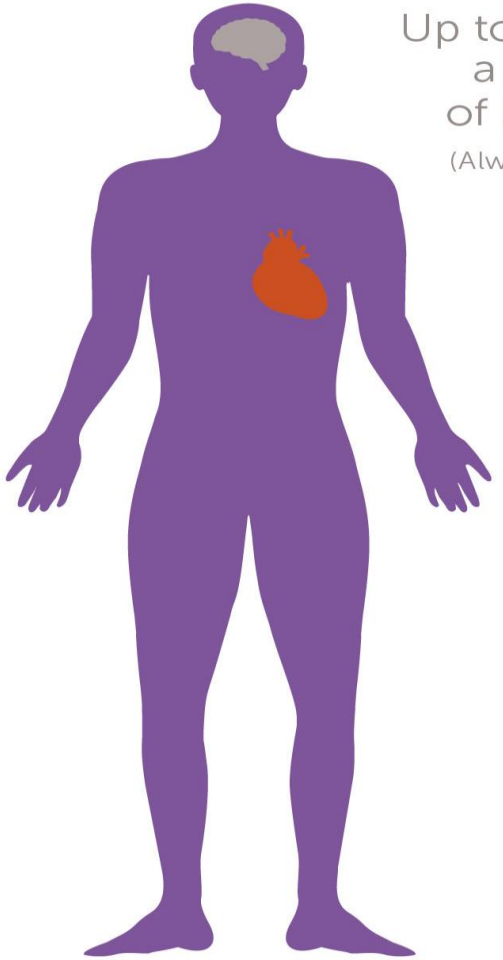
International Diabetes Federation

In studies of middle-aged people with diabetes living in high- and middle-income countries:

Up to **41%** had a history of **CVD**

includes stroke, coronary artery disease, and peripheral artery disease

(van Hateren, 2009)



Up to **10%** had a history of **STROKE**

(Alwakeel, 2008)

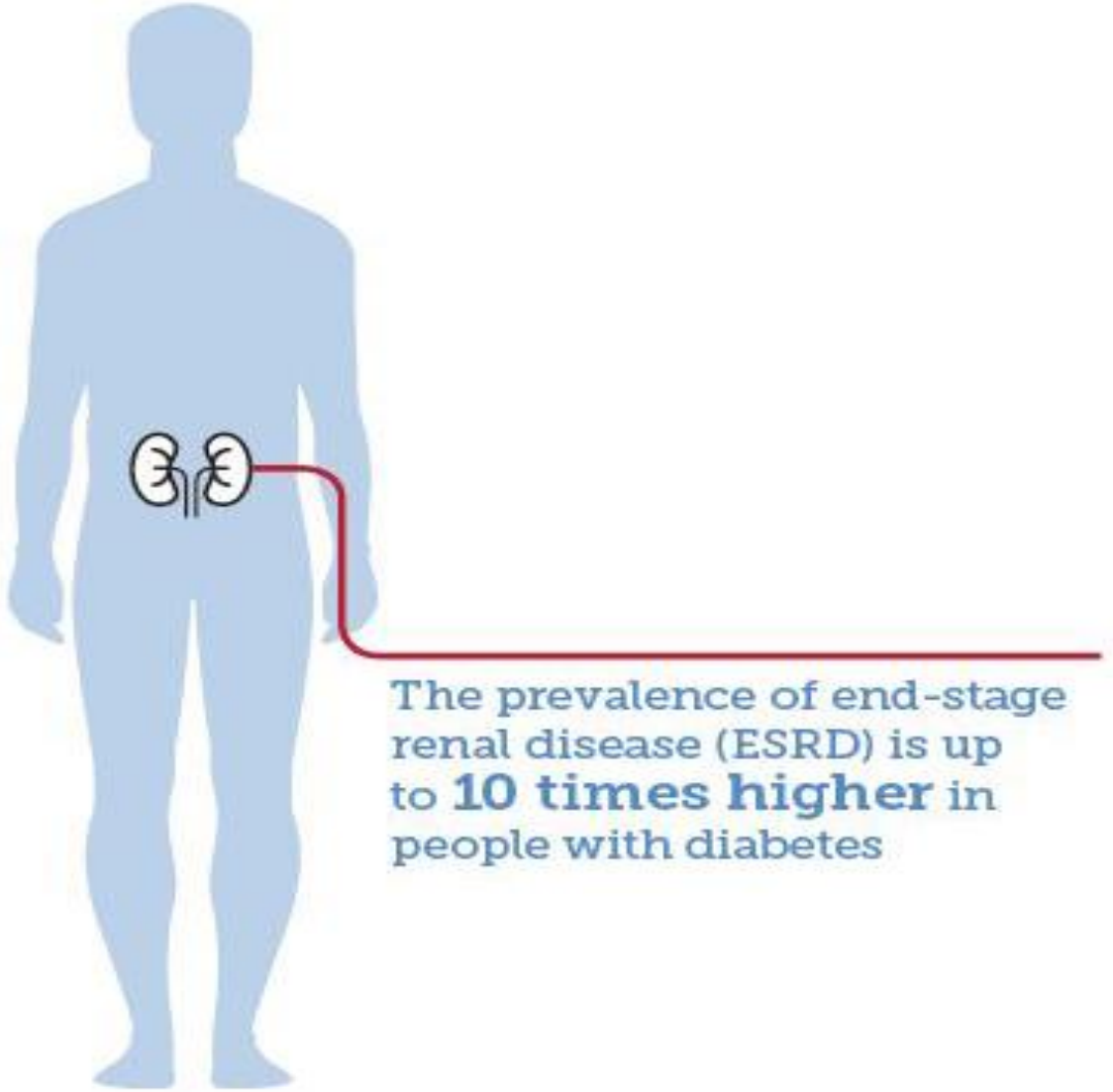
Up to **14%** had a history of **HEART ATTACK**

(Alwakeel, 2008)

Mean age of study population: 50 to 69 years

www.idf.org/cvd

DIABETES AND KIDNEY DISEASE



The prevalence of end-stage renal disease (ESRD) is up to **10 times higher** in people with diabetes

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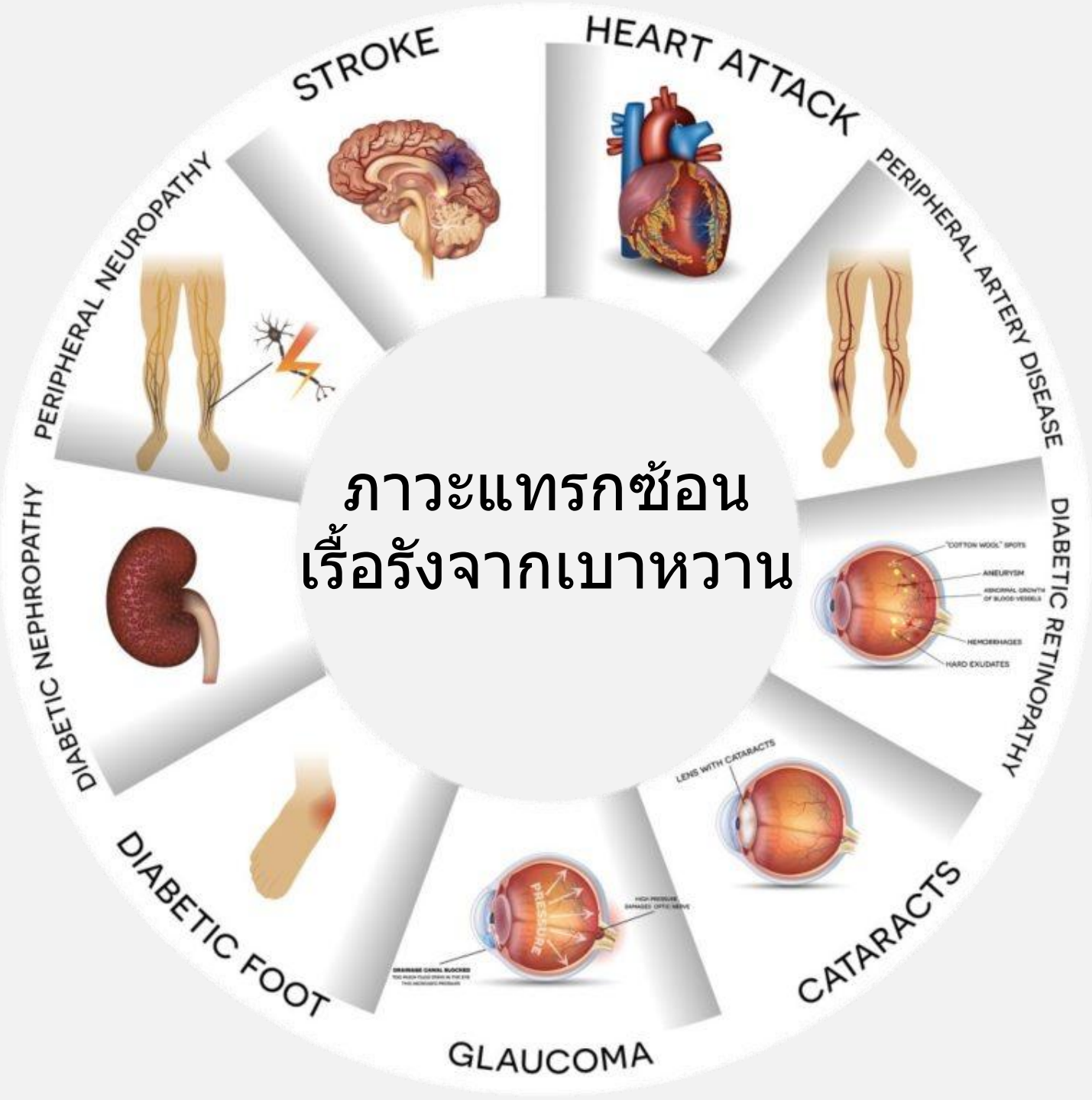

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INTERVENTION STUDIES IN TYPE 2 DIABETES

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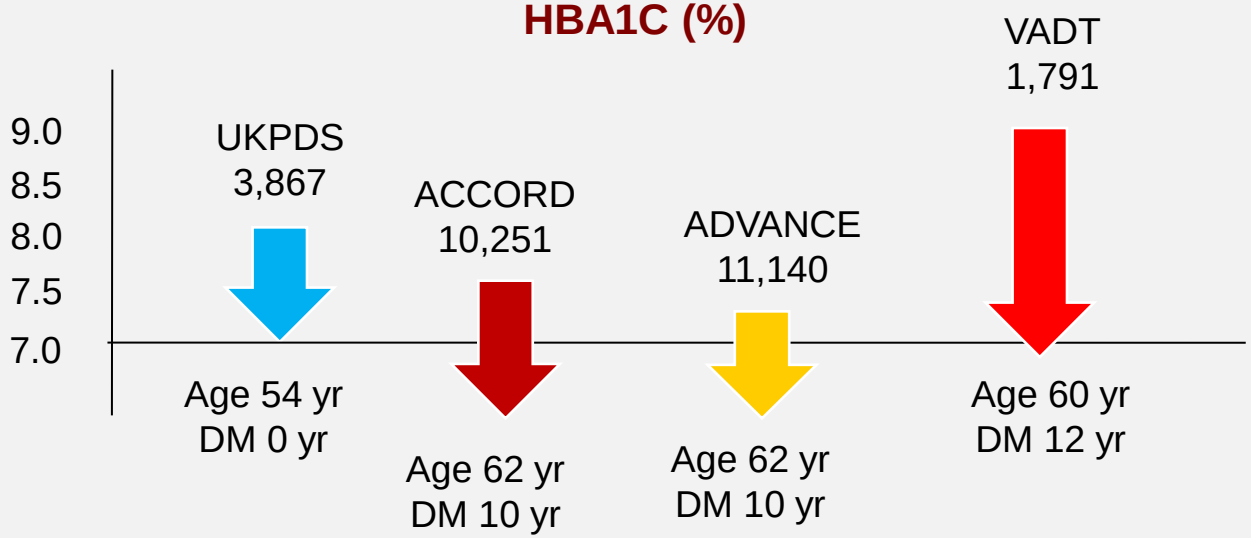
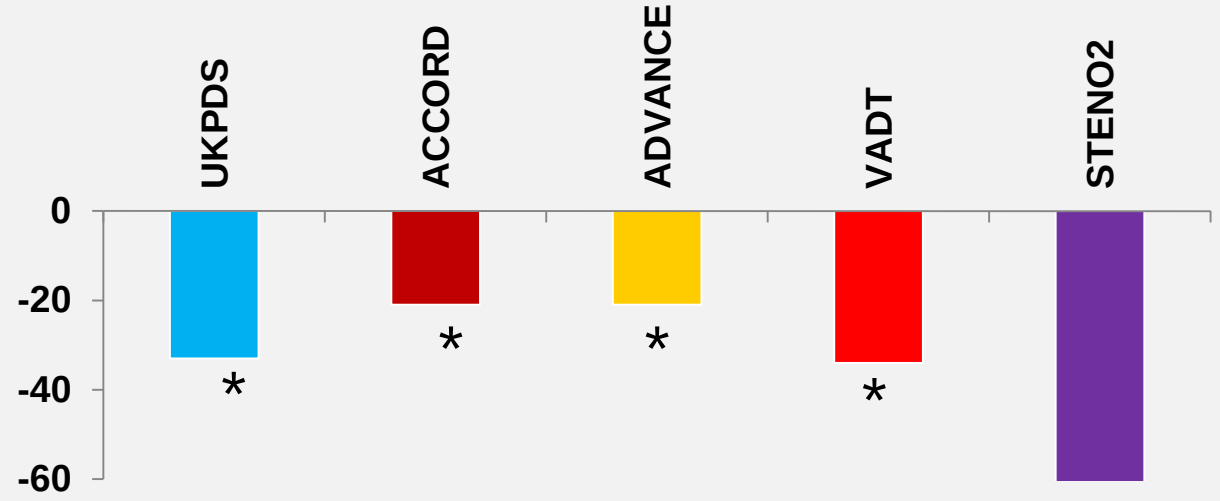
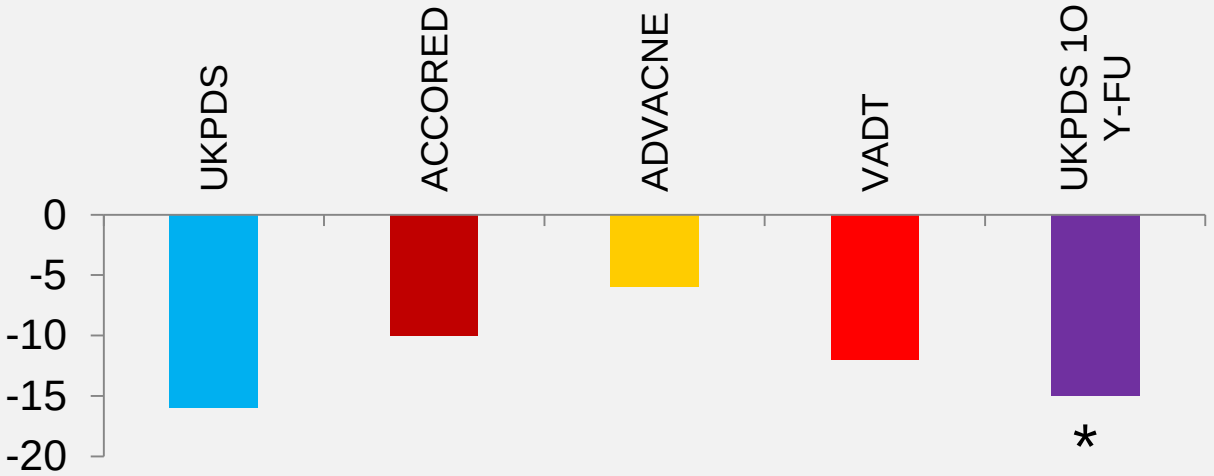
HBA1C (%)



