ENDOCRINOLOGIA

Lezione 5

Pancreas Endocrino

CORSO DI LAUREA IN SCIENZE OSTETRICHE

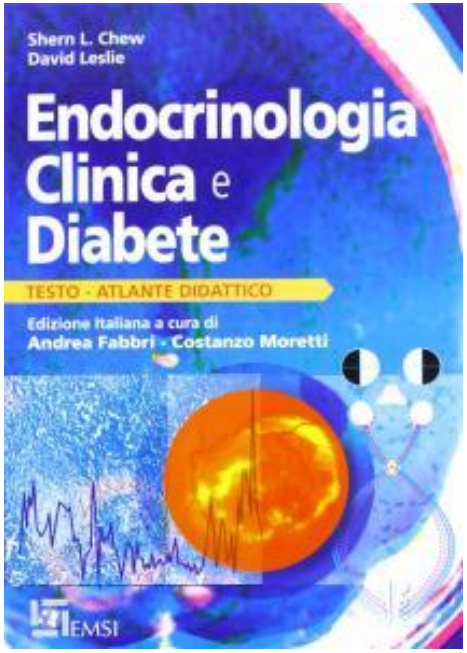
Secondo Anno – Secondo Semestre

Medicina Interna – Scienze Chirurgiche – Medicina Prenatale

Assistenza al parto ed al puerperio

Prof. Costanzo Moretti

Dipartimento di Medicina dei Sistemi



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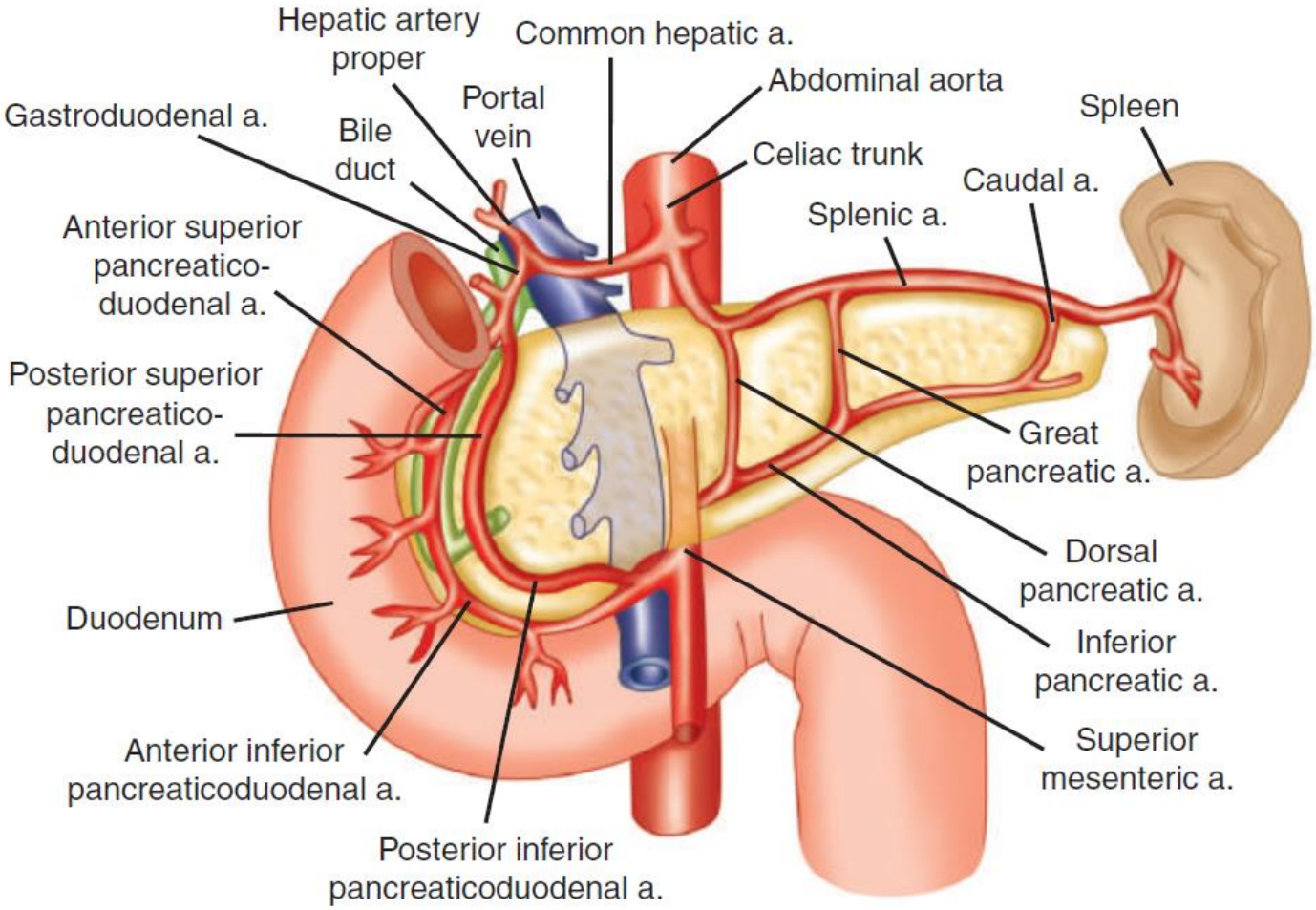
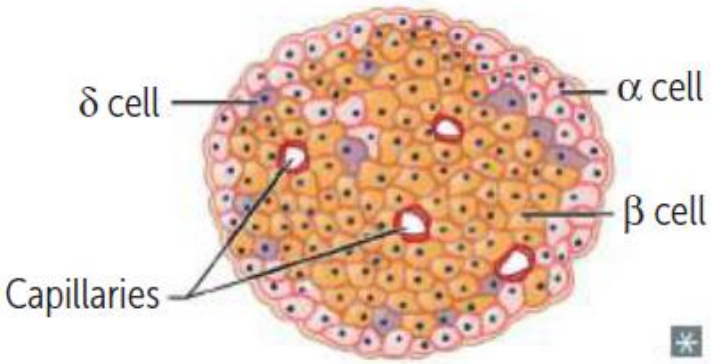
Didattica

