

FROM NOBEL PRIZE TO CARDIOVASCULAR SAFETY

Current Concept of Diabetes Care

roy panusunan sibarani

2nd jakarta emergency care, september 28th , 2017

nothing to disclose





Alliston town, Ontario



Nobel Prize for Medicine Awarded To Doctors Banting and MacLeod

(Special Cable to The Globe and The Chicago Tribune. Copyright, 1922.)



DR. F. G. BANTING.

The other Nobel awards made to Americans are: One in physics to A. A. Michelson, one in chemistry to T. W. Richards, and prizes for efforts in furthering peace to the late Theodore Roosevelt, Honorable Elihu Root, and ex-President Woodrow Wilson.

The total value of the award to be divided between Dr. Banting and Dr. MacLeod amounts to about \$40,000. It is understood that the prize was awarded jointly, in view of the fact that Professor MacLeod, as head of the Department of Physiology at the University of Toronto, directed the work in the laboratories where Dr. Banting conducted the investigations which led up to the discovery of insulin.

Professor MacLeod has not yet returned to Toronto from England, where he has been for the past month or two, and Dr. Banting could not be reached at his home here.

STOCKHOLM, Oct. 25.—The Council of Teachers of the Karolinska Institute this evening decided to give the Nobel Prize to the Canadian professors of the University of Toronto, Doctors F. G. Banting and J. J. R. MacLeod, for the discovery of insulin.

The Nobel Prize in 1922 was awarded to a professor of University College, London, Archibald Hill, because of his discoveries in the physiology of the muscles, and the second half to a professor of the University of Kiel, Otto Meyerhof, for his researches concerning oxygen, lactic acid and consumption of muscles.

This is only the second time that a Nobel Prize, for outstanding service in the field of medicine, has been awarded in America. It is the first time that any Nobel Prize has ever fallen to the lot of a Canadian.

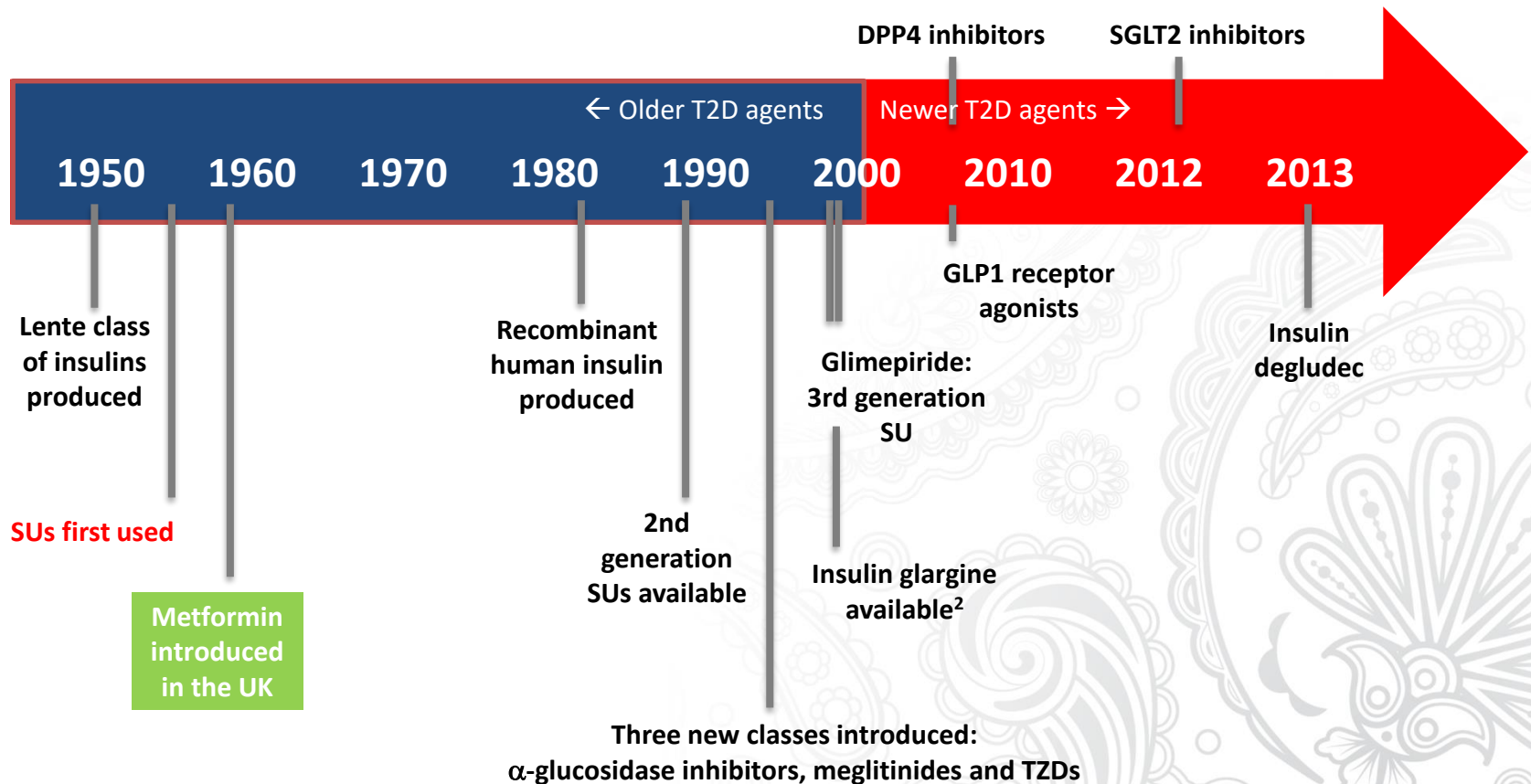
The previous award of the prize in medicine on this continent was made to Dr. Alexis Carrel in 1912, for his work in connection with surgery of the blood vessels and transplantation of tissues and organs.

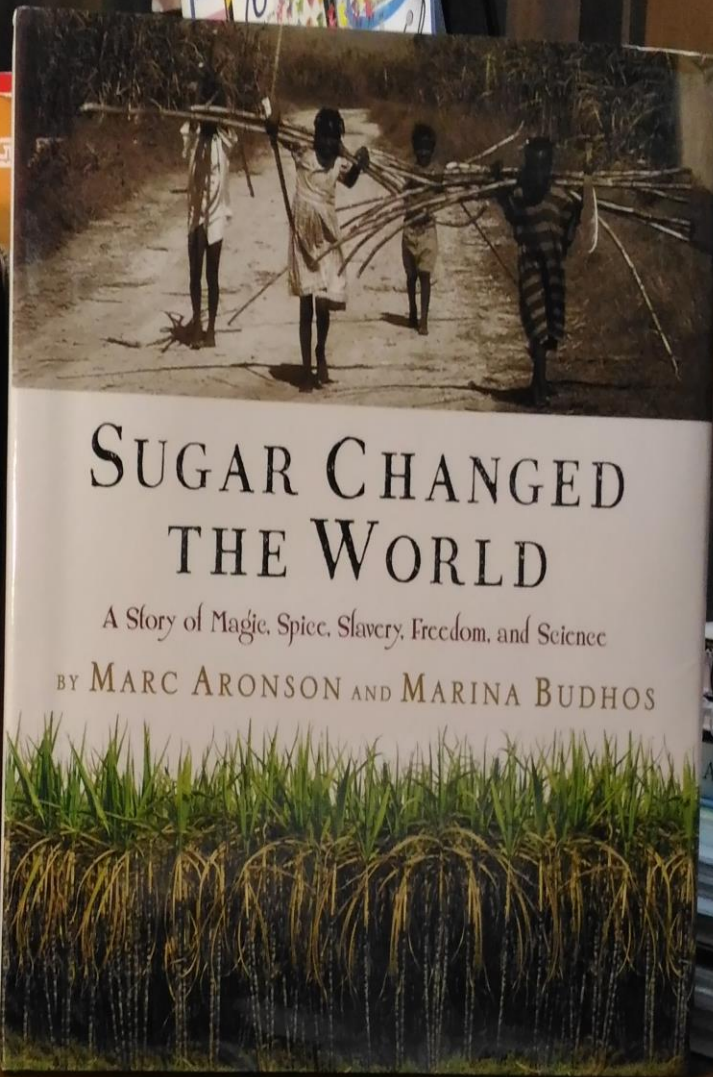


DR. J. J. R. MACLEOD.



Evolution of T2D agents







Feeding Sugar Cane Mill, Barbados, B.W.I.