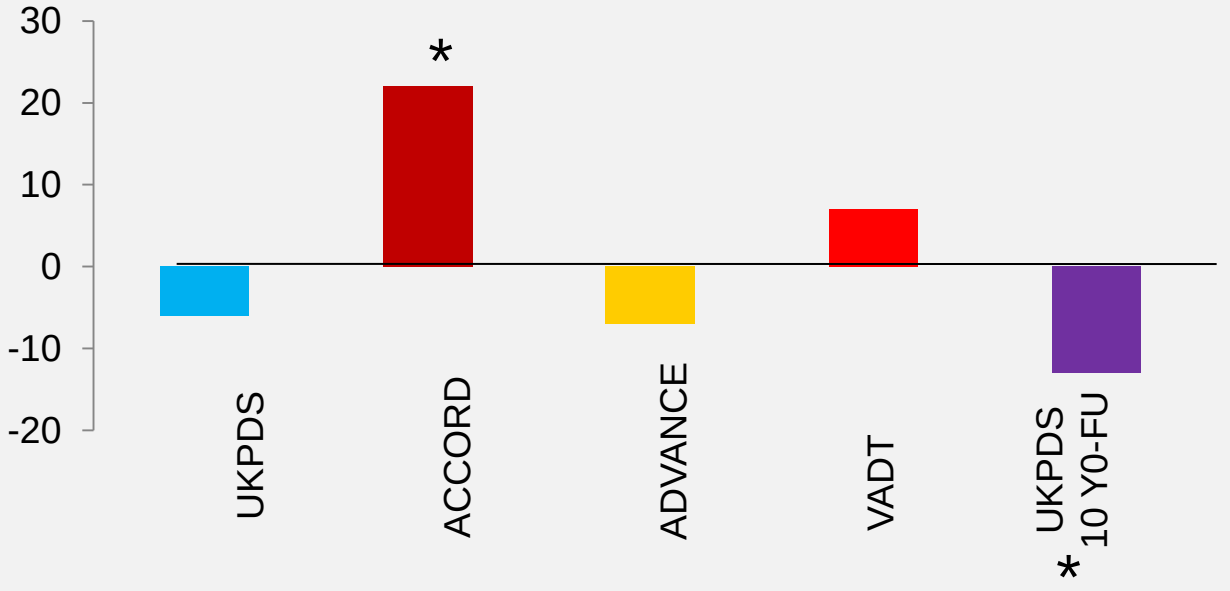
RISK REDUCTION OF DN (%)



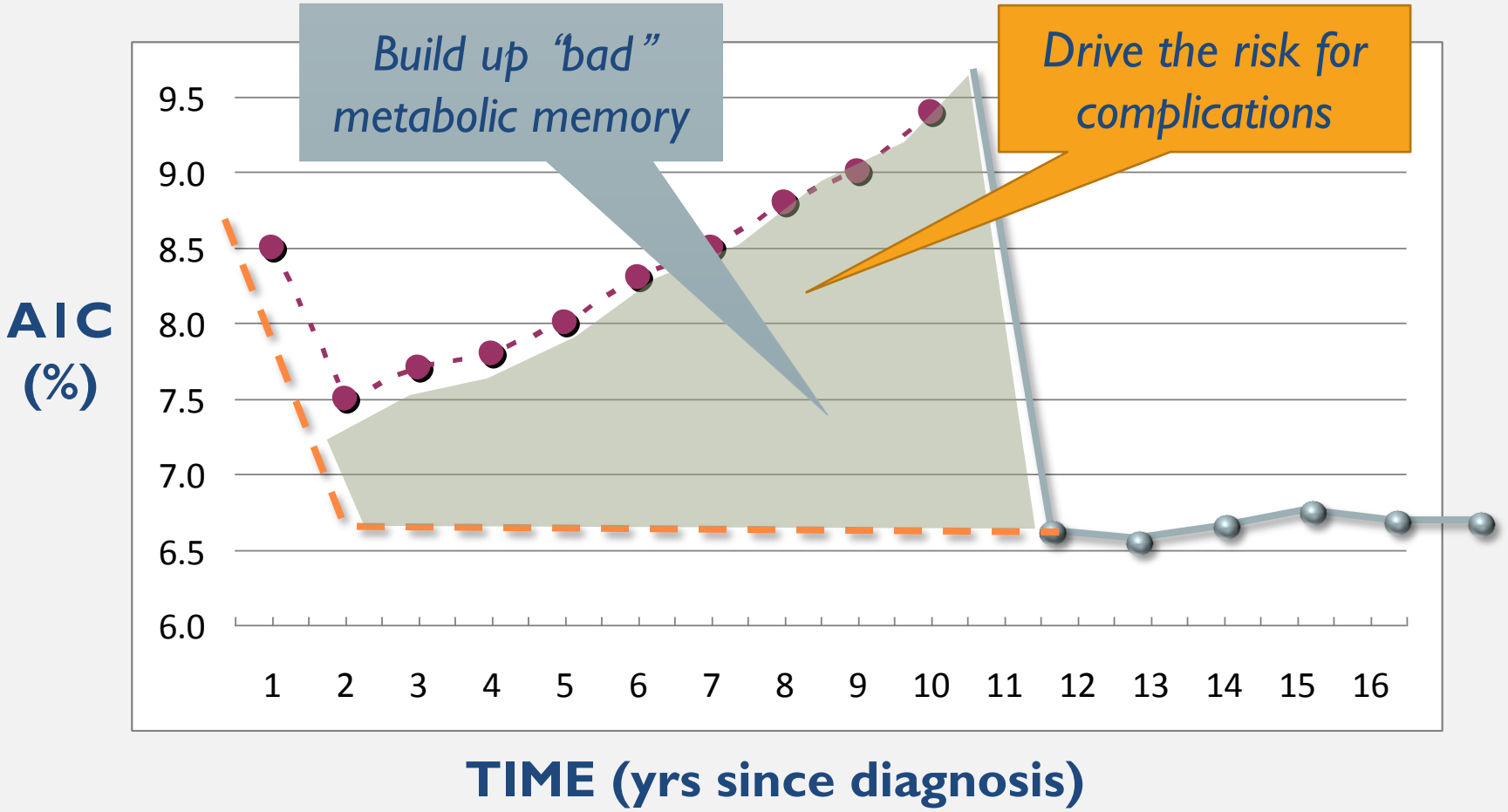
CVD EVENTS



MORTALITY



THE "NATURAL HISTORY" OF TYPE 2 DIABETES



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HYPOGLYCEMIA AND MORTALITY ACCORD

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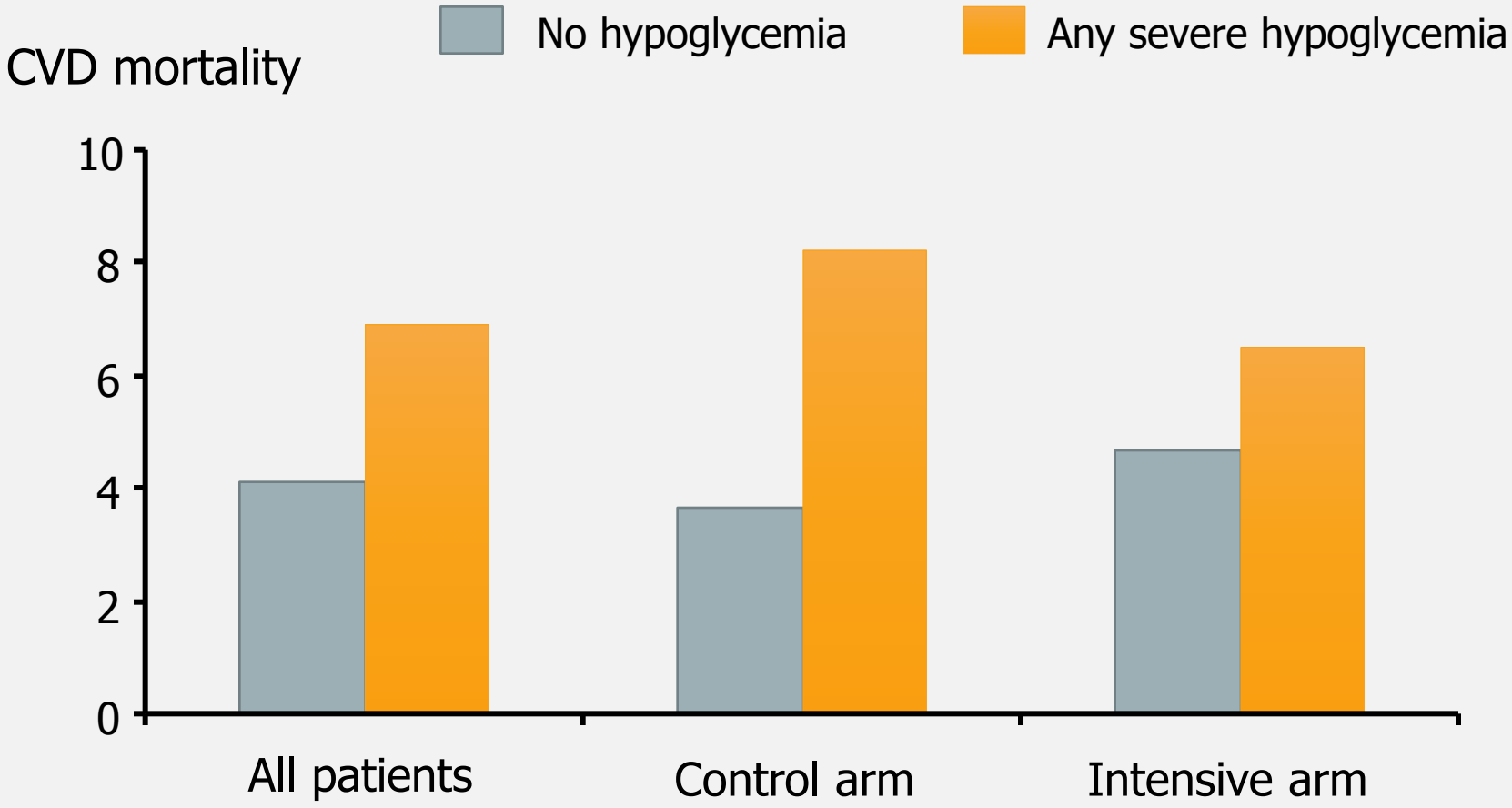
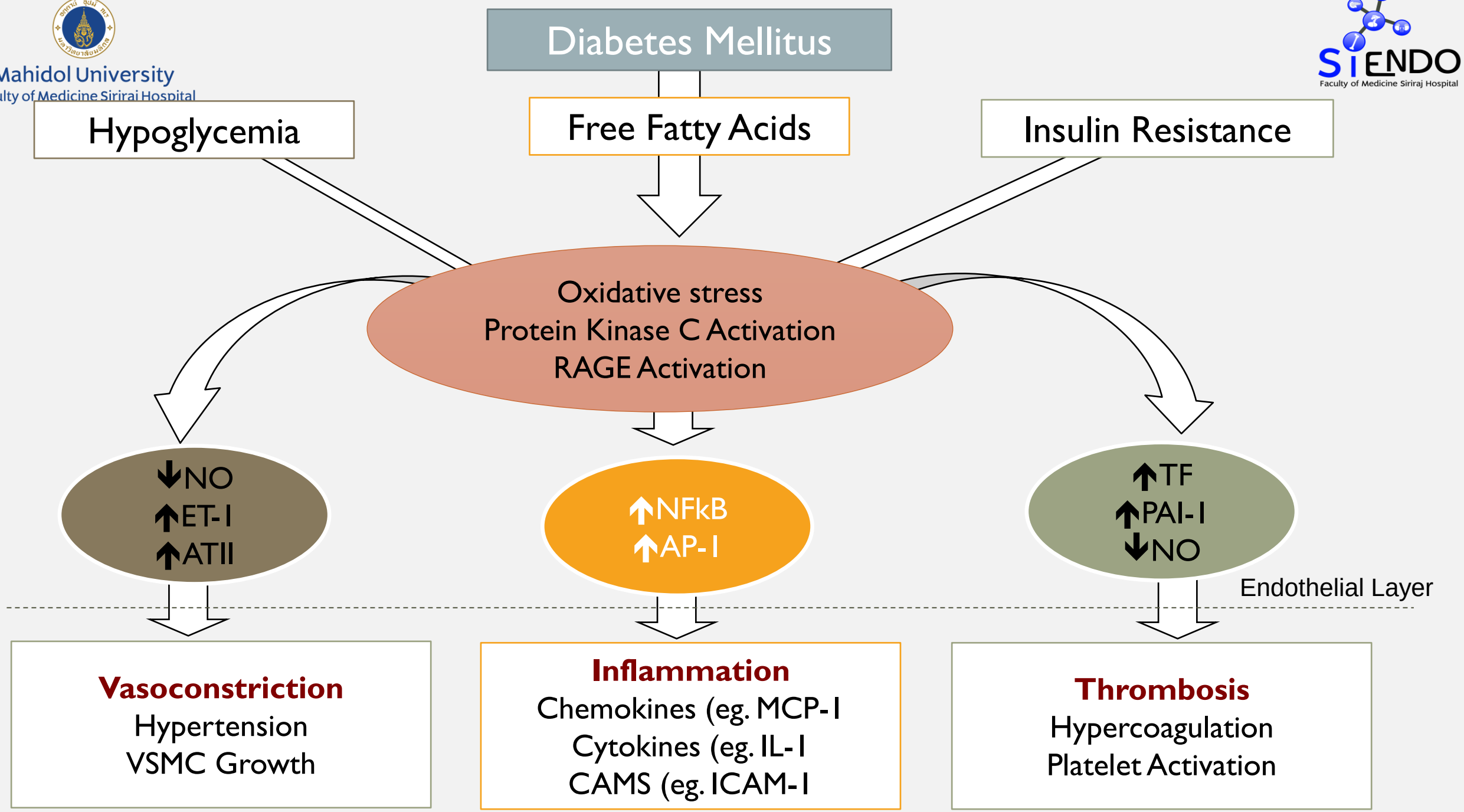


Bond D. BMJ 2010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Diabetes Mellitus
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Hypoglycemia
Free Fatty Acids
Insulin Resistance
Oxidative stress
Protein Kinase C Activation
RAGE Activation
↓NO
↑ET-1
↑ATII
↑NFkB
↑AP-1
↑TF
↑PAI-1
↓NO
Endothelial Layer
Vasoconstriction
Hypertension
VSMC Growth
Inflammation
Chemokines (eg. MCP-1
Cytokines (eg. IL-1
CAMS (eg. ICAM-1
Thrombosis
Hypercoagulation
Platelet Activation

BALANCING BETWEEN HYPER- AND HYPOGLYCAEMIA...