IL PANCREAS E' UN ORGANO MULTIFUNZIONALE DEI SISTEMI ENDOCRINO E DIGESTIVO. ESSO GIOCA UN RUOLO CHIAVE NEL METABOLISMO DI CARBOIDRATI LIPIDI E PROTEINE ATTRAVERSO LA SECREZIONE DI VARI ORMONI PROTEICI DI CUI I PRINCIPALI SONO INSULINA E GLUCAGONE

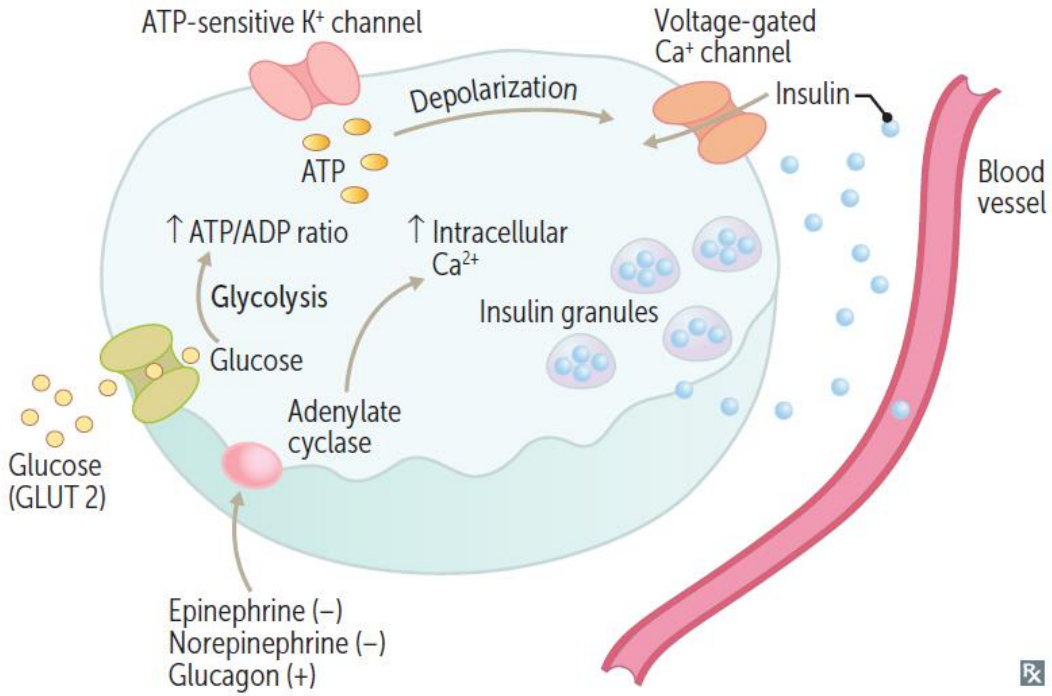
ANATOMY


Hepatic artery proper
Common hepatic a.
Abdominal aorta
Portal vein
Gastroduodenal a.
Bile duct
Celiac trunk
Spleen
Caudal a.
Splenic a.
Anterior superior pancreatico-duodenal a.
Posterior superior pancreatico-duodenal a.
Great pancreatic a.
Dorsal pancreatic a.
Duodenum
Inferior pancreatic a.
Superior mesenteric a.
Anterior inferior pancreaticoduodenal a.
Posterior inferior pancreaticoduodenal a.

ISLET CELL TYPES AND FUNCTION



CELL TYPE	QUANTITY (%)	LOCATION	HORMONE	FUNCTION
Alpha (α)	20	Peripheral	Glucagon	Increases blood glucose
Beta (β)	70	Central	Insulin	Decreases blood glucose
Delta (δ)	< 5	Variable	Somatostatin	Inhibits release of other islet cell hormones



Glucose is the most powerful stimulus for insulin release (Table 2-27). Glucose enters β-cells via the glucose transporter **GLUT 2** via facilitated diffusion, meaning that intracellular glucose concentration equilibrates with serum glucose concentration. Increases in serum glucose within β-cells are shunted into the glycolytic pathway. Increased glucose catabolism leads to a rise in the intracellular ATP:ADP ratio, which causes the **ATP-sensitive potassium channel** on the surface of β-cells to close. Closure of this potassium channel leads to depolarization of the cell, resulting in opening of voltage-gated calcium channels. The subsequent rise in intracellular calcium facilitates fusion of insulin-containing vesicles with the cell membrane, releasing insulin from the cell