Freedom or Slavery? The In-Between



The current landscape in Type 2 diabetes

387 million

People are living with diabetes worldwide...

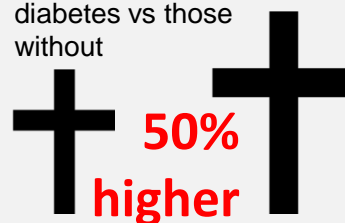


....that's 1 in every 12 people

4.9 million

deaths due to diabetes in 2014

Risk of death for
adults with
diabetes vs those
without



1 in 9

Health care dollars
spent on diabetes



Medical costs for
people in
diabetes

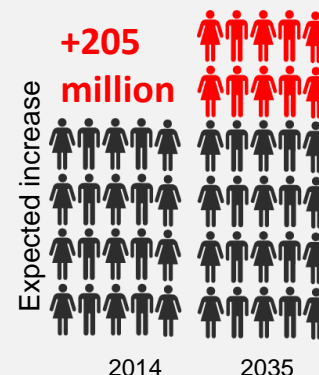
double

those for people
without diabetes



1 in 3

of us will develop Type
2
diabetes in our lifetime



Kriteria Diagnosis DM

Pemeriksaan glukosa plasma puasa ≥ 126 mg/dl. Puasa adalah kondisi tidak ada asupan kalori minimal 8 jam. (B)

Atau

Pemeriksaan glukosa plasma sewaktu ≥ 200 mg/dl 2 jam setelah *Tes Toleransi Glukosa Oral* (TTGO) dengan beban 75 gram (B)

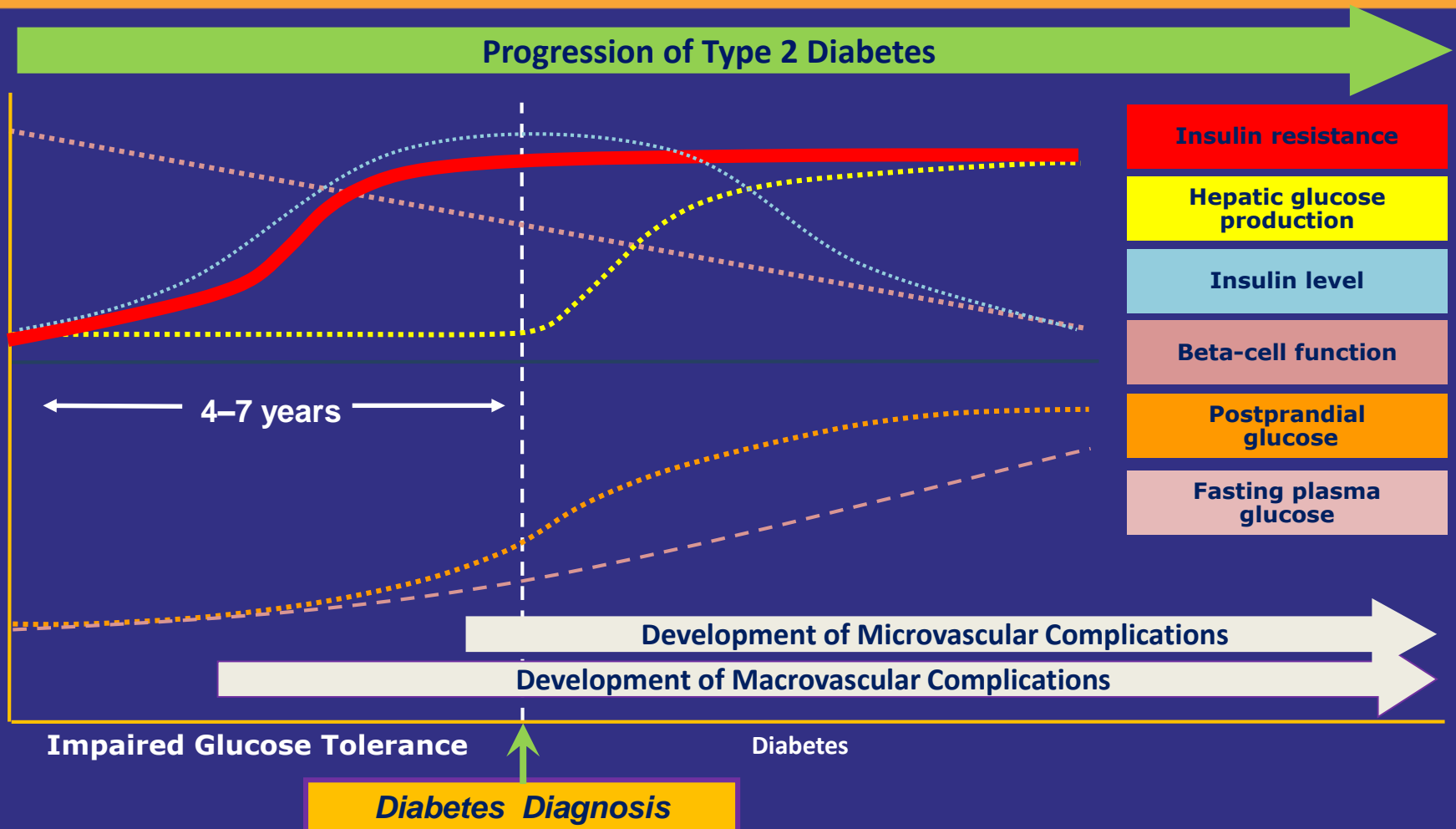
Atau

Pemeriksaan glukosa plasma sewaktu ≥ 200 mg/dl dengan keluhan klasik

Atau

Pemeriksaan HbA1c $\geq 6.5\%$ dengan menggunakan metode *High-performance Liquid Chromatography* (HPLC) yang terstandarisasi oleh *National Glycohaemoglobin Standardization Program* (NGSP). (B)