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GLYCEMIC TARGET

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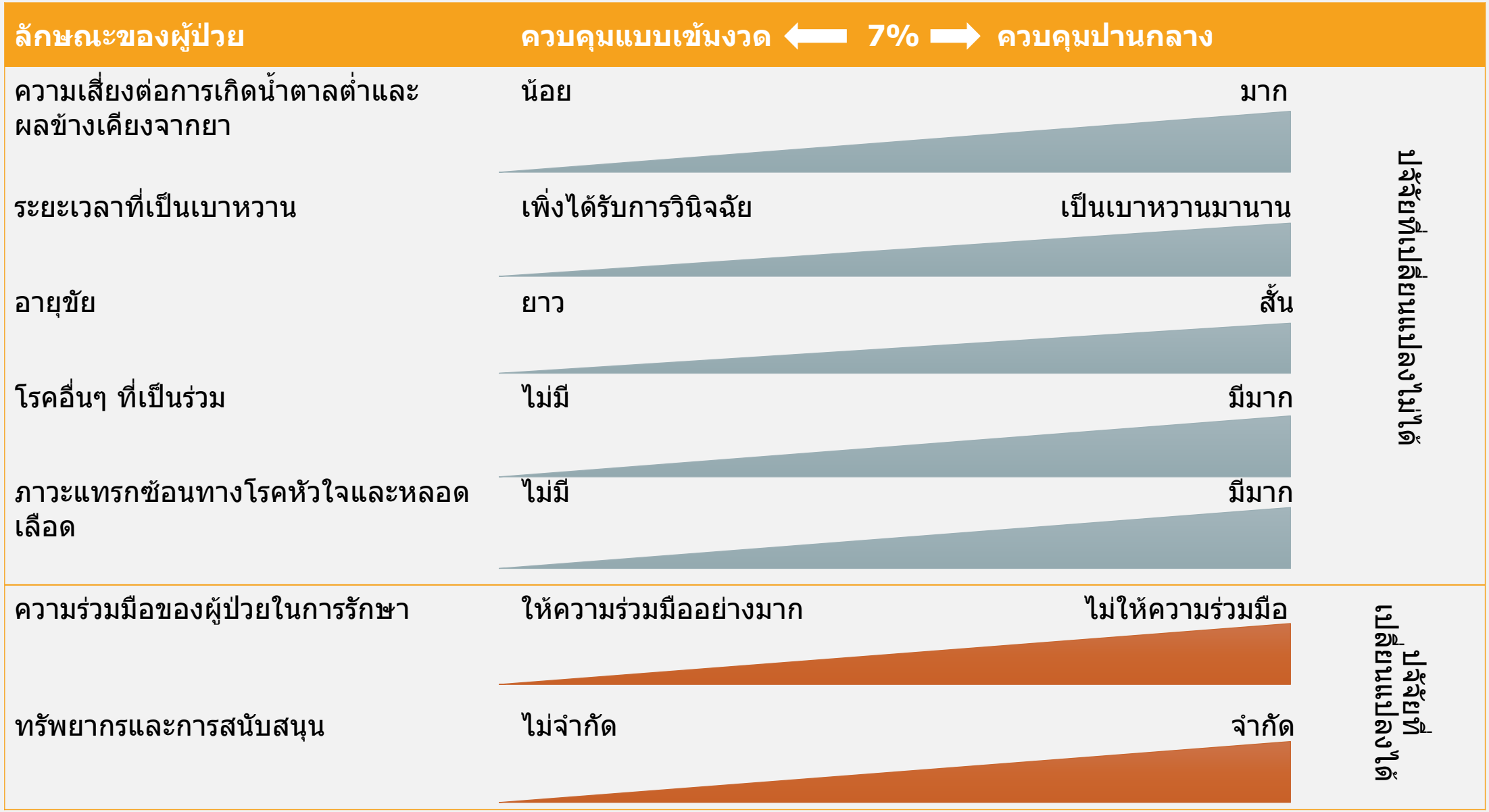
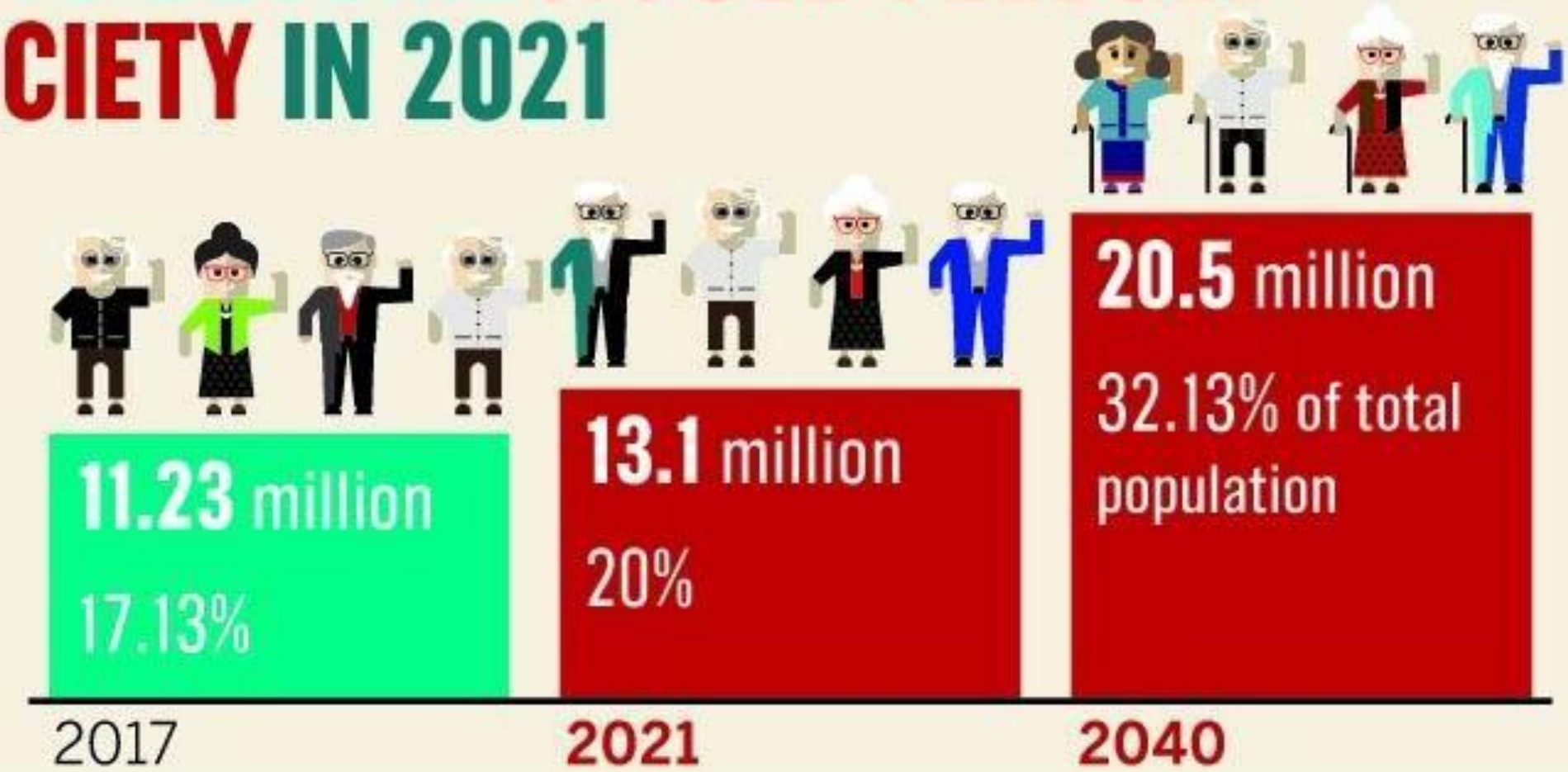


THAILAND TO BECOME A FULL-FLEDGED AGEING SOCIETY IN 2021



Source: NESDB

NATION GRAPHICS

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Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Ma**
are we
beyon

4 **Vul**
daily h
complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

This
ancy
frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

Moderate to severe Frailty
- Without DM: life expectancy 30 months
- With DM: life expectancy 23 months

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Inspiring Minds

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เป้าหมายระดับฮีโมโกลบิน เอวันซี ในผู้สูงอายุ

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สมาพันธ์เบาหวานประเทศแคนาดา		สมาพันธ์เบาหวานประเทศอเมริกา		สมาพันธ์เบาหวานระหว่างประเทศ ((IDF)		สมาคมเบาหวานแห่งประเทศไทย	
แข็งแรงดี	≤ 7.0%	แข็งแรงดี	≤ 7.5%	พึ่งตนเองได้	7.0-7.5%	พึ่งตนเองได้	7.0-7.5%
		เริ่มมีปัญหาสุขภาพ	≤ 8.0%	ต้องพึ่งคนอื่น	7.0-8.0%		
เปราะบาง	≤ 8.5%	เปราะบาง	≤ 8.5%	เปราะบาง	≤ 8.5%	เปราะบาง	≤ 8.5%

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THAI GUIDELINE 2017

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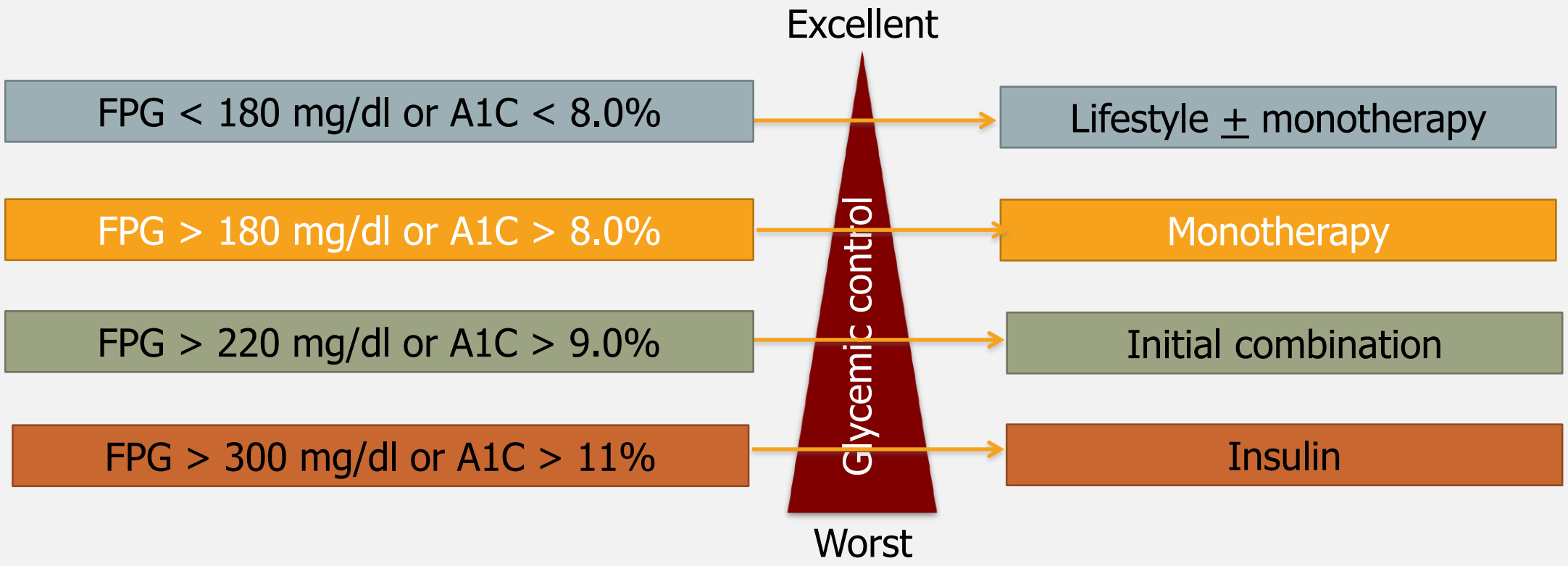

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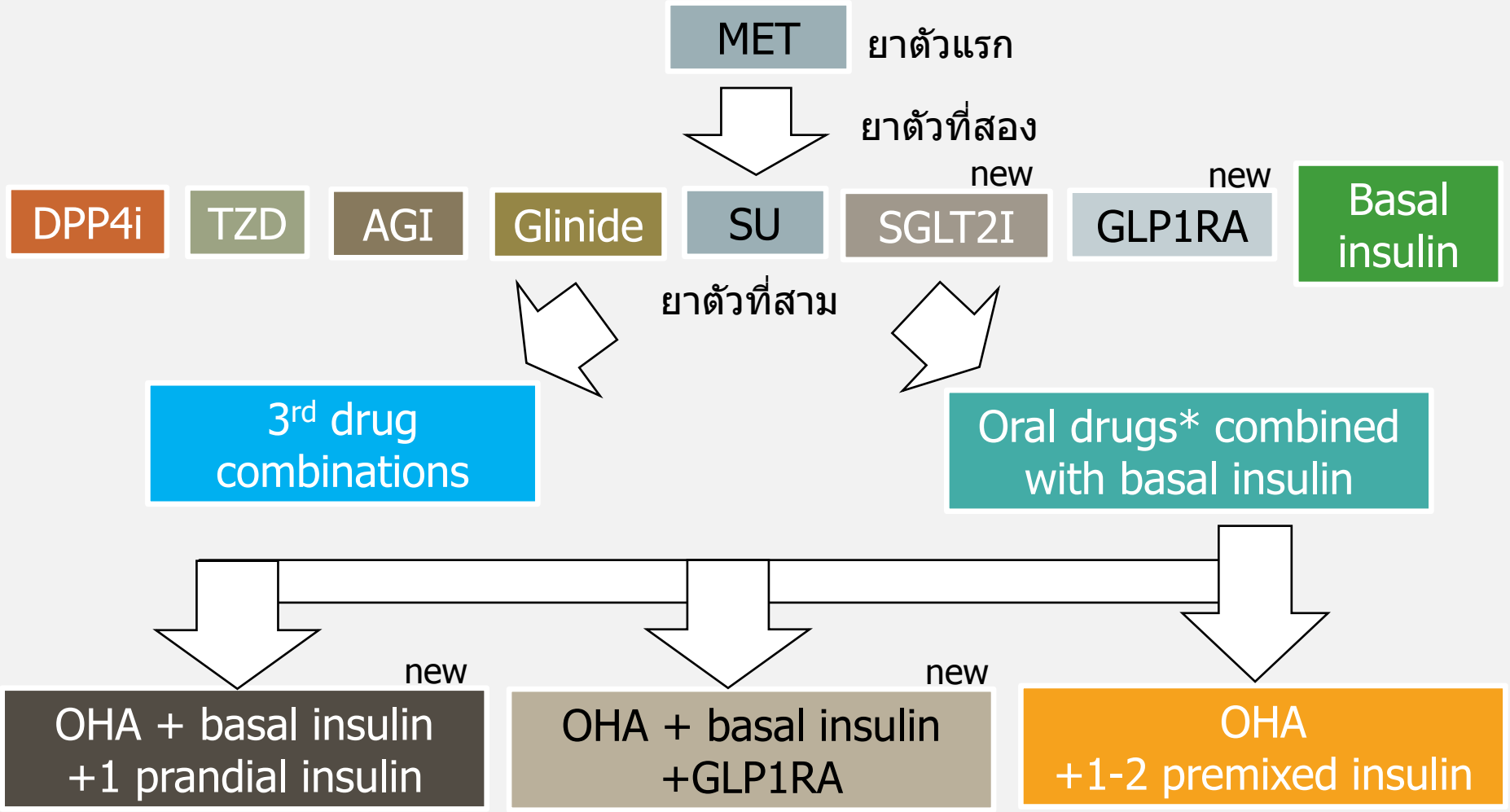
แนวทางการรักษาเบาหวาน สมาคมโรคเบาหวานแห่งประเทศไทย 2560