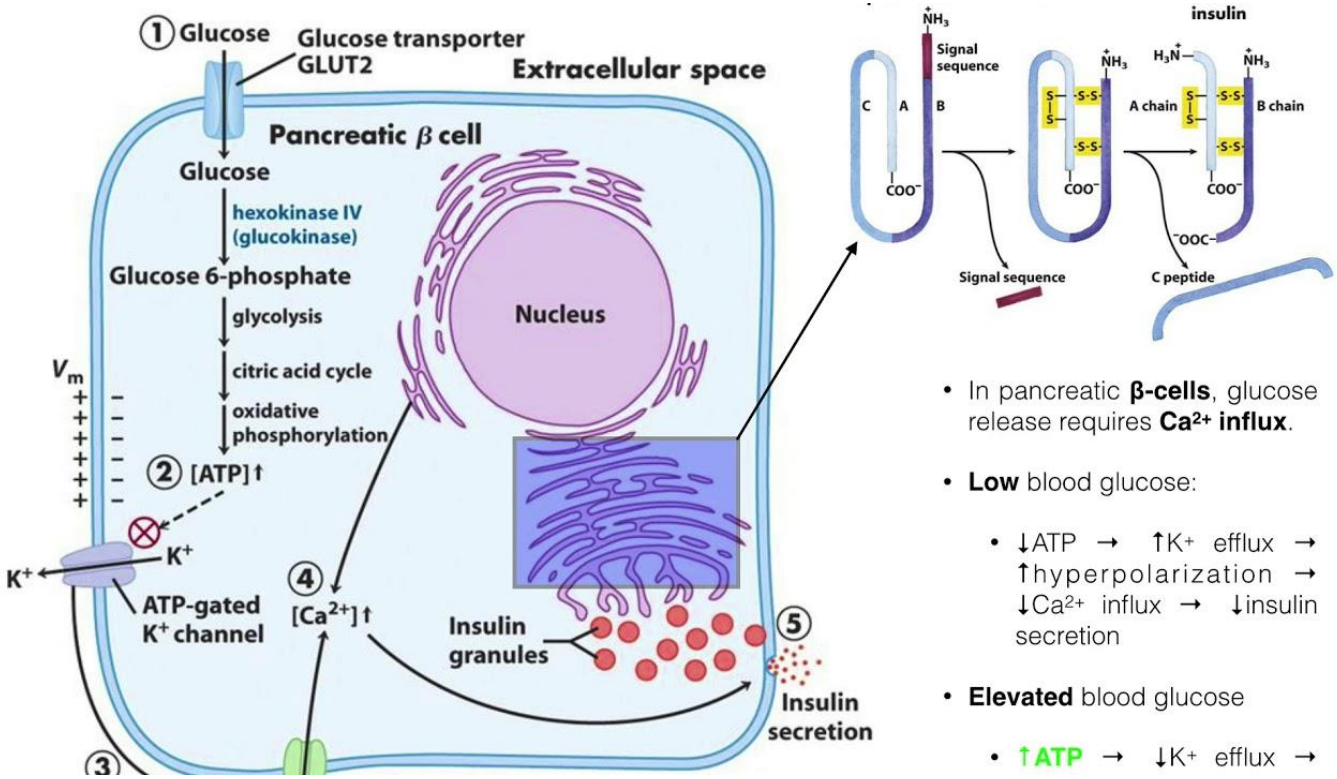


TABLE 2-27. Factors Affecting Insulin Release

PROMOTE INSULIN SECRETION	INHIBIT INSULIN SECRETION
Glucose	α-Adrenergic stimulation
Amino acids	Somatostatin
Vagal stimulation	Drugs: Phenytoin, vinblastine, colchicine
Sulfonylureas	
CCK, GIP, glucagon-like peptide	
Secretin, gastrin	
β-Adrenergic stimulation	

CCK, cholecystokinin; GIP, gastric inhibitory polypeptide.