Type 2 diabetes is a progressive disease





Gemuk

Malas olahraga

Banyak makan



hipertensi

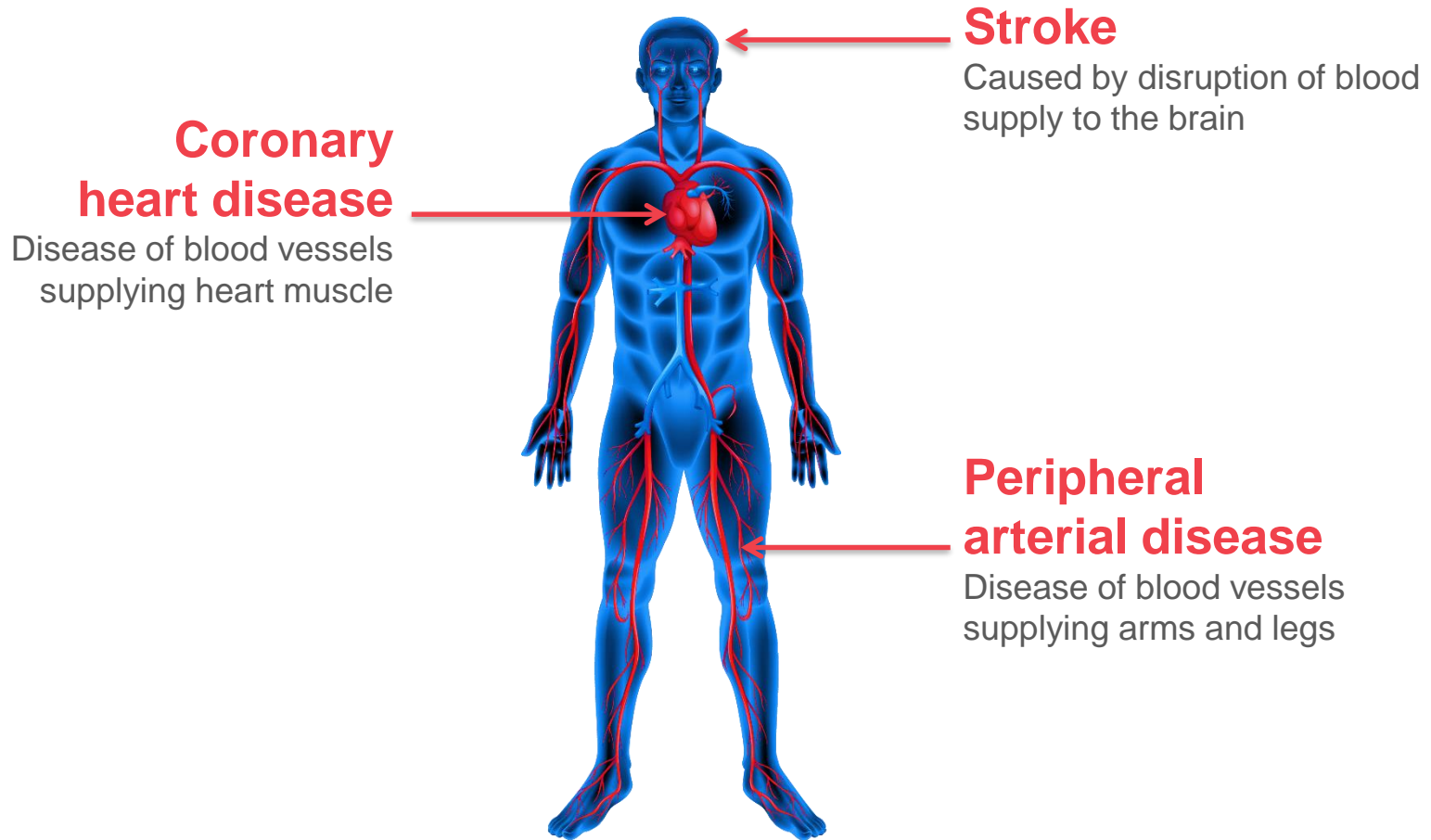
diabetes

kolesterol

resistensi insulin

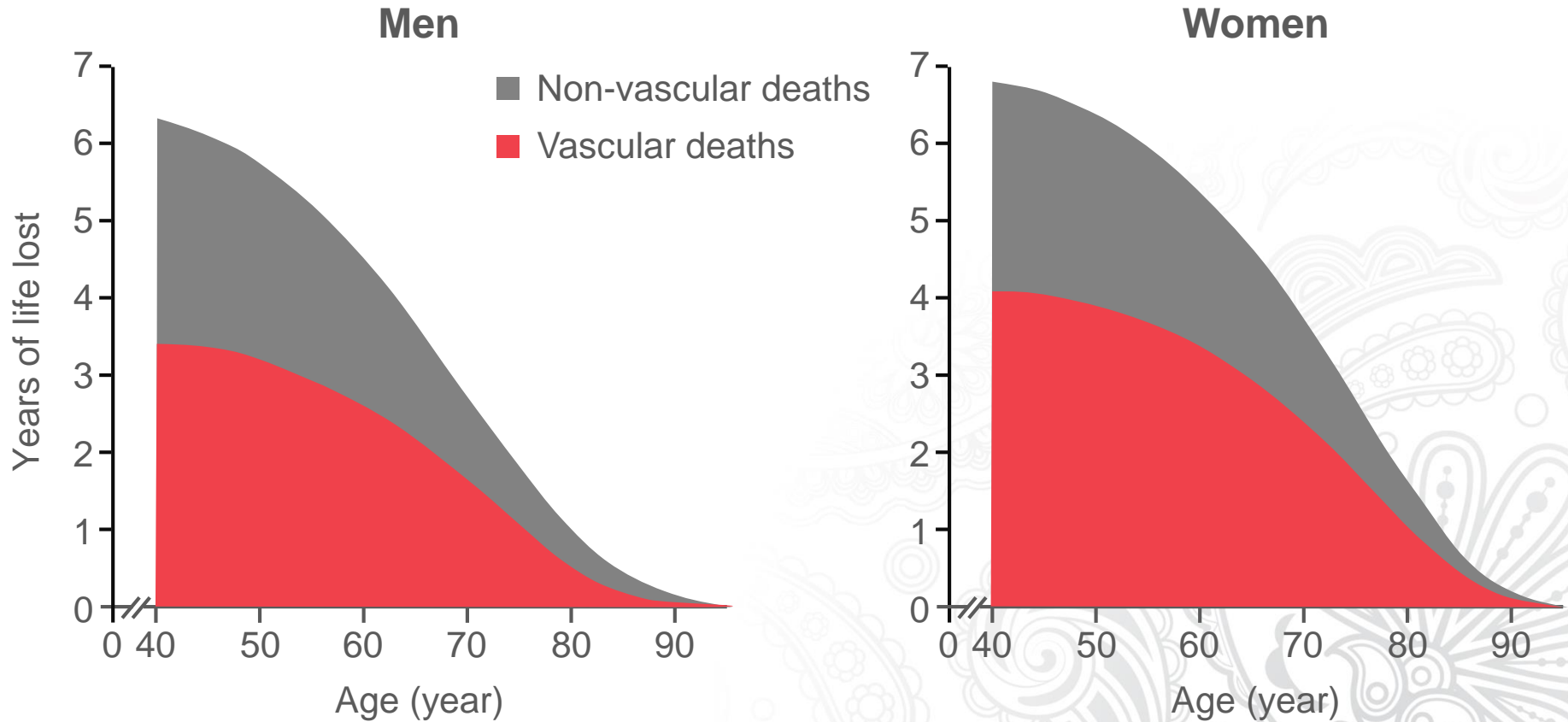


Key manifestations of CV disease¹



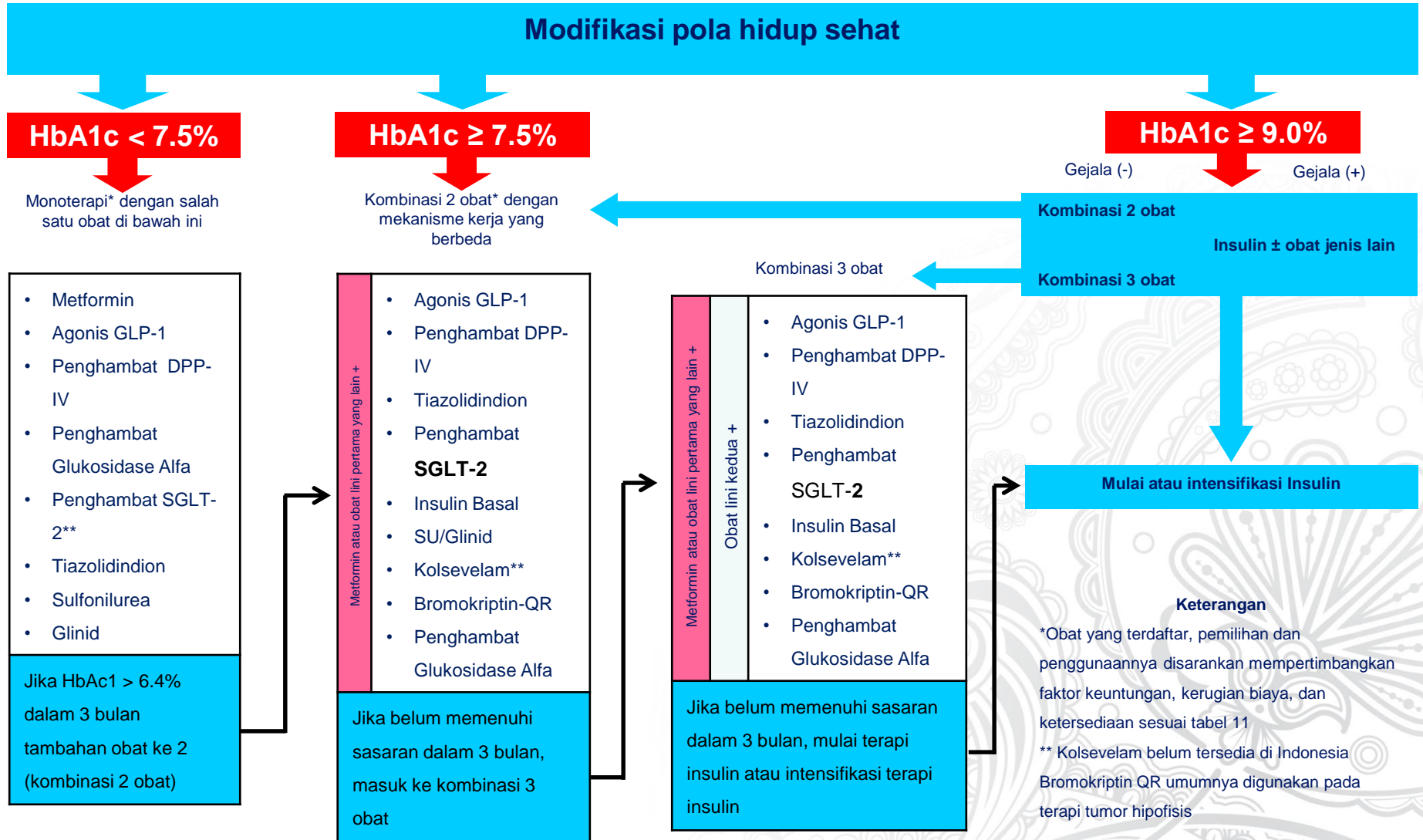
1. World Health Organization 2015: http://www.who.int/cardiovascular_diseases/en/cvd_atlas_01_types.pdf?ua=1