*continue MET/ low dose PIO

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GLUCOSE-LOWERING MEDICINES

Class of medicine	Expected decrease in HbA_{1C}	Advantage	Disadvantage
Biguanide	1.0 - 2.0%	Weight loss, Low risk of hypoglycemia, Reduces macrovascular risk, Low costs	Gastrointestinal side effects, Lactic acidosis (rare in patients without contraindication)
Sulfonylureas	1.0 - 2.0%	Low costs	Rapid secondary drug failure, Weight gain, Risk of hypoglycemia
Glinides	0.5-1.5%	Reduces postprandial glucose Convenience	No outcomes data, Hypoglycemia, Weight gain, High costs
TZDs	0.5-1.4%	More sustained glucose control, Low risk of hypoglycemia	Weight gain, Peripheral edema, Increased incidence of CHF, Increased risk of distal fractures in women, High cost
α-glucosidase inhibitors	0.5-0.8%	Weight neutral, Low risk of hypoglycemia, Serious side effects extremely rare	No robust cardiovascular outcomes data, Gastrointestinal side effects, Modest efficacy
GLP-1 agonists	0.5-1.0%	Low risk of hypoglycemia Weight loss Cardiovascular benefit in high risk	GI side effects, ? Pancreatitis, High costs, Injection
DPP4 inhibitors	0.5-0.8%	Low risk of hypoglycemia, Weight neutral	High costs
SGLT-2 inhibitors	0.5-0.8%	Low risk of hypoglycemia Weight loss, Cardiovascular benefit in high risk	UTI, genital tract infection, High costs

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PROPOSED METFORMIN USE IN CKD

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CKD stage	eGFR	Maximal total daily dose, mg	Remark
1	≥90	2550	
2	60-<90	2550	
3A	45-<60	2000	- Avoid if kidney function is or expected to become unstable
3B	30-<45	1000	- Do not initiate therapy BUT drug may be continued and need revised dose - Avoid if kidney function is or expected to become unstable
4	15-<30	Do not use	
5	<15	Do not use	

Inzucchi SE, et al. JAMA. 2014;312(24):2668-2675.

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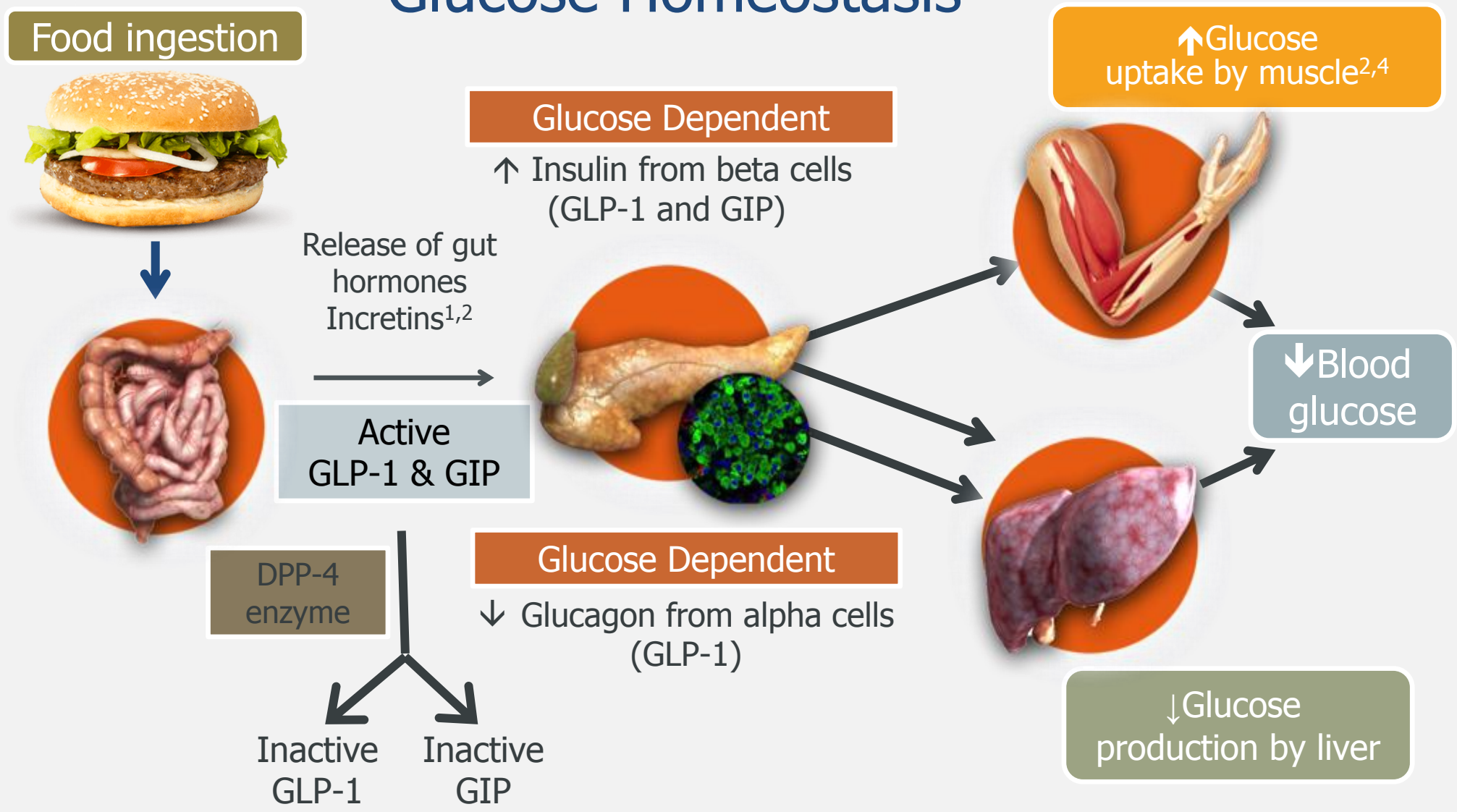
Incretins: Role in Glucose Homeostasis



1. Kieffer TJ, Habener JF. *Endocr Rev*. 1999;20:876–913. 2. Ahrén B. *Curr Diab Rep*. 2003;2:365–372. 3. Drucker DJ. *Diabetes Care*. 2003;26:2929–2940. 4. Holst JJ. *Diabetes Metab Res Rev*. 2002;18:430–441.

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GLP-1: BEYOND GLUCOSE METABOLISM

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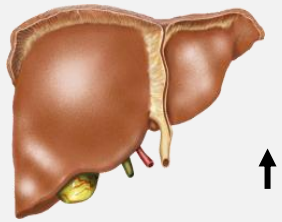
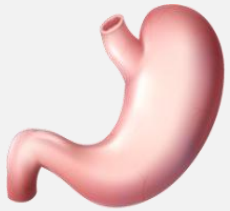


Liver
↑ Glycogen storage

Brain
↑ Neuroprotecti
↑ Neurogenesis
Memory

Heart
↑ Myocardial contractility
↑ Heart rate
↑ Myocardial glucose uptake
↓ Ischaemia-induced myocardial damage



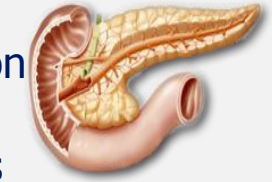
GI tract
↓ Motility

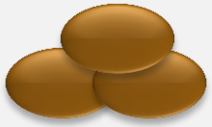
DPP-4

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Lys Ala Ala Gln Gly Glu Leu Tyr Ser Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly

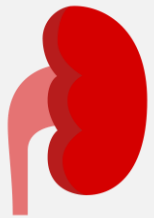
GLP-1

Pancreas
↑ New β-cell formation
↓ β-cell apoptosis
↑ Insulin biosynthesis





Fat cells
↑ Glucose uptake
↑ Lipolysis



Kidney
↑ Natriuresis

Blood vessel
↑ Endothelium-dependent vasodilation

Skeletal muscle
↑ Glucose uptake

Meier JJ et al. *Nat Rev Endocrinol* 2012;8:728–42

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INCRETIN-BASED THERAPY

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DPP-IV Inhibitor

- ไม่มีน้ำตาลต่ำ เพราะออกฤทธิ์แบบ glucose dependence insulin secretion
- ความเสี่ยงน้อยต่อการเกิดระดับน้ำตาลในเลือดต่ำ
- ใช้ได้ในผู้ป่วยโรคไตโดยปรับขนาดตามระดับ GFR
- เป็นยากิน
- ↓A1C ~0.5-0.8%
- ไม่เพิ่มน้ำหนัก

GLP-1 receptor agonist

- ไม่มีน้ำตาลต่ำ เพราะออกฤทธิ์แบบ glucose dependence insulin secretion
- ความเสี่ยงน้อยต่อการเกิดระดับน้ำตาลในเลือดต่ำ
- ใช้ได้ในผู้ป่วยโรคไตที่ GFR > 30
- เป็นยาฉีด
- ↓A1C ~1.0-1.5%
- น้ำหนักลด

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SGLT2 INHIBITION – MODE OF ACTION

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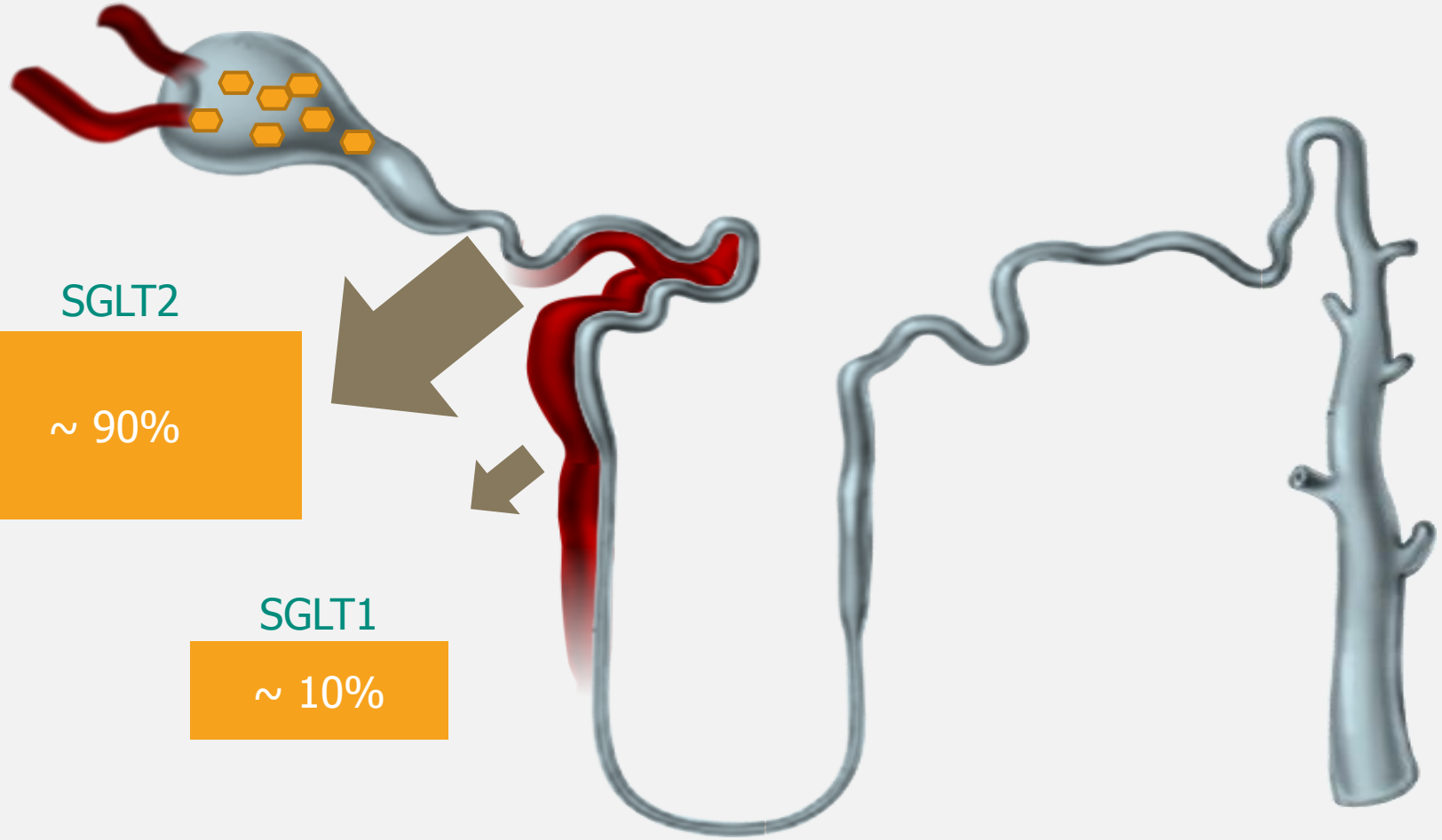
Renal glucose re-absorption under healthy conditions

Filtered glucose load 180 g/day



SGLT2

~ 90%

SGLT1

~ 10%

Virtually all of the filtered glucose is re-absorbed in the proximal tubules through SGLT2 and SGLT1, with SGLT2 accounting for ~ 90% in the S1 and S2 segments and SGLT1 accounting for ~ 10% in the S3 segment

SGLT, sodium glucose co-transporter.