Diabetes Mellitus (DM)

DM eventually → microvascular and macrovascular complications

–Microvascular: retinopathy, nephropathy, and peripheral neuropathy
–Macrovascular: coronary heart disease (CHD), stroke, and peripheral vascular disease (PVD)

Glucose Contributions to HbA_{1c}

HbA_{1c} =

Fasting Glucose, Influenced by:

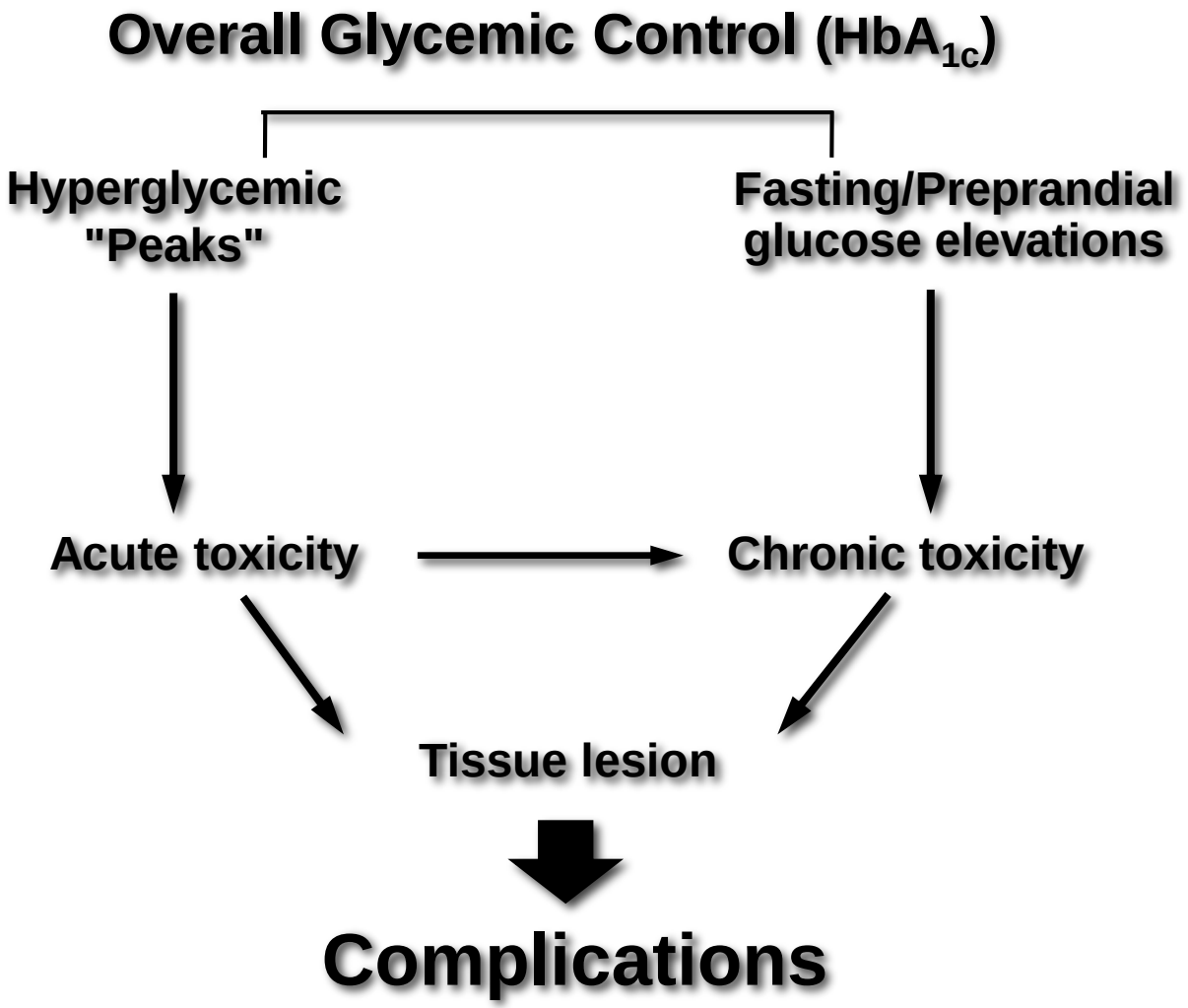
- Hepatic glucose production
- Hepatic sensitivity to insulin