Diabetes is associated with significant loss of life years



On average, a 50-year old with diabetes but no history of vascular disease is ~6 years younger at time of death than a counterpart without diabetes

Algoritme Pengelolaan DM Tipe 2 di Indonesia KONSENSUS PERKENI 2015



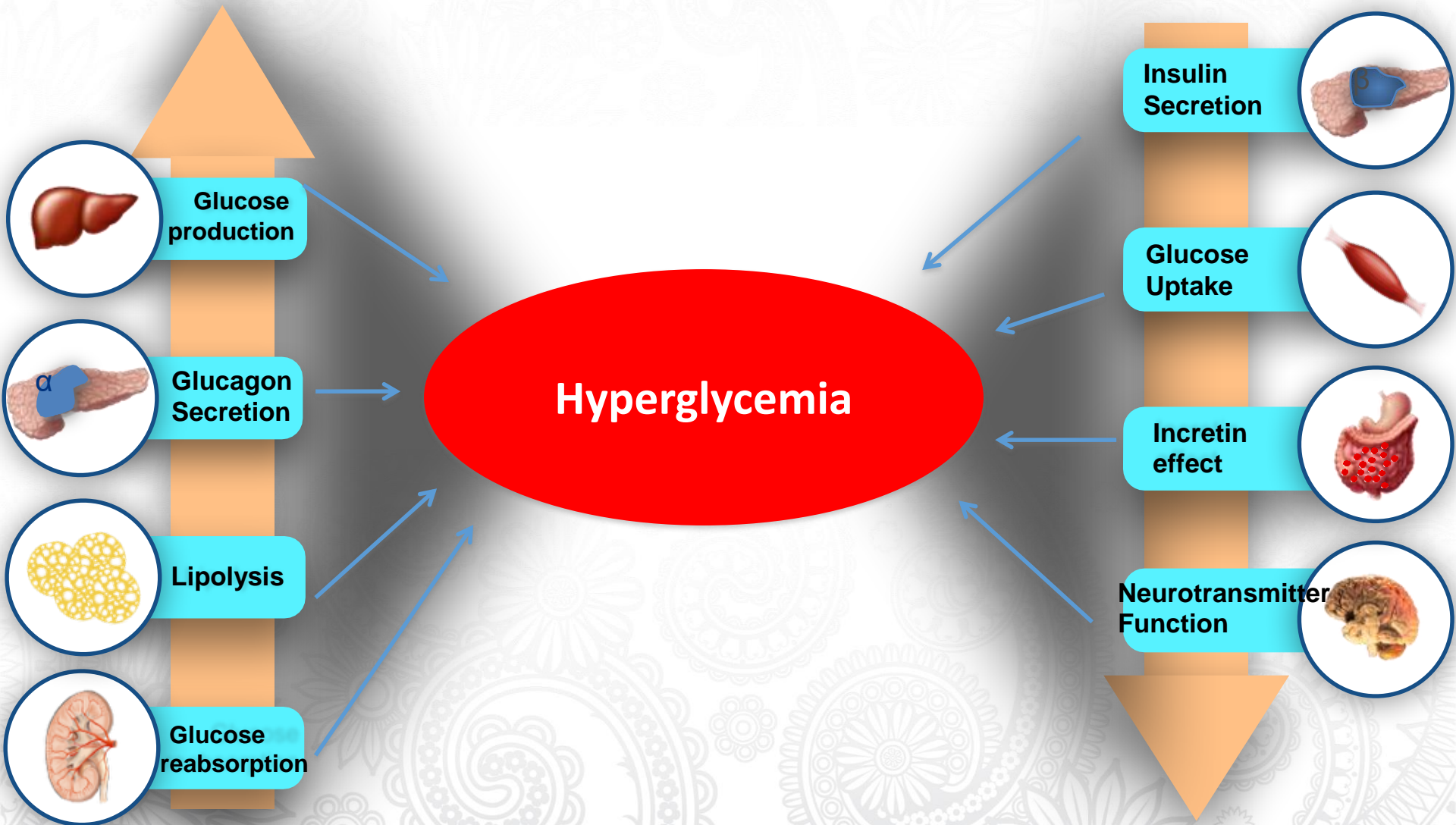
Guidelines for Glycemic, Blood Pressure, and Lipid Control

American Diabetes Association Goals

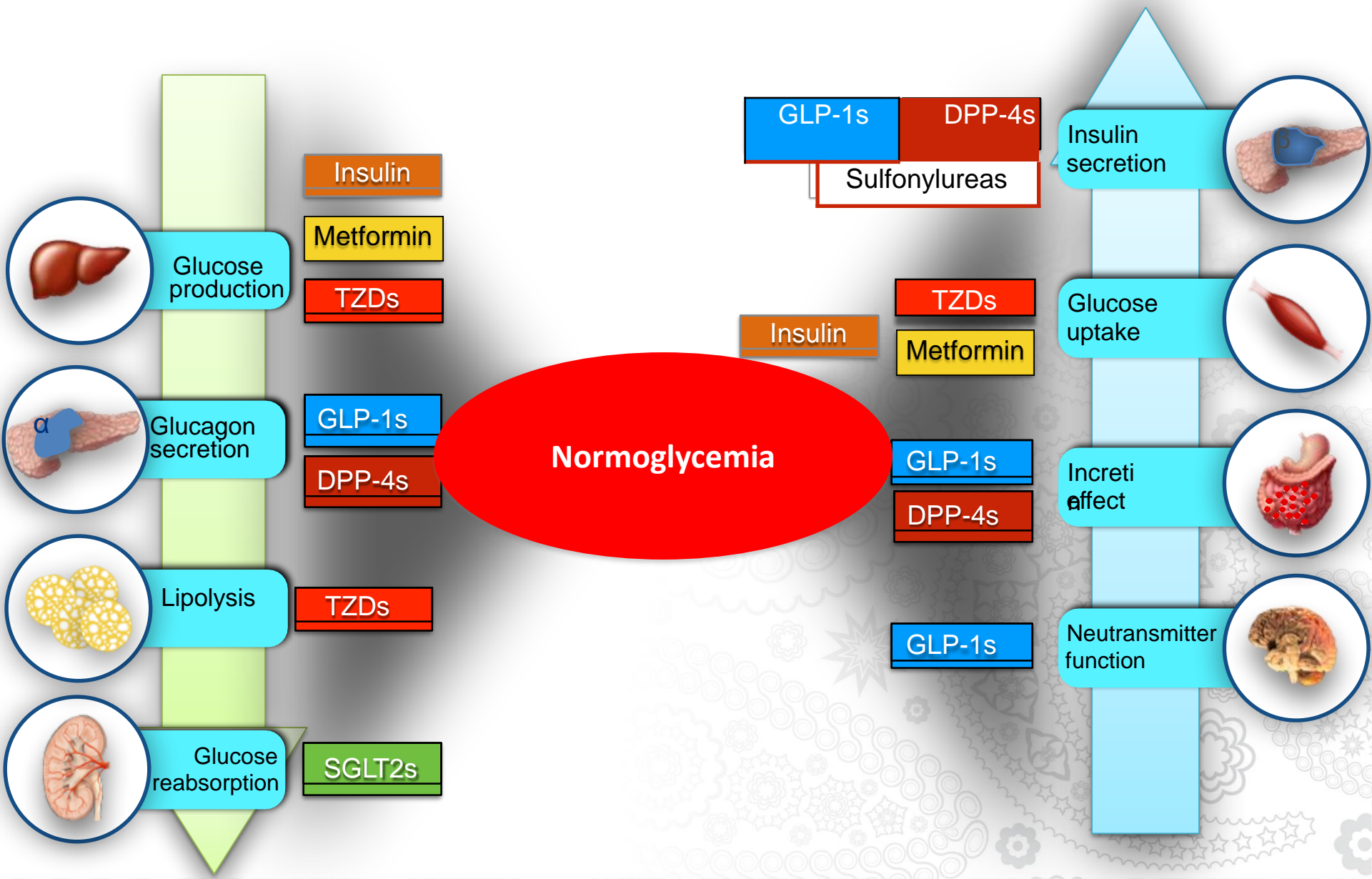
HbA1c	<7.0% (individualization)	
Preprandial glucose	70-130mg/dL (3.9-7.2 mmol/L)	
Postprandial glucose	<180 mg/dL	
Blood pressure	<130/80 mm Hg	
Lipids	LDL	<100 mg/dL (2.59 mmol/L)
		<70 mg/dL (1,81 mmol/L) (with overt CVD)
	HDL	♂ > 40 mg/dL (1.04 mmol/L)
		♀ > 50 mg/dL (1.30 mmol/L)
	TG	< 150 mg/dL (1.69 mmol/L)