1. Gerich JE. *Diabet Med.* 2010;27:136–142; 2. Bakris GL, et al. *Kidney Int.* 2009;75;1272–1277;
3. Ferrannini E et al *Nat Rev Endocrinol* 2012; 8: 495. Figure reprinted by permission
from McMillan Publishers Ltd *Nat Rev Endocrin* 2012

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SGLT2 INHIBITION – MODE OF ACTION

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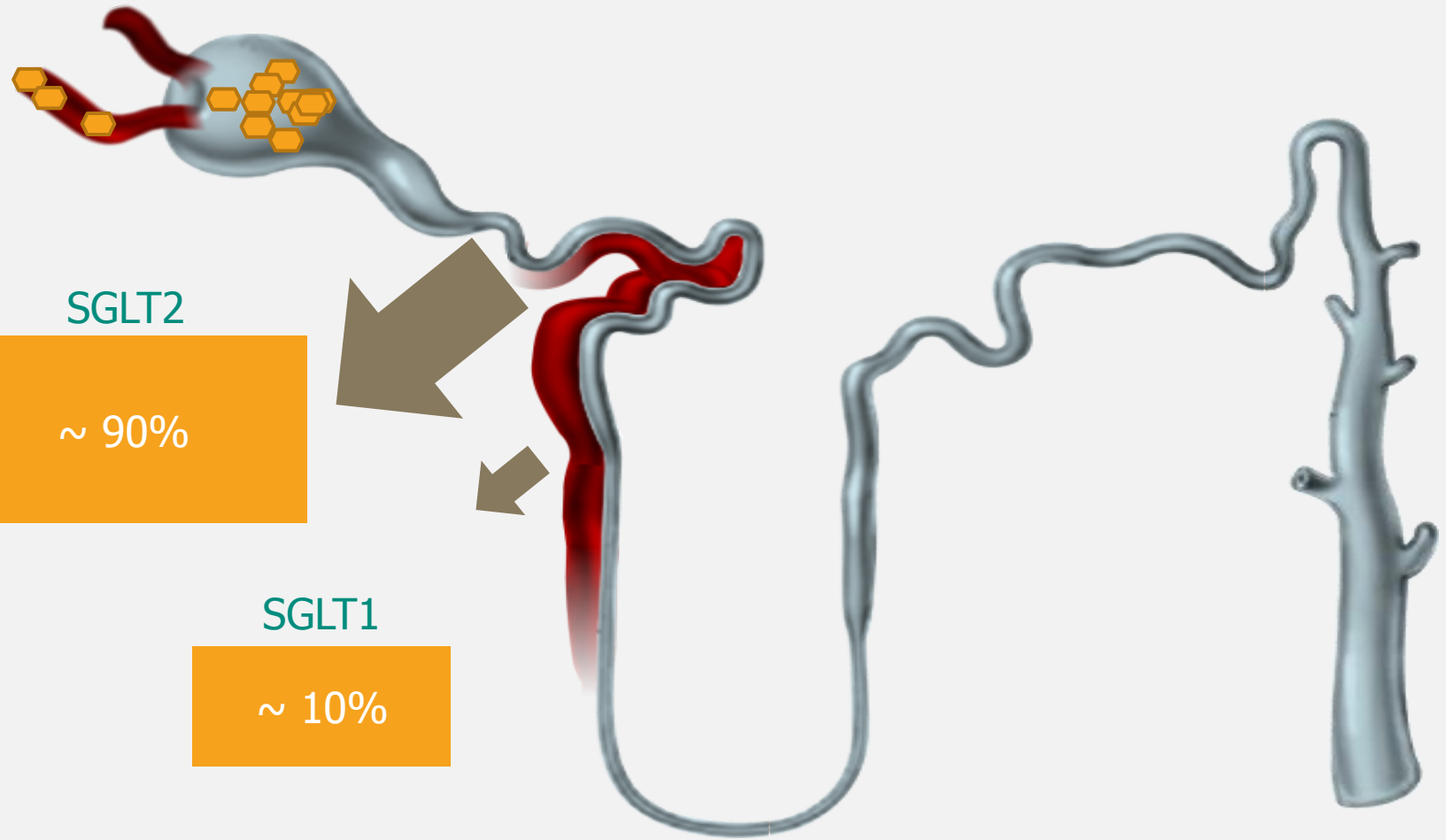
Renal glucose re-absorption in T2DM

Filtered glucose load > 180 g/day



SGLT2

~ 90%

SGLT1

~ 10%

When blood glucose increases above the renal threshold (~ 11 mmol/L or 198 mg/dL), the capacity of the transporters is exceeded, resulting in urinary glucose excretion

SGLT, sodium glucose co-transporter.

1. Gerich JE. Diabet Med. 2010;27:136–142; 2. Bakris GL, et al. Kidney Int. 2009;75;1272–1277;
3. Ferrannini E et al *Nat Rev Endocrinol* 2012; 8: 495. Figure reprinted by permission
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SGLT2 INHIBITION – MODE OF ACTION

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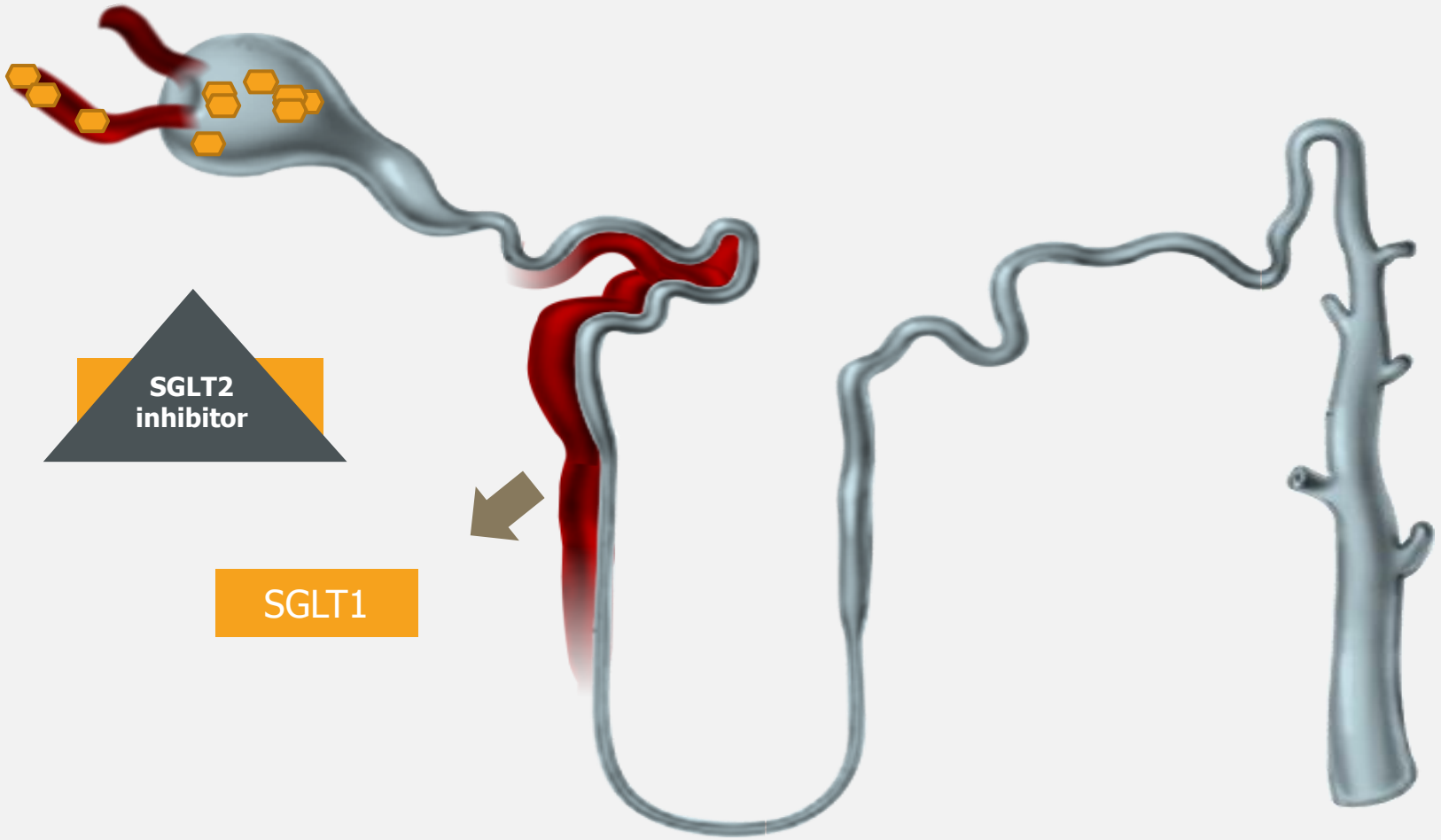
Urinary glucose excretion via SGLT2 inhibitor

Filtered glucose load > 180 g/day



SGLT2 inhibitors reduce glucose re-absorption in the proximal tubule, leading to urinary glucose excretion* and osmotic diuresis

SGLT, sodium glucose co-transporter. *Loss of ~ 78 g of glucose per day = 312 calories/day.

1. Gerich JE. Diabet Med. 2010;27:136–142; 2. Bakris GL, et al. Kidney Int. 2009;75;1272–1277;
3. Ferrannini E et al *Nat Rev Endocrinol* 2012; 8: 495. Figure reprinted by permission from McMillan Publishers Ltd *Nat Rev Endocrin* 2012

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PERSPECTIVES ON SGLT-2 INHIBITION

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Potential Advantages	Concerns
• Once daily administration • Decreases FPG, PPG, A1c • Weight loss (60g urine glucose = 240 kcal/day = 0.3 kg/week) • No/low risk of hypoglycemia • Modest blood pressure lowering • Effect independent of insulin secretion or insulin resistance • Use complementary with other T2D Rx?T1D,? Pre-diabetes? • Potential for use in Type 1 Diabetes • long-term effects on kidney and on CV outcomes	• Bacterial urinary tract infections • Fungal genital infections • May not be as effective in patients with renal impairment • Transient initial period of dehydration, polyuria, thirst • No known Added cost to diabetes therapy • Euglycemic DKA

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HOW TO PREVENT SGLT2 I ASSOCIATED DKA

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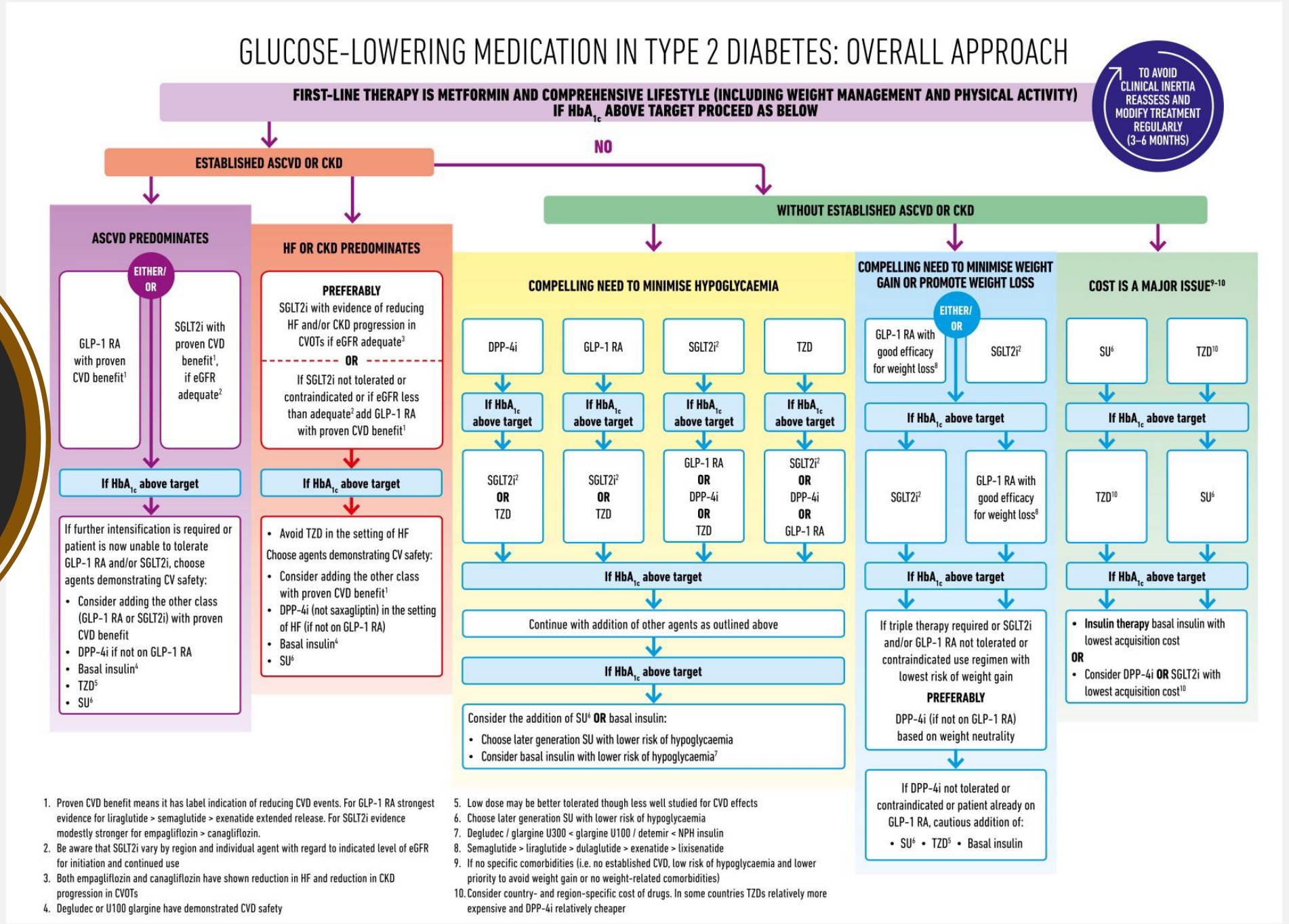
Precipitant	Action Regarding SGLT2 I
Acute illness	Hold at onset Restart when feeling well and able to eat and drink
Major surgical procedures	Hold 3 days before surgery Restart when feeling well and able to eat and drink
Risk of dehydration	Hold until able to maintain hydration
Low-CHO diet	Hold until normal diet resumes
Bariatric surgery	Hold while on preoperative low-CHO diet Reevaluate postoperatively
Excessive alcohol intake	Stop immediately

R.M. Goldenberg et al. Clinical Therapeutics/Volume 38, Number 12, 2016

NEW CVOT IN DIABETES

		3P-MACE	CV Death	MI	Stroke	Any death	HHF	Renal benefit
SGLT-2 I	EMPA-REG	↓	↓	↔	↔	↓	↓	↓
	CANVAS	↓	↔	↔	↔	↔	↓	↓
	DECLARE	↔	↔	↔	↔	↔	↓	↓
	CREDENCE	↓	↔	↔	↔	↔	↓	↓
GLP-1 RA	ELIXA	↔	↔	↔	↔	↔	↔	↔
	LEADER	↓	↓	↔	↔	↓	↔	↓
	SUSTAIN-6	↓	↔	↔	↓	↔	↔	↓
	EXECEL	↔	↔	↔	↔	↔	↔	↔
	HARMONY	↓	↔	↓	↔	↔	↔	↔
	REWIND	↓	↔	↔	↓	↔	↔	↓
	PIONEER-6	↔	↓	↔	↔	↔	↔	