+

Postprandial Glucose, Influenced by:

- Preprandial glucose
- Glucose load from meal
- Insulin secretion
- Insulin sensitivity in peripheral tissues and liver

Possible Pathogenesis of Diabetic Complications



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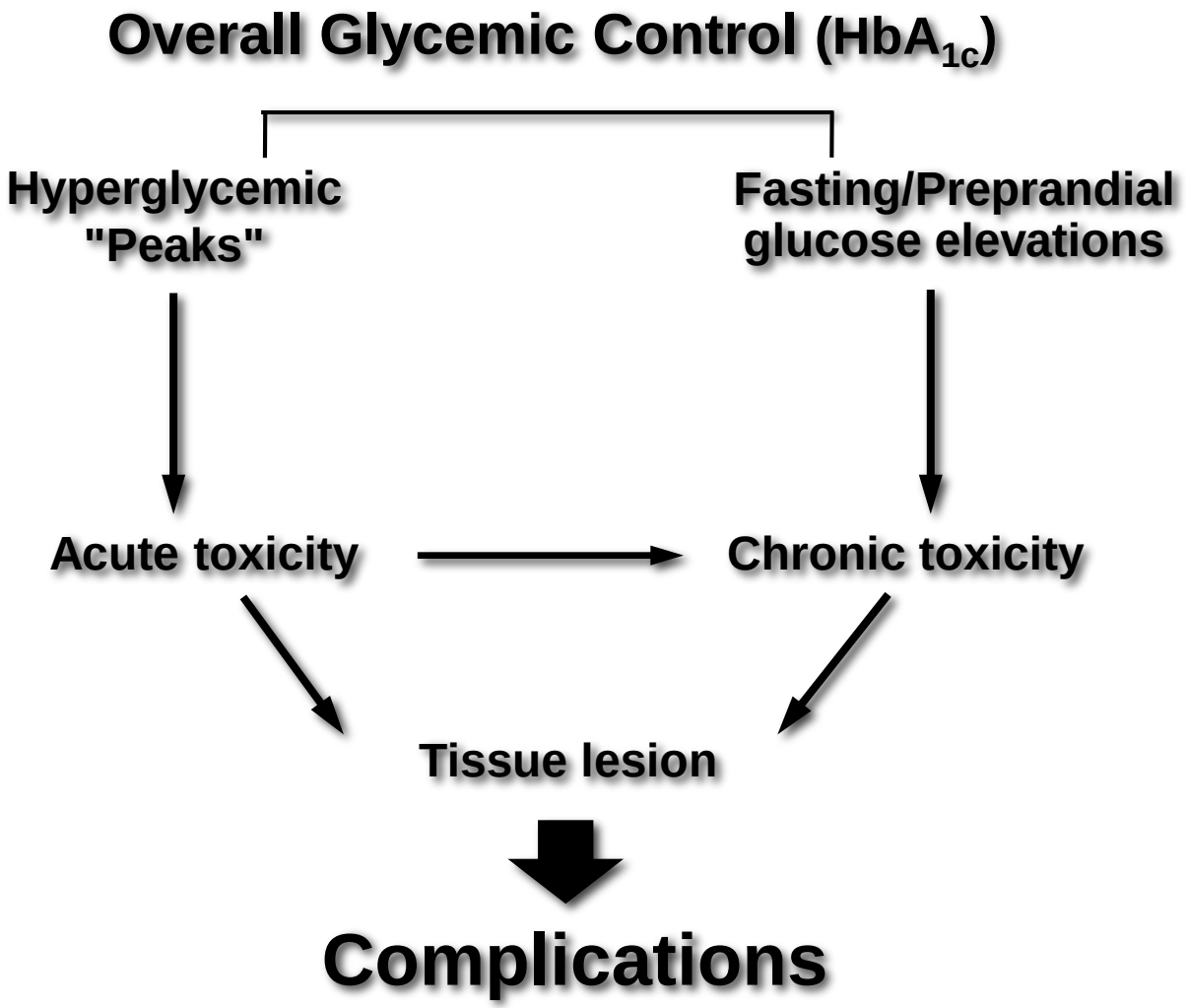