TG=triglycerides

Patofisiologi DM 2 The Ominous Octet



Mekanisme kerja Anti Diabetik Oral





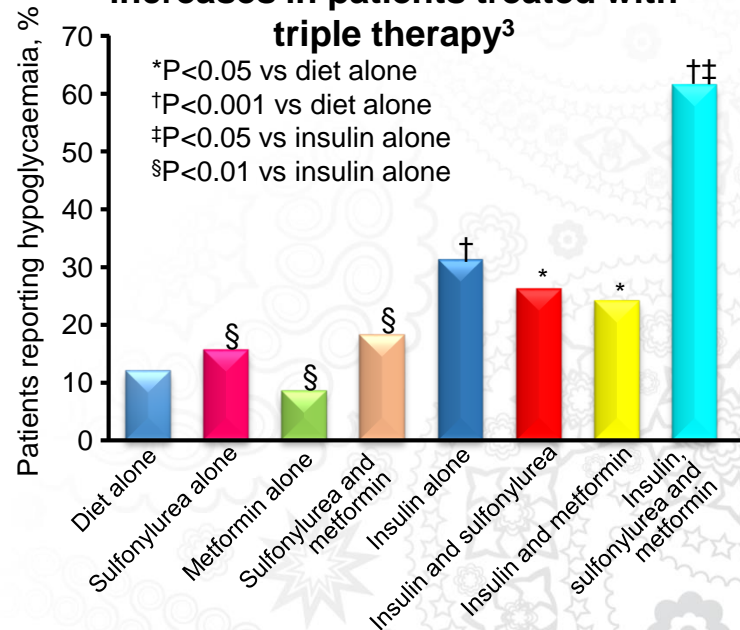
Treatment Regimen

Important Predictor Of Hypoglycaemia

Increased risk of hypoglycaemia
with some glucose-lowering
agents^{1,2}

High risk	Low risk
Insulin	Metformin
Sulphonylureas	Alpha-glucosidase inhibitors
Glinides	Pioglitazone
	GLP-1 receptor agonists
	DPP-4 inhibitors

Prevalence of hypoglycaemia
increases in patients treated with
triple therapy³



Does **hypoglycaemia** impact CV risk?

YES!

1. Khunti et al. Diabetes Care 2015;38:316–22.
2. Gerstein for ACCORD. N Engl J Med 2008;358:2545–59.
3. Bonds et al. BMJ 2010;340:b4909.
4. Turnbull et al. Diabetologia 2009;52:2288–98.
5. Goto et al. BMJ. 2013;347:f4533.

Does **hypoglycaemia** impact CV risk?

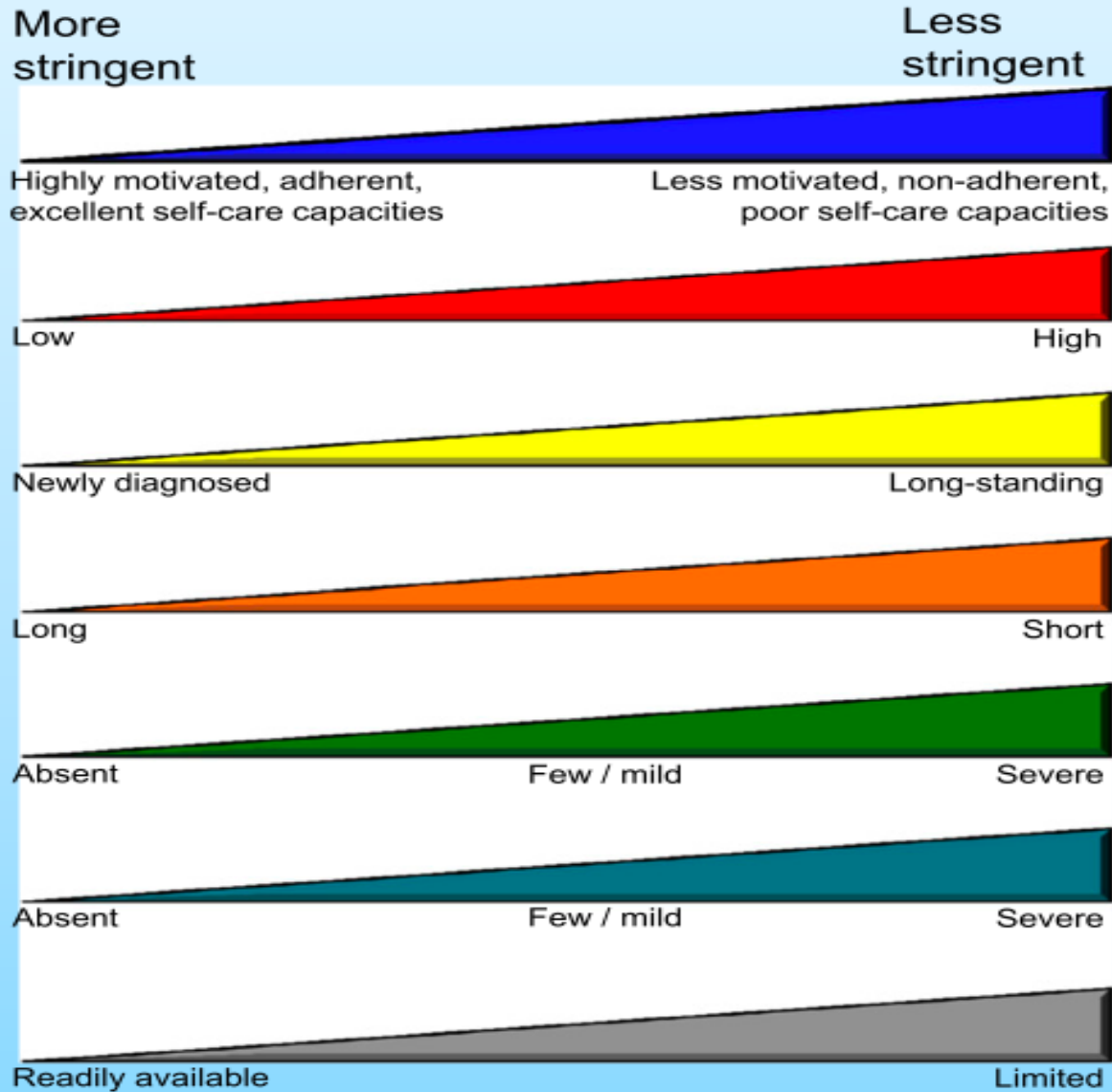
- Hypoglycaemia may be associated with co-morbidities that impact CVD
- A UK cohort study showed hypoglycaemia was associated with increased CV risk and mortality¹
- In ACCORD, severe hypoglycaemia was more frequent in the intensive glucose-lowering than in the standard arm²
 - Severe hypoglycaemia associated with increased risk of death in both arms but in patients who experienced hypoglycaemia, risk of death was lower in the intensive than in the standard arm³
- Meta-analysis of major glycaemic control trials associated intensive glucose control with increased risk of severe hypoglycaemia, but with no increase in CV events⁴
- Systematic review of prospective and retrospective datasets suggested severe hypoglycaemia associated with **2-fold increase** in CVD⁵
 - Co-morbidities alone could not account for this association

1. Khunti et al. Diabetes Care 2015;38:316–22. 2. Gerstein for ACCORD. N Engl J Med 2008;358:2545–59.

3. Bonds et al. BMJ 2010;340:b4909. 4. Turnbull et al. Diabetologia 2009;52:2288–98. 5. Goto et al. BMJ. 2013;347:f4533.

ADA-EASD 2012: Patient-centered approach

Approach to management of hyperglycemia:



Patient-Centered Approach

“...providing care that is respectful of and responsive to individual patient preferences, needs, and values – ensuring that patient values guide all clinical decisions.”

- Gauge patient's preferred level of involvement.
- Explore, where possible, therapeutic choices. Consider using decision aids.
- Shared Decision Making – a collaborative process between patient and clinician, using best available evidence and taking into account the patient's preferences and values
- Final decisions regarding lifestyle choices ultimately lie with the patient.