New Updated ADA/EASD 2018



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NEW UPDATED 2018 ADA/EASD GUIDELINE FOR MANAGEMENT OF T2DM

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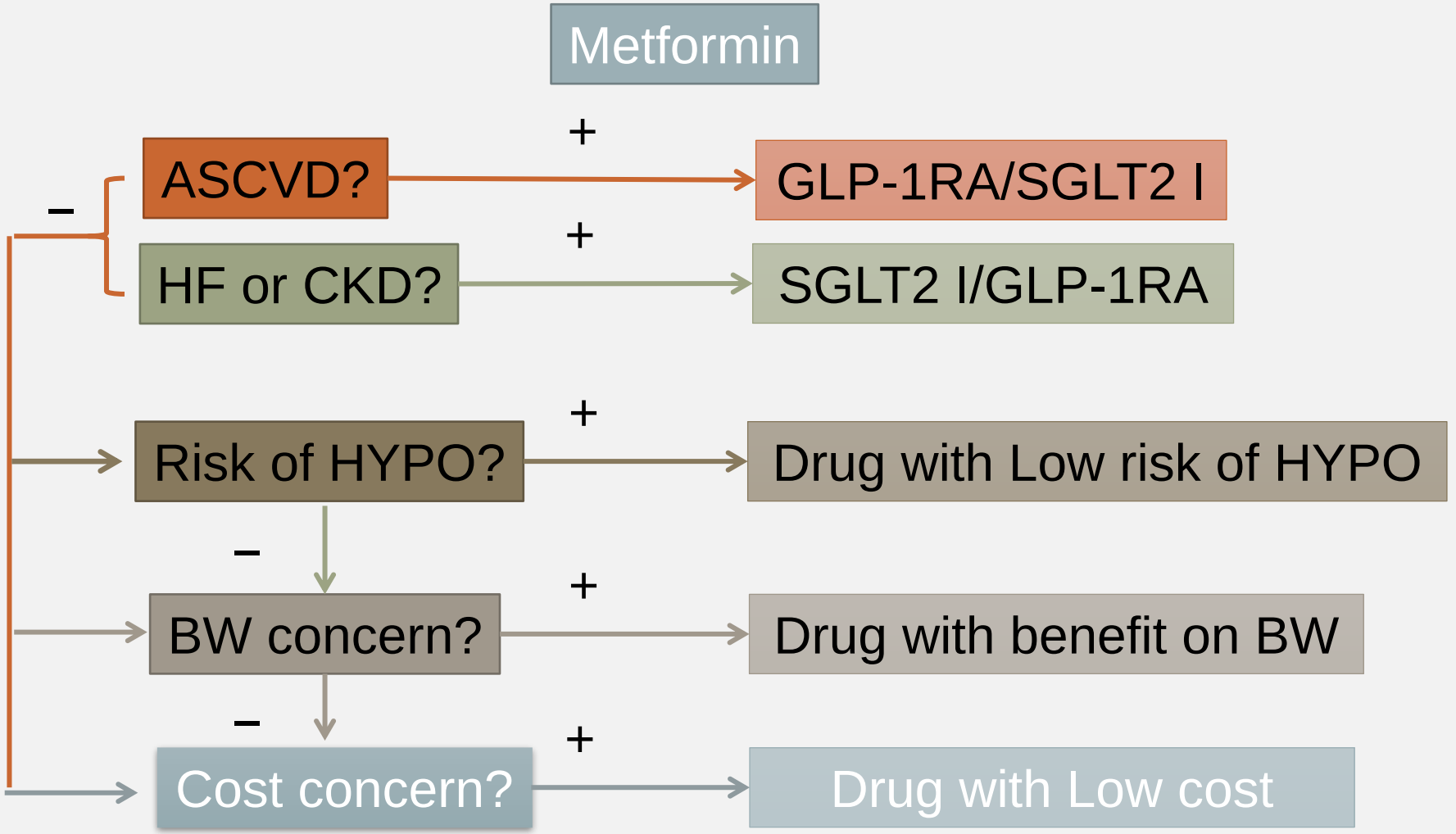

Personalized Treatment

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การศึกษา STENO-2: การติดตามผู้เข้าร่วมโครงการเป็นระยะเวลา 21 ปี

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อัตราการเสียชีวิตจาก
โรคหลอดเลือดหัวใจ (%)

Gæde P, et al. Diabetologia. 2016;59(11):2298-2307

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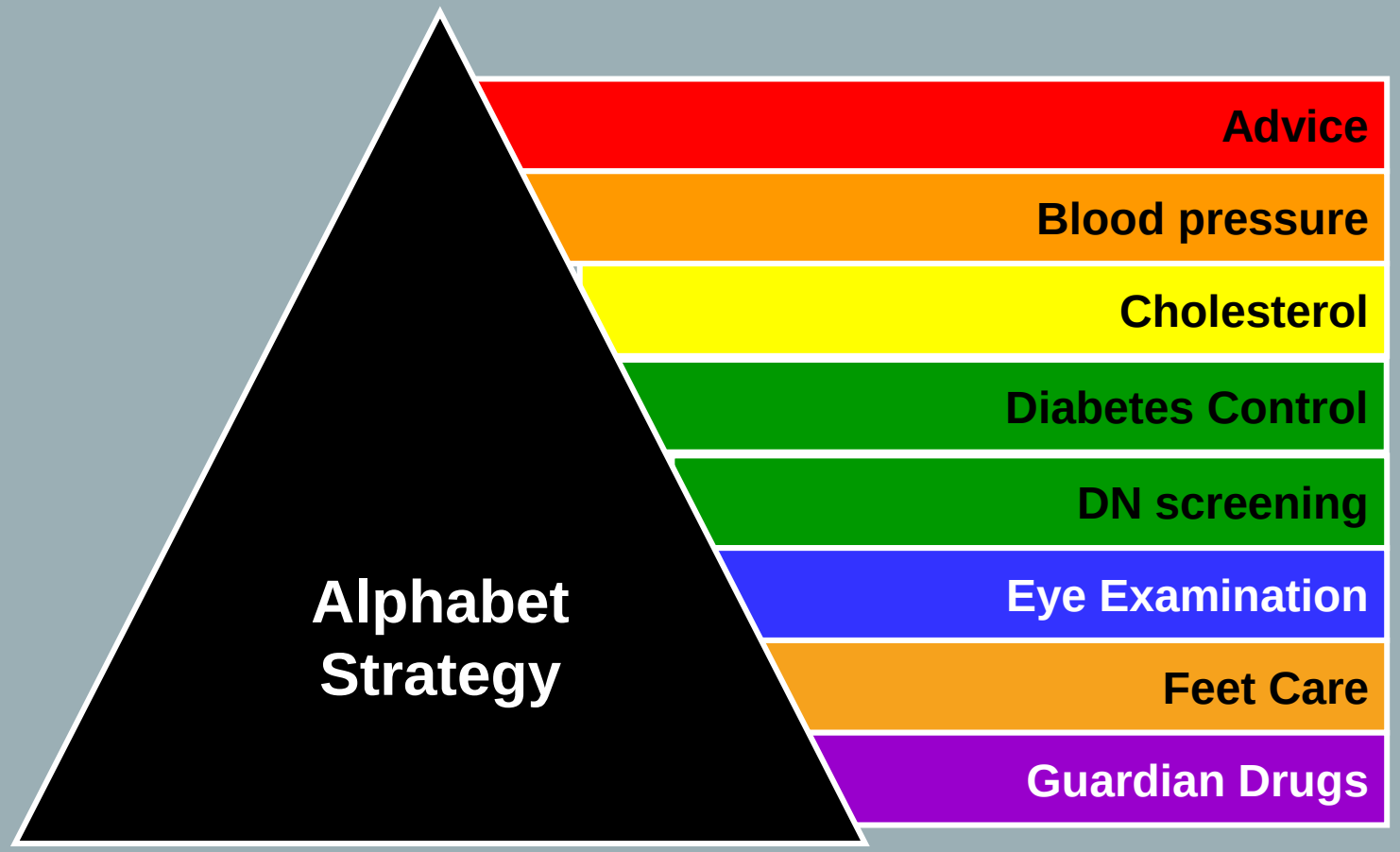
DIABETES CARE:
THE ALPHABET STRATEGY



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ADA 2019 RECOMMENDATION FOR BP MANAGEMENT

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- DM + HT + high CV risk (existing ASCVD or 10-year ASCVD risk >15%)
  - A blood pressure target of <130/ 80 mmHg may be appropriate
  - If it can be safely attained
- DM + HT + lower risk for CV (10-year ASCVD risk <15%)
  - Treat to a blood pressure target of <140/90 mmHg
- Patient at high risk of adverse effects may prefer higher blood pressure targets to enhance quality of life

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ADA 2019 RECOMMENDATION FOR BP MANAGEMENT

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- All hypertensive patients with diabetes should monitor their blood pressure at home
- Those who are not meeting BP targets on 3 classes of anti HT, including a diuretic should be considered
  - Search for secondary HT
  - Prescribed mineralocorticoid receptor antagonist

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ASCVD RISK ESTIMATOR PLUS

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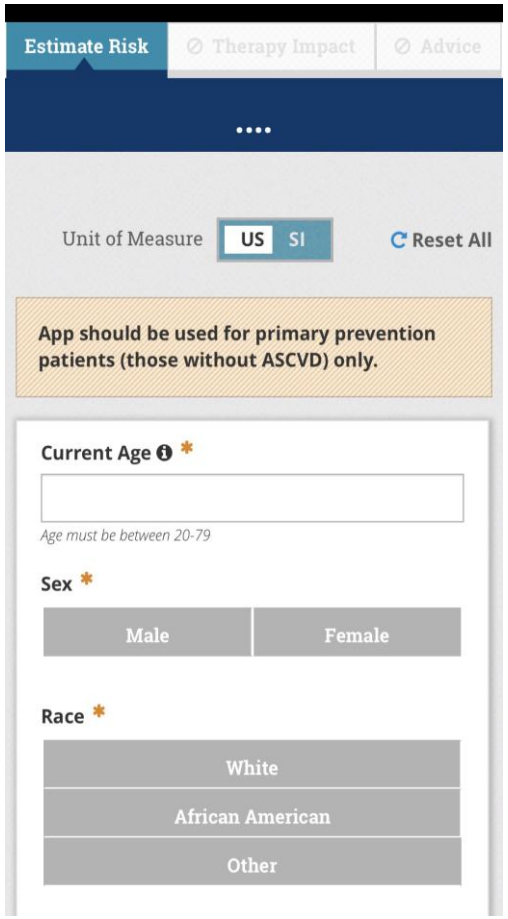
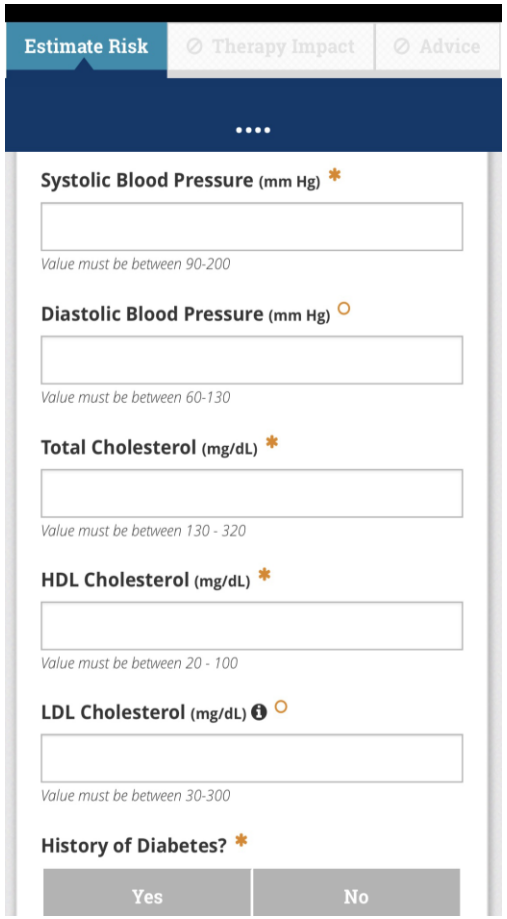
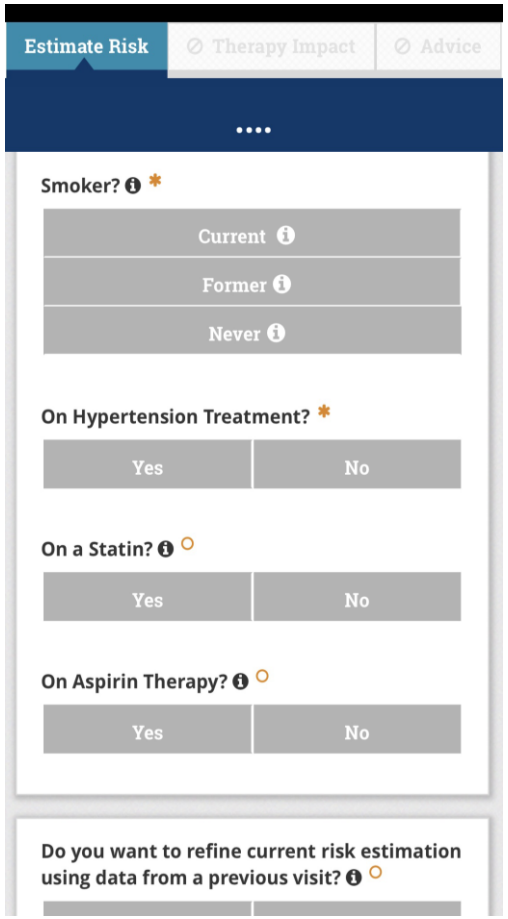
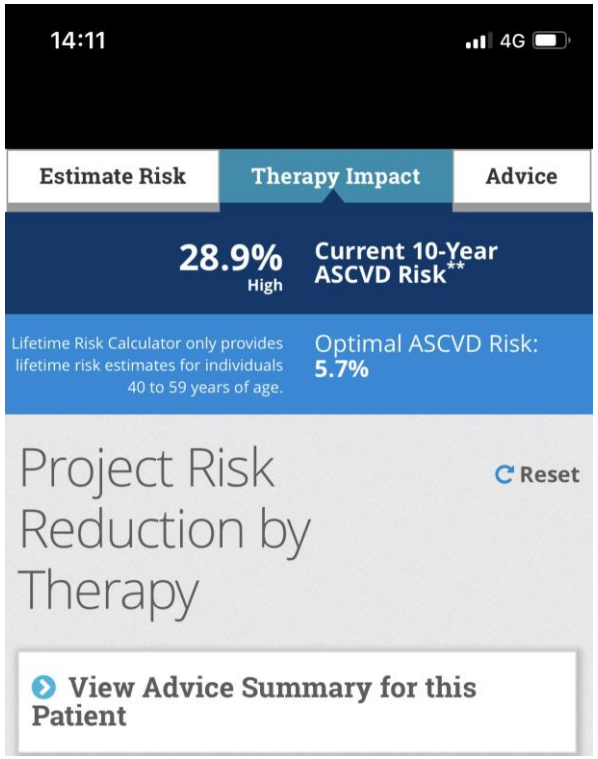