Type 1 Diabetes

Absolute deficiency in insulin
β-cell destruction

Type 1 Diabetes Mellitus

- Characterized by absolute insulin deficiency
- Pathophysiology and etiology
  - Result of pancreatic beta cell destruction
    - Prone to ketosis
  - Total deficit of circulating insulin
  - Autoimmune
  - Idiopathic

Pathogenesis of Type 1 diabetes.

Autoimmune Type 1 Diabetes

- Beta cells destroyed via autoimmune mechanism.
- Genetically predisposed people:triggering factor = production of islet cell Ab
- Islet cell Ab destroy Beta cells.
- Insulin production decreases.

Pathogenesis of Type 1 diabetes.

Autoimmune Type 1 Diabetes

- Viruses + other environmental agents have been shown to be triggering factors.
- Viruses can damage beta cells by:
  1. Direct invasion.
  2. Triggering an autoimmune response.

Pathogenesis of Type 1 diabetes.

Autoimmune Type 1 Diabetes

- Implicated viruses:

  mumps, intrauterine rubella, coxsackie B virus, echo virus, gytomegalo virus and herpes virus.

- Chemical substances that reduce diabetes:

  alloxan, streptozotosin and dietary nitrosamides

Pathogenesis of Type 1 diabetes.

Idiopathic Type 1 Diabetes

- No known aetiology.
- Permanent insulinopaenia.
- This form is strongly inherited.
- Not HLA associated.

Epidemiology

- **Average onset is in childhood or early adulthood (usually before 30 years of age)**

- **Characterized by autoimmune destruction of pancreatic β-cells → absolute insulin deficiency**

- **Patients dependent on exogenous insulin**

Incidence of Type 1 diabetes

- ✓ **Incidence peaks at 11-13 years.**
- ✓ **Seasonal variation: lowest rates in spring and summer.**
- ✓ **Geographical variation: Japan has a very low incidence.**
- ✓ **10% of Type 1 diabetics are over 65 years of age.**