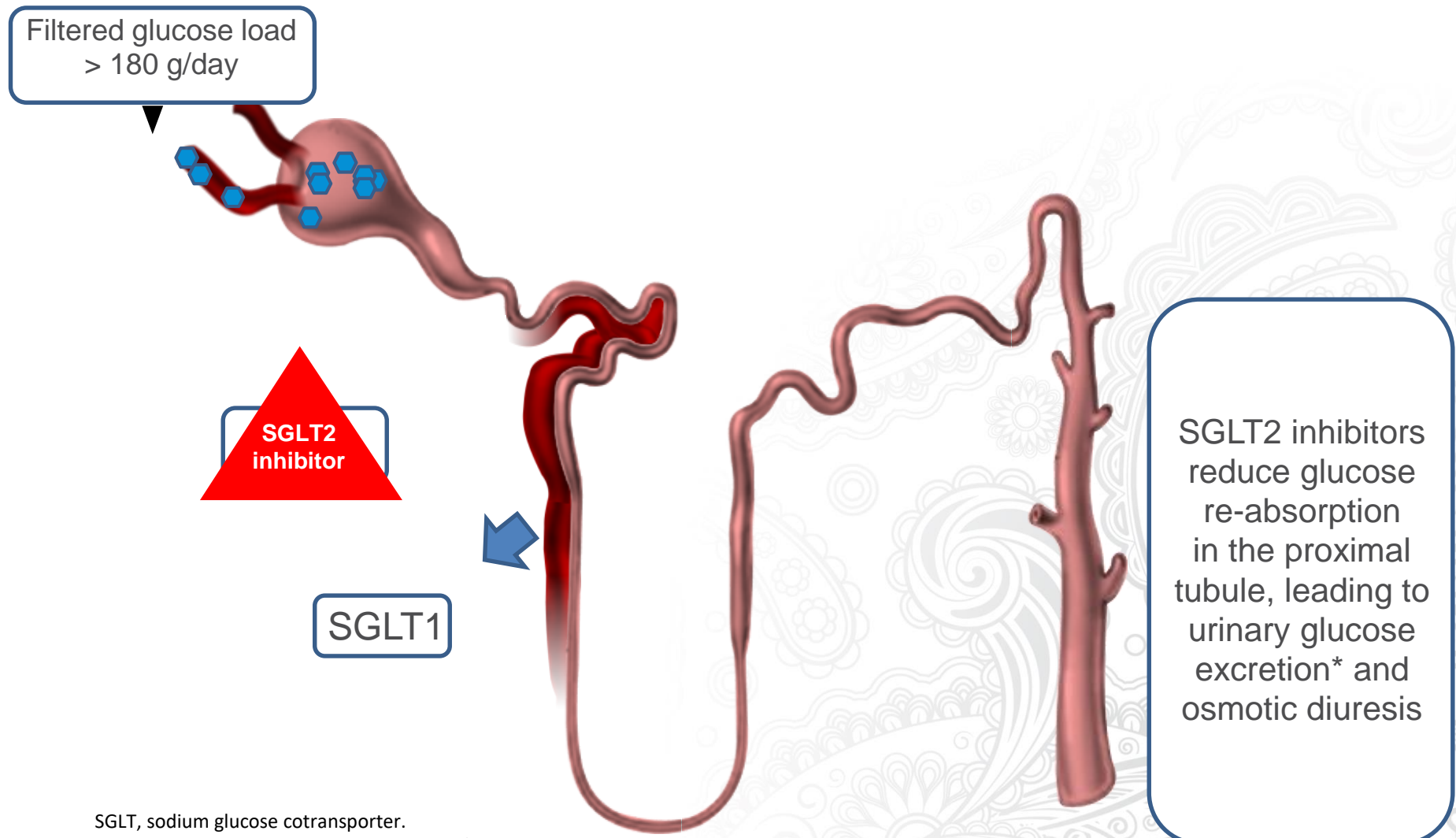
Why do we need more oral agents and not start insulin therapy sooner ?

- Insulin associated with more hypoglycemia
- Insulin still “refused” by many patients
- Worse adherence to insulin injections
insulin persistence with basal insulin 65%
at 1 year versus 86% on oral agents
- Weight gain

Novel Therapies for Type 2 Diabetes

- GLP-1 Agonists
- DPP-IV Inhibitors
- Bile acid sequestrant
- Bromocriptine
- Sodium Glucose Co-Transporter 2 Inhibitors

Inhibiting Sodium-glucose cotransporter¹



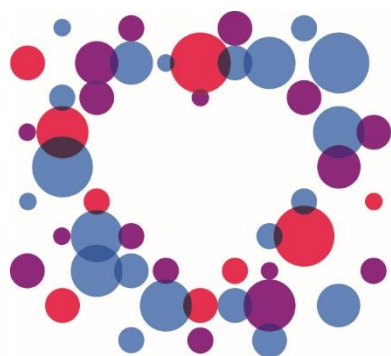
SGLT, sodium glucose cotransporter.

*Loss of ~ 80 g of glucose per day = 240 cal/day.

1. Bakris GL, et al. *Kidney Int.* 2009;75;1272–1277.

Introduction

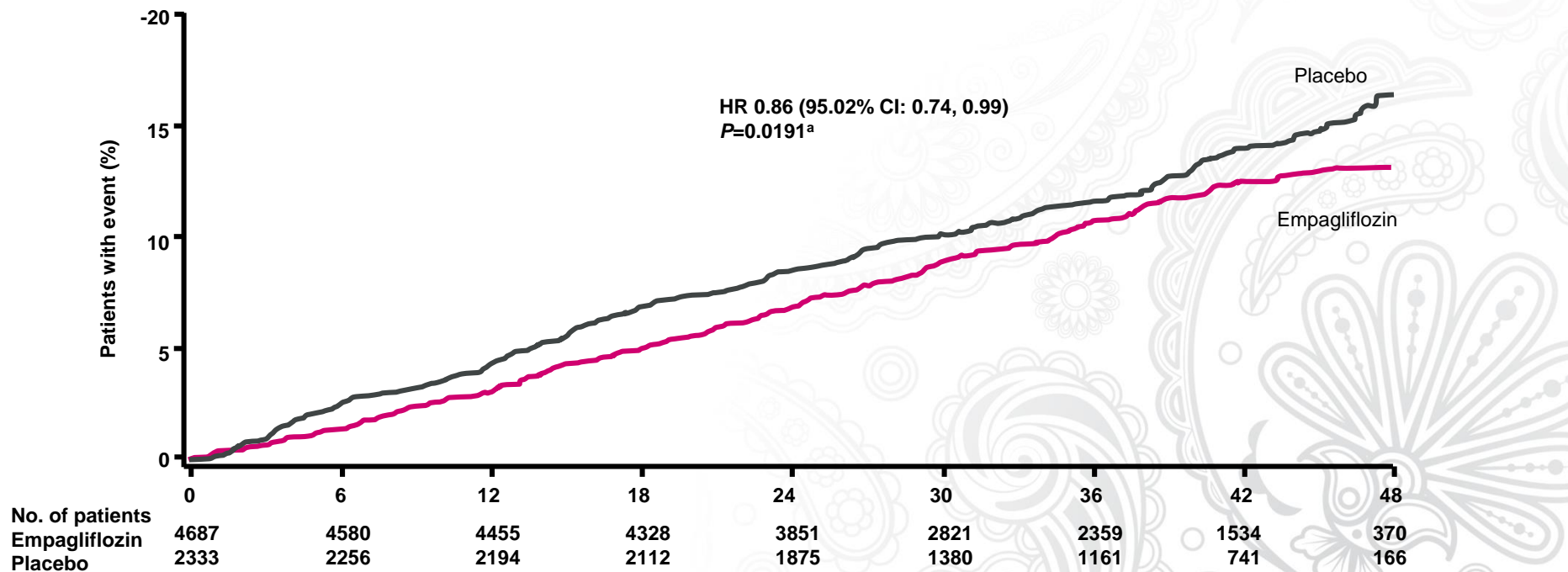
Bernard Zinman CM, MD, FRCP, FACP
Director, Leadership Sinai Centre for Diabetes
Professor of Medicine, University of Toronto