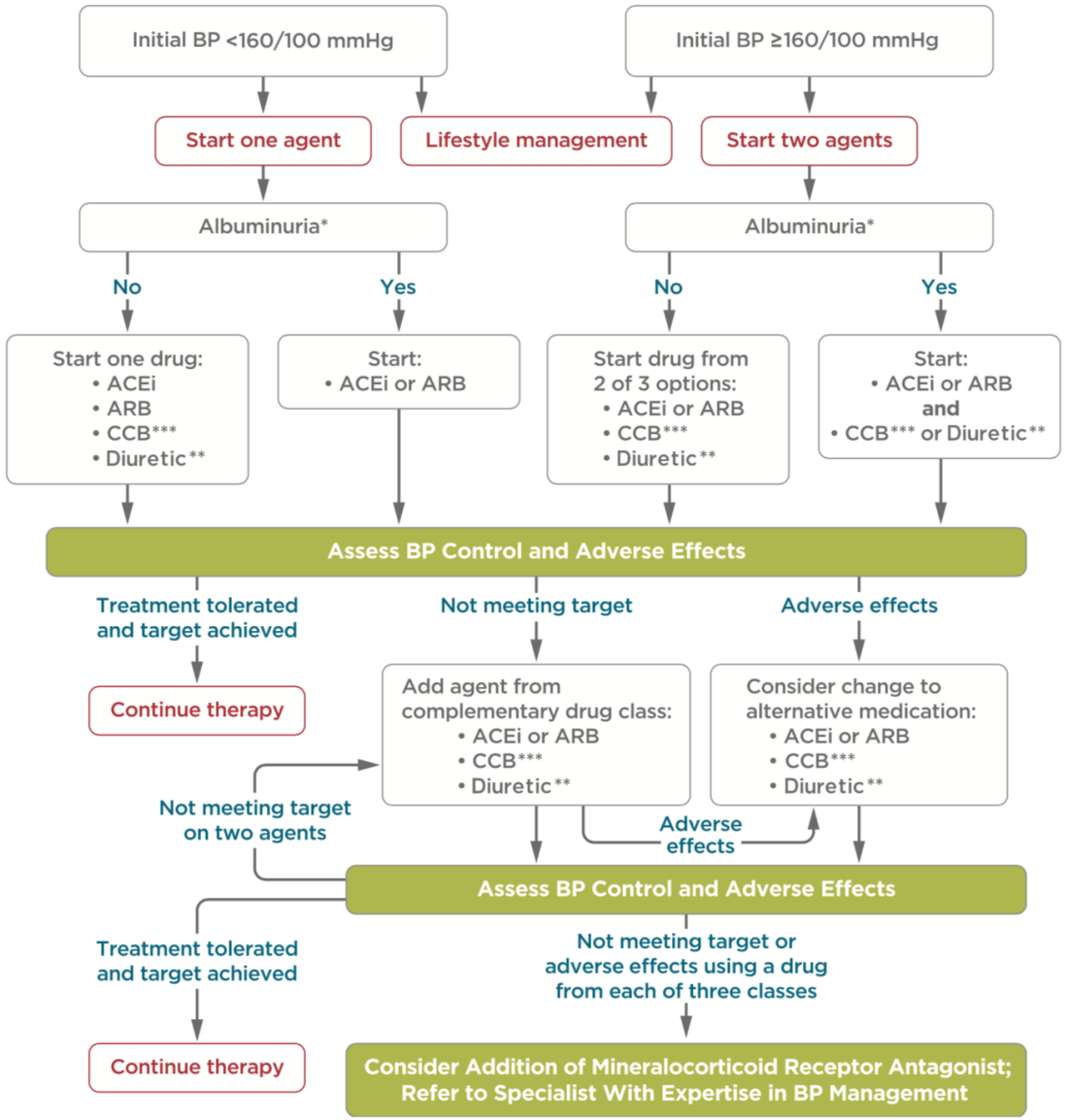






http://tools.acc.org/ASCVD-+Risk-Estimator-Plus

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

Initial BP <160/100 mmHg

Initial BP ≥160/100 mmHg

Start one agent

Lifestyle management

Start two agents

Albuminuria*

Albuminuria*

No

Yes

No

Yes

Start one drug:
- ACEi
- ARB
- CCB***
- Diuretic**

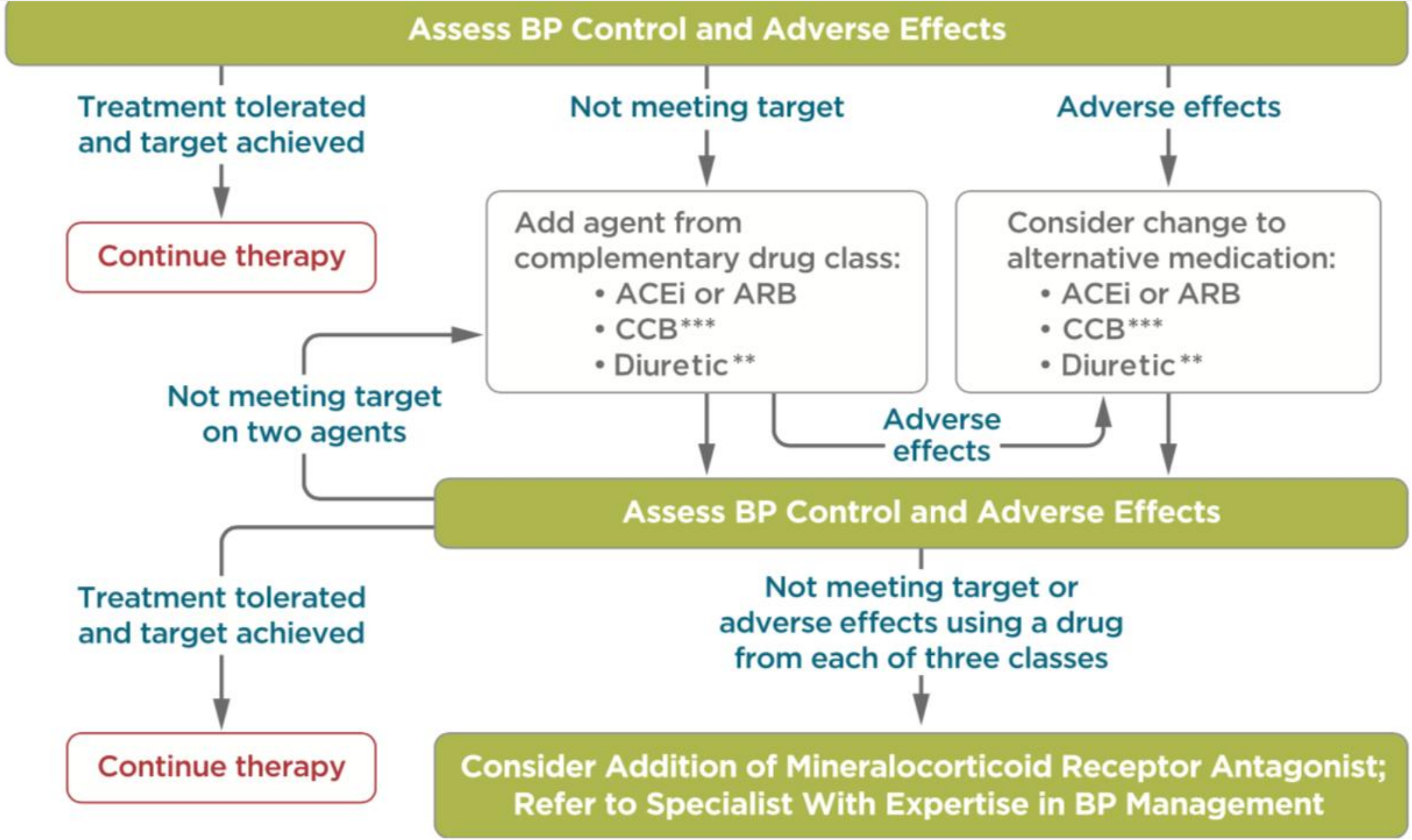
Start:
- ACEi or ARB

Start drug from 2 of 3 options:
- ACEi or ARB
- CCB***
- Diuretic**

Start:
- ACEi or ARB

and

- CCB*** or Diuretic**


Assess BP Control and Adverse Effects
Treatment tolerated and target achieved
Not meeting target
Adverse effects
Continue therapy
Add agent from complementary drug class:
• ACEi or ARB
• CCB***
• Diuretic**
Consider change to alternative medication:
• ACEi or ARB
• CCB***
• Diuretic**
Not meeting target on two agents
Adverse effects
Assess BP Control and Adverse Effects
Treatment tolerated and target achieved
Not meeting target or adverse effects using a drug from each of three classes
Continue therapy
Consider Addition of Mineralocorticoid Receptor Antagonist; Refer to Specialist With Expertise in BP Management

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ADA 2019 LIPID MANAGEMENT RECOMMENDATION

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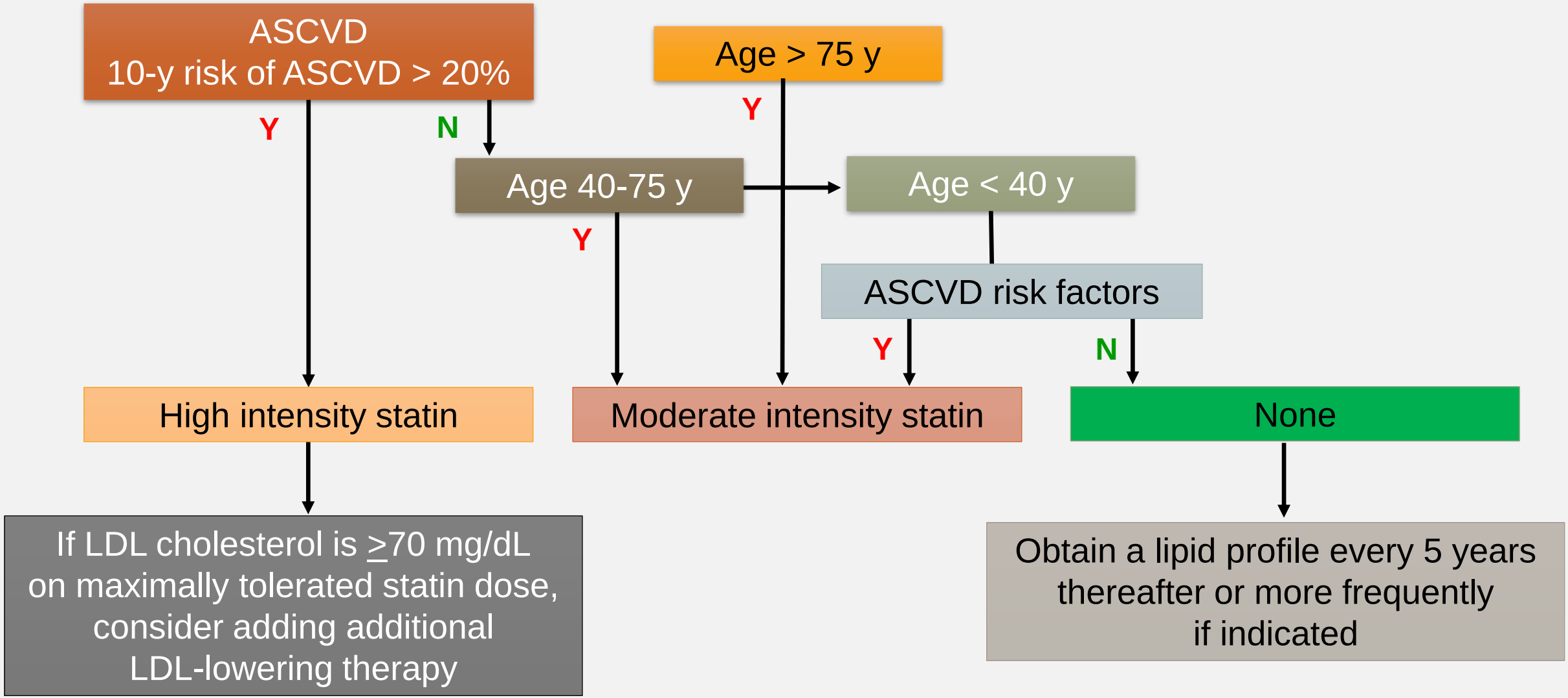

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INTENSITY OF STATIN

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High intensity	*Moderate intensity*	*Low intensity*
Daily dosage lowers LDL-C by approximately ≥ 50% on average	Daily dosage lowers LDL-C by approximately 30% to 50% on average	Daily dosage lowers LDL-C by < 30% average
Atorvastatin (Lipitor), 40† to 80 mg	**Atorvastatin, 10** *(20)* **mg**	*Simvastatin, 10 mg*
Rosuvastatin (Crestor), 20 *(40)* **mg**	**Rosuvastatin,** *(5)* **10 mg**	**Pravastatin, 10 to 20 mg**
	Simvastatin (Zocor), 20 to 40 mg‡	**Lovastatin, 20 mg**
	Pravastatin (Pravachol), 40 *(80)* **mg**	*Fluvastatin, 20 to 40 mg*
	Lovastatin (Mevacor), 40 mg	*Pitavastatin, 1 mg*
	Fluvastatin XL (Lescol XL), 80 mg	
	Fluvastatin, 40 mg twice daily	
	Pitavastatin (Livalo), 2 to 4 mg	

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SIMVASTATIN RESTRICTIONS

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Maximum Dose

Limit use of the 80-mg dose to patients who have been taking it for ≥12 months without evidence of myopathy

Contraindicated

Strong CYP3A4 Inhibitors:

Antifungals
- Itraconazole *(Sporanox)*
- Ketoconazole *(Nizoral)*
- Posaconazole *(Noxafil)*
- Voriconazole *(Vfend)*

Antibacterials
- Clarithromycin *(Biaxin)*
- Erythromycin *(Ery-Tabs)*
- Isoniazid (INH)
- Telithromycin *(Ketek)*

HIV Protease Inhibitors

Other Drugs:
- Gemfibrozil *(Lopid)*
- Cyclosporine *(Neoral)*
- Danazol
- Grapefruit juice (>1 qt/d)

Simvastatin Dosing Restrictions

Maximum 10 mg/day with:
- Amiodarone *(Cordarone)*
- Diltiazem *(Cardizem)*
- Verapamil *(Calan)*

Maximum 20 mg/day with:
- Amlodipine *(Norvasc)*
- Ranolazine *(Ranexa)*

Caution

- ≥1 gm/day niacin in Chinese patients
- Fibrates (other than gemfibrozil)

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ADA 2019 RECOMMENDATION FOR ANTIPLATELETS

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- Secondary prevention
  - Aspirin 75–162 mg/day in DM + ASCVD
  - Clopidogrel 75 mg/day in those with aspirin allergy
- Primary prevention
  - Aspirin 75–162mg/day may be considered in DM + increased CV risk, after a discussion about benefits versus increased risk of bleeding