EMPA-REG
OUTCOME®

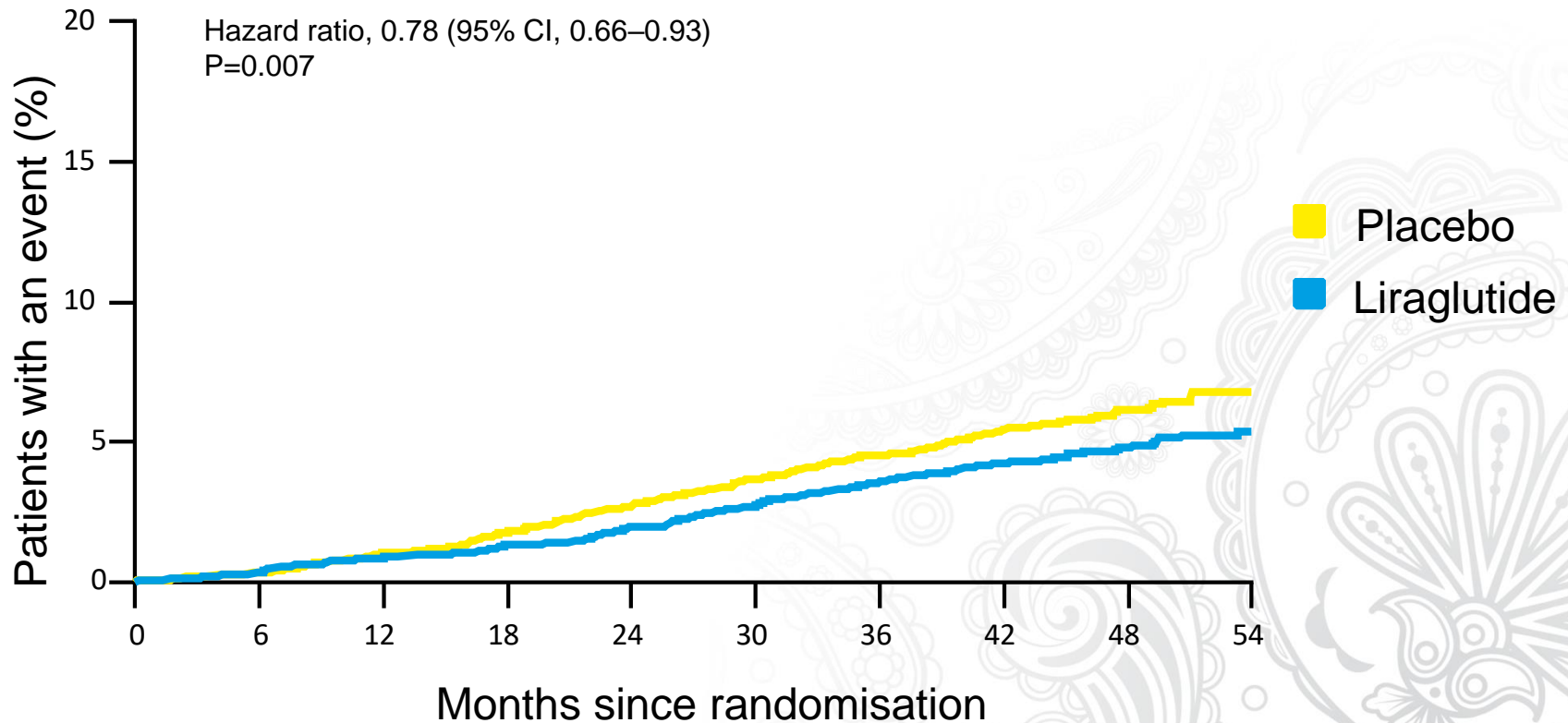
EMPA-REG demonstrated improved CV outcomes in patients with established CVD

EMPA-REG - Type 2 diabetes with established CVD: primary outcome: 3-point MACE



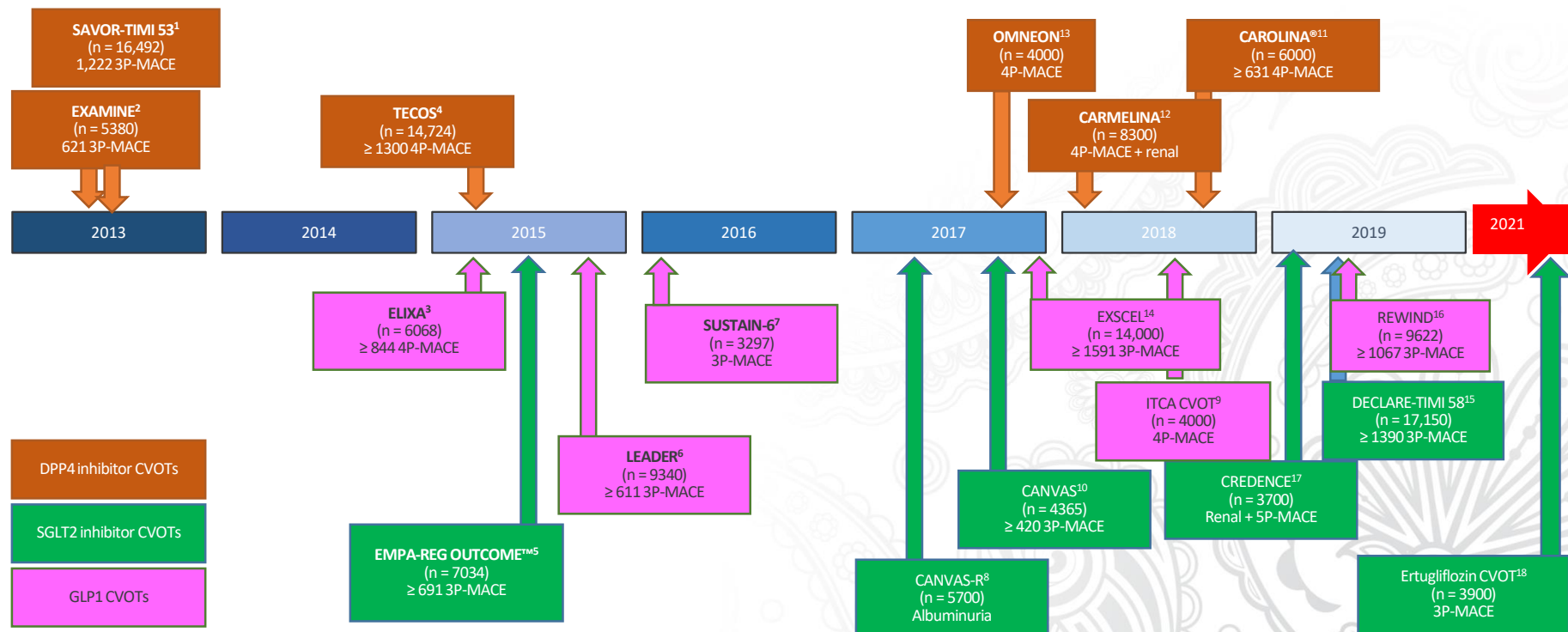
Cumulative incidence function; ^aTwo-sided tests for superiority were conducted (statistical significance was indicated if $P \leq 0.0498$)
CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; MACE, major adverse cardiovascular event; SGLT2, sodium-glucose co-transporter 2
Zinman B, et al. *New Engl J Med* 2015;373:2117-2128