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ASSOCIATION OF ASPIRIN USE FOR PRIMARY PREVENTION WITH CV EVENTS AND BLEEDING EVENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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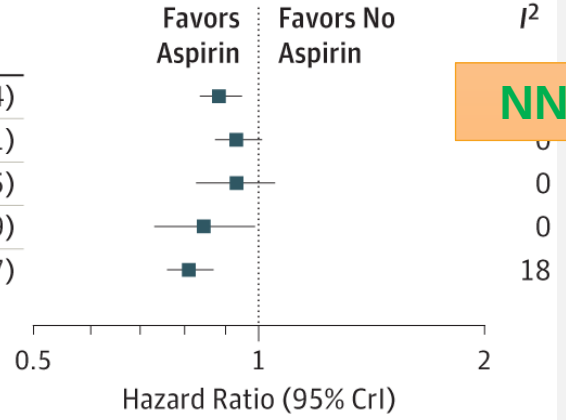
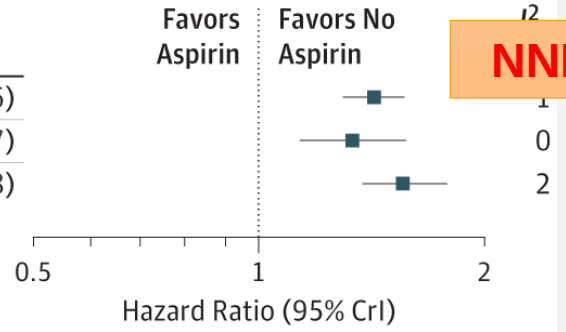
Total of 13 trials randomizing 164 225 participants without cardiovascular disease

Cardiovascular Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Reduction, % (95% CI)	HR (95% CrI)
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Composite CV outcome	13	2911	79717	3342	80057	0.41 (0.23 to 0.59)	0.89 (0.84-0.94)
All-cause mortality	13	3622	81623	3588	80057	0.13 (-0.07 to 0.32)	0.94 (0.88-1.01)
CV mortality	13	995	81623	997	80057	0.07 (-0.04 to 0.17)	0.94 (0.83-1.05)
Myocardial infarction	13	1469	81623	1599	80057	0.28 (0.05 to 0.47)	0.85 (0.73-0.99)
Ischemic stroke	10	831	65316	942	63752	0.19 (0.06 to 0.30)	0.81 (0.76-0.87)



NNT 241

Bleeding Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Increase, % (95% CI)	HR (95% CrI)
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Major bleeding	11	1195	74715	834	73143	0.47 (0.34 to 0.62)	1.43 (1.30-1.56)
Intracranial bleeding	12	349	80985	257	79419	0.11 (0.04 to 0.18)	1.34 (1.14-1.57)
Major GI bleeding	10	593	70336	380	70465	0.30 (0.20 to 0.41)	1.56 (1.38-1.78)



NNH 210

Sean LZ, et al. JAMA. 2019;321(3):277-287. doi:10.1001/jama.2018.20578

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ASSOCIATION OF ASPIRIN USE FOR PRIMARY PREVENTION WITH CV EVENTS AND BLEEDING EVENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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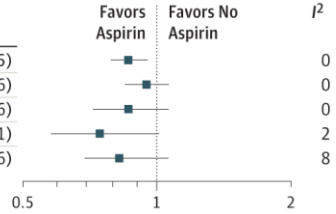
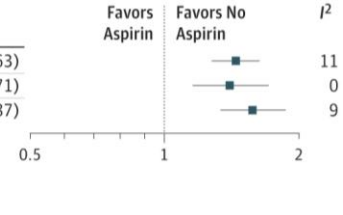
LOW CV RISK

Cardiovascular Outcomes	No. of Studies	Aspirin No. of Events	Aspirin No. of Participants	No Aspirin No. of Events	No Aspirin No. of Participants	Absolute Risk Reduction, % (95% CI)	HR (95% CrI)	I^2
Composite CV outcome	6	1559	56212	1753	56354	0.34 (0.14 to 0.52)	0.87 (0.79-0.95)	0
All-cause mortality	6	1903	56212	1905	56354	0.01 (-0.27 to 0.27)	0.95 (0.85-1.06)	0
CV mortality	6	405	56212	448	56354	0.07 (-0.03 to 0.16)	0.87 (0.72-1.06)	0
Myocardial infarction	6	649	56212	793	56354	0.27 (0.00 to 0.49)	0.75 (0.58-1.01)	2
Ischemic stroke	5	508	49942	593	50078	0.16 (0.02 to 0.29)	0.83 (0.69-1.06)	8

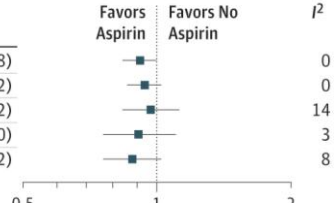


Bleeding Outcomes	No. of Studies	Aspirin No. of Events	Aspirin No. of Participants	No Aspirin No. of Events	No Aspirin No. of Participants	Absolute Risk Increase, % (95% CI)	HR (95% CrI)	I^2
Major bleeding	5	665	49942	465	50078	0.40 (0.25 to 0.57)	1.45 (1.28-1.63)	11
Intracranial bleeding	6	245	56212	175	56354	0.13 (0.05 to 0.22)	1.41 (1.16-1.71)	0
Major GI bleeding	5	359	48992	228	49110	0.27 (0.15 to 0.40)	1.58 (1.34-1.87)	9

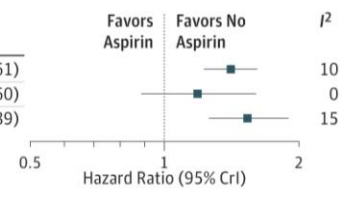


HIGH CV RISK

Cardiovascular Outcomes	No. of Studies	Aspirin No. of Events	Aspirin No. of Participants	No Aspirin No. of Events	No Aspirin No. of Participants	Absolute Risk Reduction, % (95% CI)	HR (95% CrI)	I^2
Composite CV outcome[a]	8	1645	25411	1649	23703	0.63 (0.18 to 1.04)	0.91 (0.84-0.98)	0
All-cause mortality	7	1719	25411	1683	23703	0.43 (-0.02 to 0.84)	0.94 (0.86-1.02)	0
CV mortality	7	590	25411	549	23703	0.04 (-0.27 to 0.32)	0.97 (0.84-1.12)	14
Myocardial infarction[a]	8	820	25411	806	23703	0.32 (-0.16 to 0.74)	0.91 (0.76-1.10)	3
Ischemic stroke[a]	6	323	15374	350	13674	0.28 (-0.12 to 0.63)	0.88 (0.76-1.02)	8

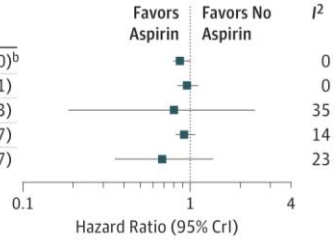


Bleeding Outcomes	No. of Studies	Aspirin No. of Events	Aspirin No. of Participants	No Aspirin No. of Events	No Aspirin No. of Participants	Absolute Risk Increase, % (95% CI)	HR (95% CrI)	I^2
Major bleeding	6	530	24773	369	23065	0.64 (0.35 to 0.97)	1.41 (1.23-1.61)	10
Intracranial bleeding	6	104	24773	82	23065	0.07 (-0.04 to 0.21)	1.19 (0.89-1.60)	0
Major GI bleeding	5	34	19452	30	19444	0.39 (0.16 to 0.69)	1.54 (1.26-1.89)	15

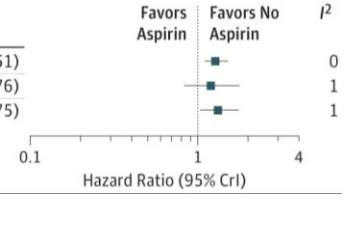


DIABETES

Cardiovascular Outcomes	No. of Studies	Aspirin No. of Events	Aspirin No. of Participants	No Aspirin No. of Events	No Aspirin No. of Participants	Absolute Risk Reduction, % (95% CI)	HR (95% CrI)	I^2
Composite CV outcome	8	977	14916	1072	14898	0.65 (0.09 to 1.17)	0.90 (0.82-1.00)[b]	0
All-cause mortality	5	1028	11938	1055	11946	0.24 (-0.49 to 0.91)	0.97 (0.85-1.11)	0
CV mortality	4	264	10159	279	10167	0.05 (-1.27 to 0.94)	0.82 (0.19-2.43)	35
Myocardial infarction	8	472	11788	490	11700	0.26 (-0.47 to 0.88)	0.94 (0.83-1.07)	14
Ischemic stroke	3	275	9535	317	9511	0.83 (-0.50 to 1.70)	0.70 (0.36-1.37)	23



Bleeding Outcomes	No. of Studies	Aspirin No. of Events	Aspirin No. of Participants	No Aspirin No. of Events	No Aspirin No. of Participants	Absolute Risk Increase, % (95% CI)	HR (95% CrI)	I^2
Major bleeding	3	370	10029	287	10047	0.80 (0.29 to 1.39)	1.29 (1.11-1.51)	0
Intracranial bleeding	2	63	9002	52	9017	0.12 (-0.09 to 0.43)	1.21 (0.84-1.76)	1
Major GI bleeding	2	142	9002	105	9017	0.41 (0.06 to 0.86)	1.35 (1.05-1.75)	1



ANTIPLATELETS AS A PRIMARY PREVENTION

Shared decision-making for use of aspirin in primary prevention of CVD

1 Assessment of patient's baseline level of understanding and patient activation to engage in discussion with sample questions

What have you heard about aspirin use in preventing cardiovascular events such as heart attack and stroke?

Would you be interested in learning more about this today?

2 Review of potential benefits and harms

Benefits
- Reduced CVD mortality
- Reduced myocardial infarction risk
- Reduced stroke occurrence
- Reduced colorectal cancer mortality

Harms
- Intracranial bleeding
- Major and minor gastrointestinal bleeding
- Nuisance bleeding and bruising
- Increased costs and follow-up visits

3 Assessment of patient preferences with sample questions

Familiarity with and concerns about the conditions prevented by aspirin

What's your experience with heart attack, stroke, and cancer?

How concerned are you about developing one of these conditions?

Familiarity with and concerns about the adverse effects of aspirin use

What's your experience with excess bleeding?

How concerned are you about the risk of bleeding while on aspirin?

How do you feel about minor bleeding or bruising as a side effect?

How do you feel about medication side effects in general?

Willingness to take a long-term medication

How do you feel about continuing daily aspirin for years?

Considerations for patients **not under current treatment** with low-dose aspirin

Consider initiation	Discuss benefits and harms	Avoid initiation
• High CVD risk (>15%) • High colorectal cancer risk • Lower bleeding risk	• Intermediate CVD risk (7.5%-15%)	• Low CVD risk (<7.5%) • Higher bleeding risk

Considerations for patients **under current treatment** with low-dose aspirin

Consider continuation	Discuss benefits and harms	Consider discontinuation
• High CVD risk (>10%) • High colorectal cancer risk • Longer duration of past aspirin use (>10 y)	• Intermediate CVD risk (7.5%-15%)	• Low CVD risk (<7.5%) • Shorter duration of past aspirin use (<5 y) • Higher bleeding risk

JAMA. 2019; online 28 Jun 2019

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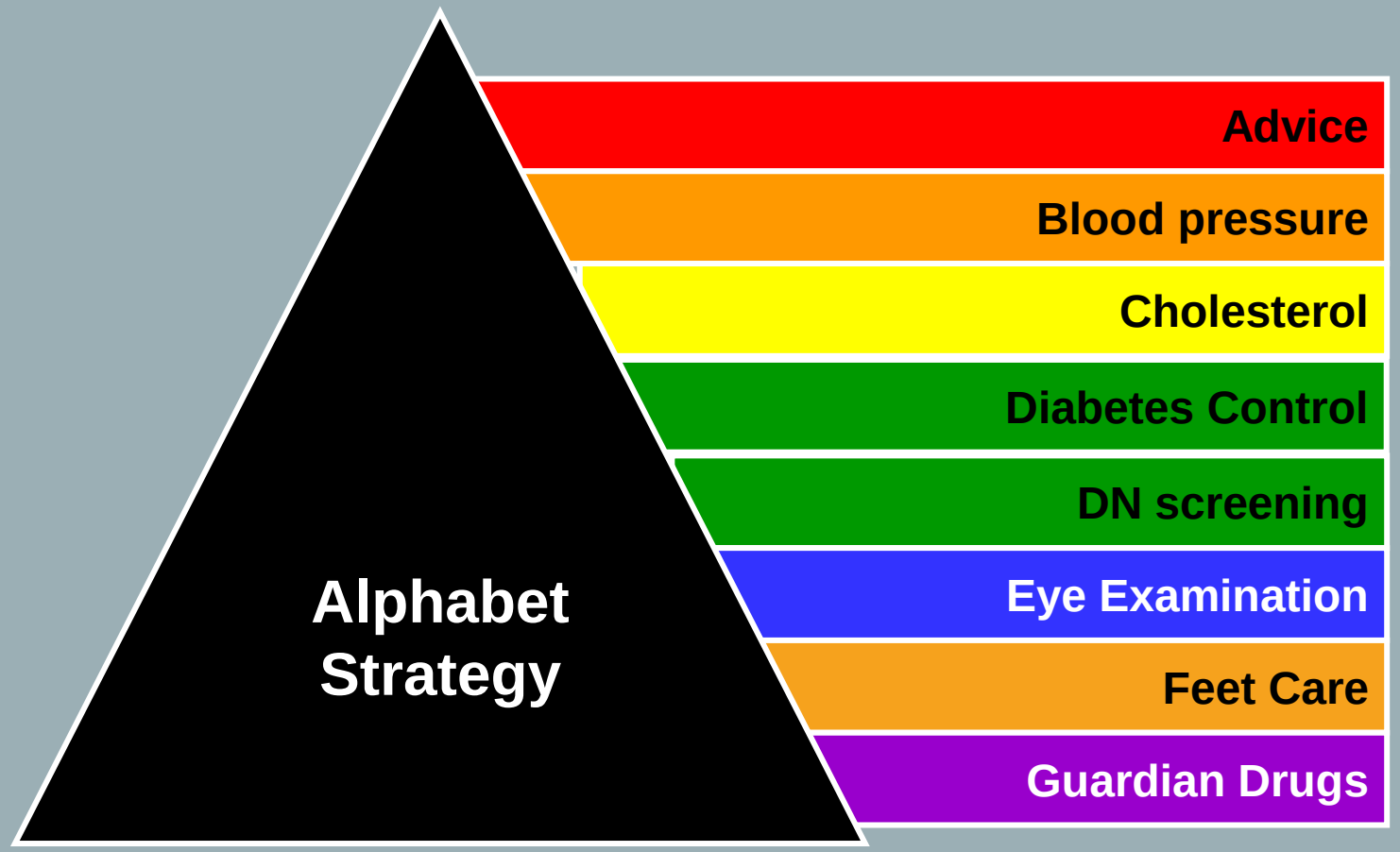
DIABETES CARE:
THE ALPHABET STRATEGY



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DIABETES CARE:
THE ALPHABET STRATEGY

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• **A**dvice	↓BW, Smoking , diet ,exercise
• **B**lood pressure	≤ 140/90 (≤ 130/80 in high risk for ASCVD)
• **C**holesterol	LDL ≤ 100 (optional 70)
• **D**iabetes control	Individualized target
• **D**N screening	Annual examination
• **E**ye examination	Annual examination
• **F**eet examination	Annual examination
• **G**uardian drugs	Aspirin, ACEI, statins


ขอบคุณค่ะ