LEADER trial: Death from Cardiovascular Causes



Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results (LEADER) trial

CV safety trials are being conducted for each compound within the newer classes

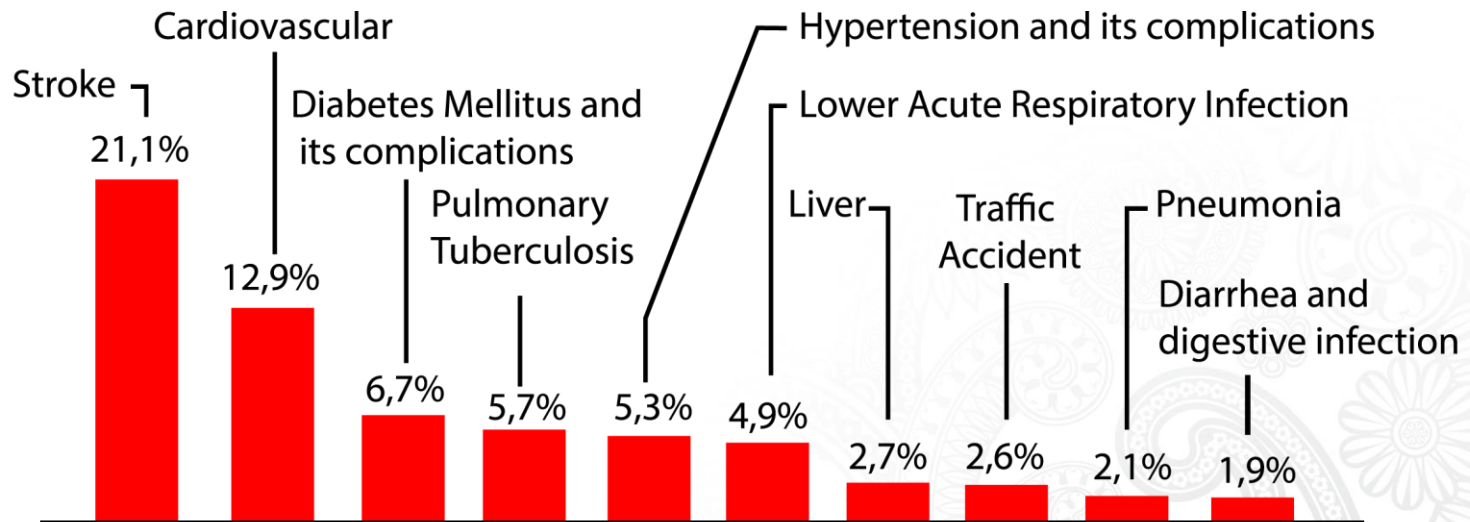


Timings represent estimated completion dates as per ClinicalTrials.gov

Adapted from Johansen. World J Diabetes 2015; in press (references 1–18 expanded in slide notes)

The Top 10 Causes of Death in Indonesia 2014

Men and Women



Men		Women	
Stroke	1	Stroke	
Cardiovascular	2	Cardiovascular	
Pulmonary Tuberculosis	3	Diabetes Mellitus and its complications	
Lower Acute Respiratory	4	Hypertension and its complications	
Diabetes Mellitus and its complications	5	Pulmonary Tuberculosis	
Hypertension and its complications	6	Lower Acute Respiratory Infection	
Traffic Accident	7	Pneumonia	
Liver	8	Diarrhea and digestive infection	
Pneumonia	9	Liver	
Diarrhea and digestive infection	10	Breast Cancer	

Data from 41.590 death in Indonesia, January-December 2014 Indonesia Health Research and Development, Ministry of Health

Managemen Diabetes Melitus

Diagnosis

Empat Pilar

I

edukasi

II

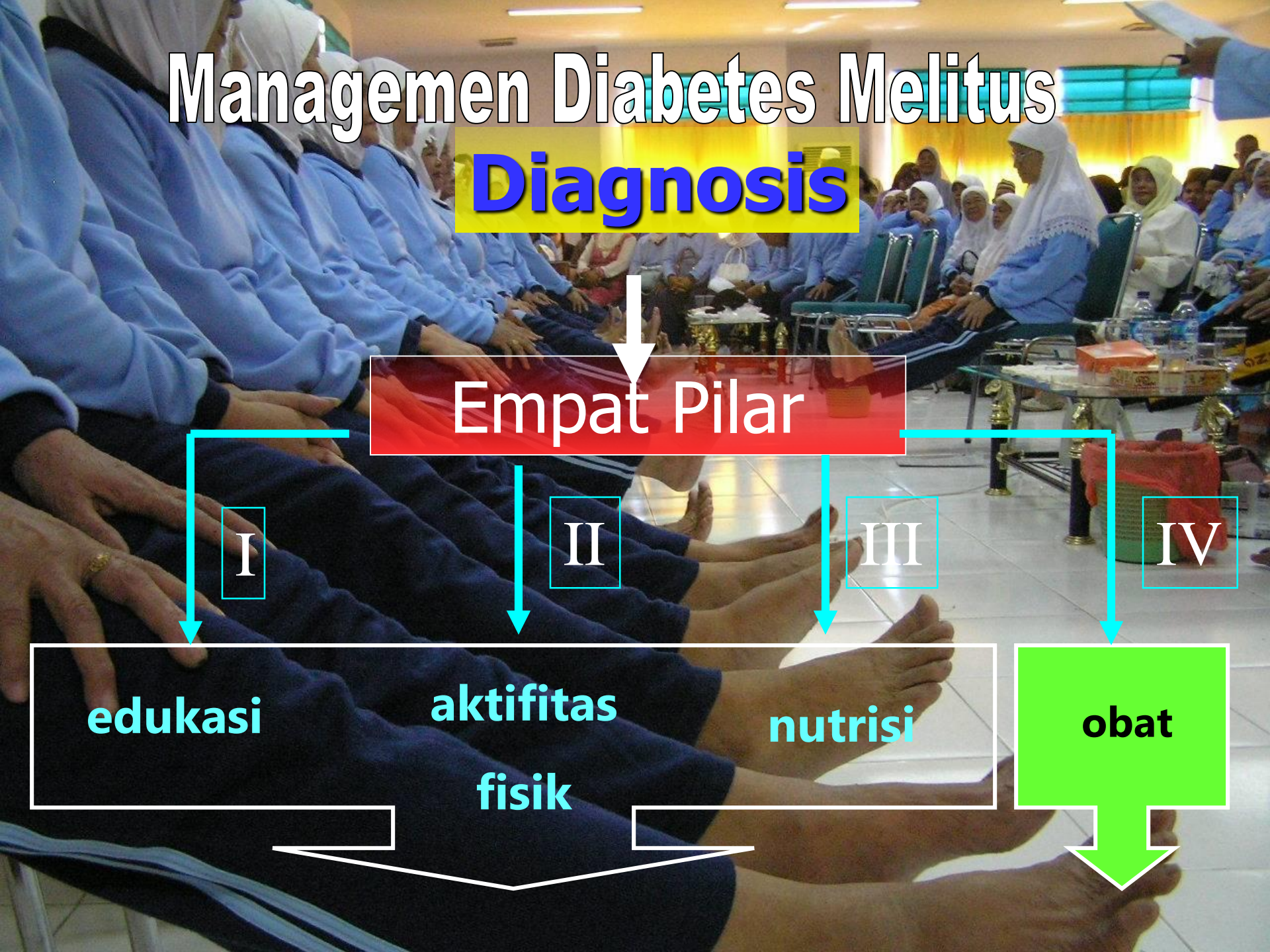
aktifitas
fisik

III

nutrisi

IV

obat



Education Is The Key



If I begin taking insulin

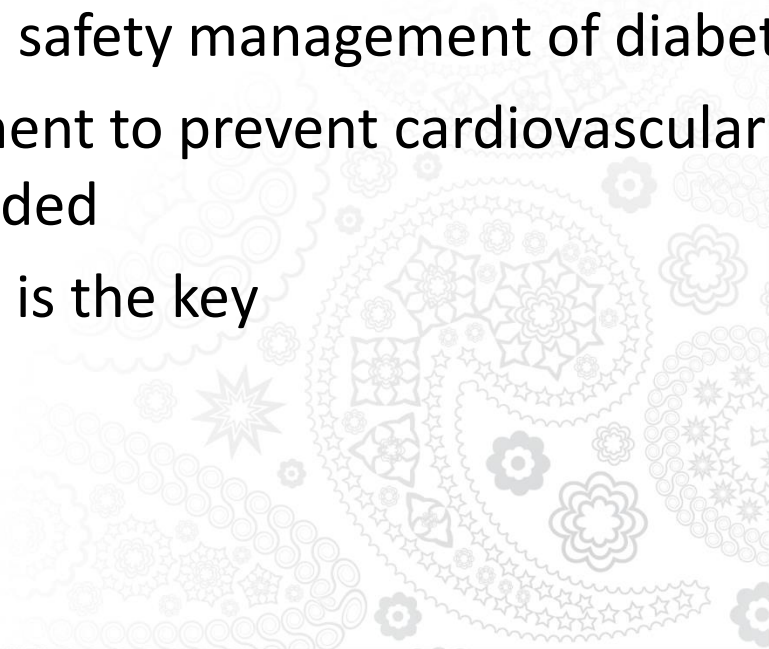
I will have to take it for the rest of my life



- For type 1
- Many insulin users find that by controlling their diet and following an exercise program, they can reduce the amount and type of insulin
- insulin is a hormone, so it is not "habit-forming" or addictive.

Take Home Notes

- Diabetes is a progressive disease
- Insulin resistance is a major cause of diabetes
- After discovery of insulin, more medications are developed to find a safety management of diabetes
- A holistic management to prevent cardiovascular complication is needed
- Diabetes education is the key



Thank you!

MeetMed

www.meetmed.net