Pathophysiology

- Immune-mediated destruction of pancreatic β- cells

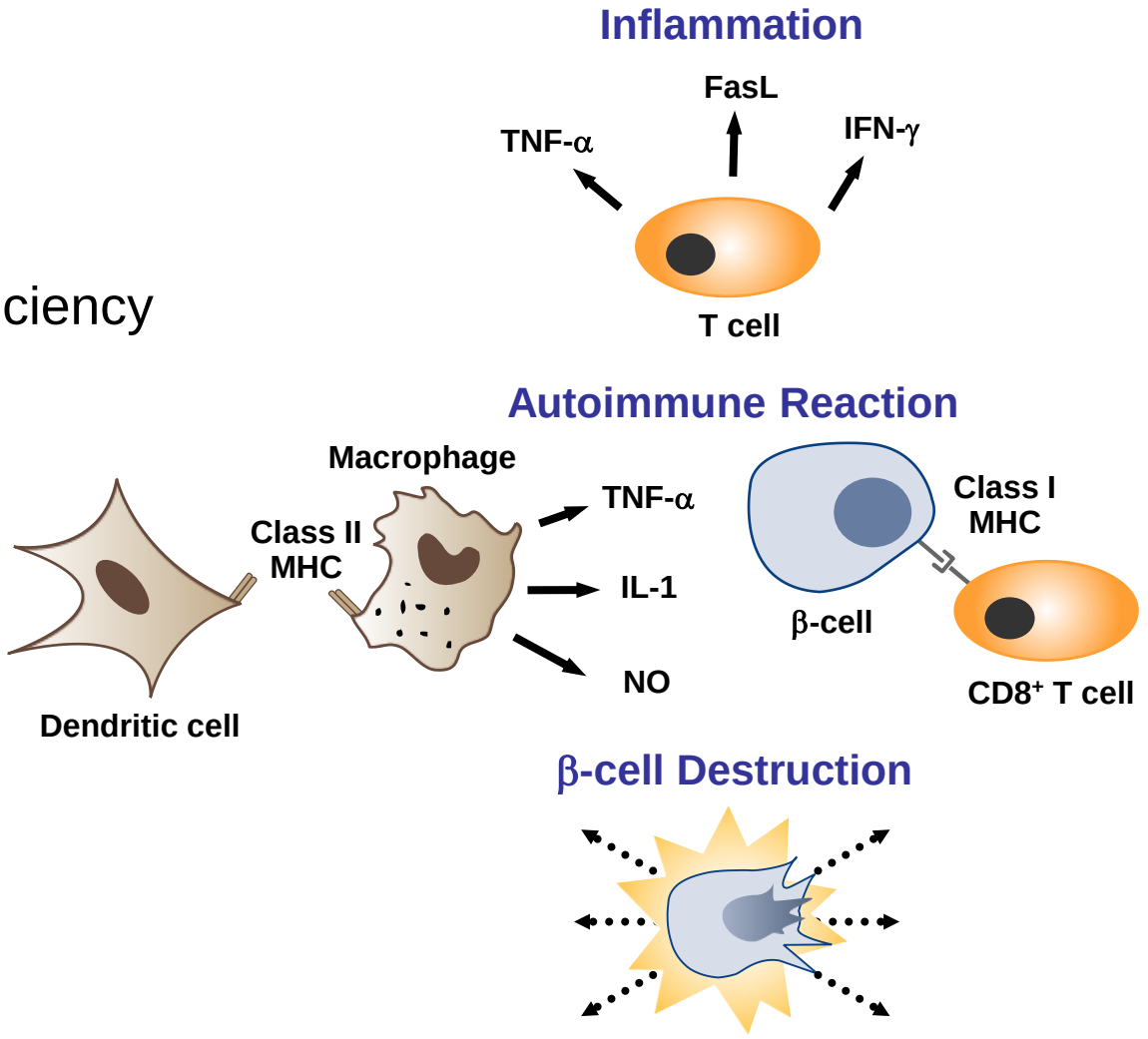
- Certain antibodies detected in blood:
  - Islet cell antibody (ICA)
  - Glutamic acid decarboxylase (GAD65) antibody
  - Insulin autoantibody (IAA)

- HLA-DR3 and HLA-DR4 as well as DQA and DQB genes are strongly associated with type 1 DM

- Strong familial genetic link

Type 1 Diabetes Pathophysiology

- β-cell destruction
  - Usually leading to absolute insulin deficiency
- Immune mediated
- Idiopathic



CD8, cluster of differentiation 8; FasL, Fas ligand; IFN-γ, interferon γ; IL-1, interleukin 1; MHC, major histocompatibility complex; NO, nitric oxide; TNF-α, tumor necrosis factor α.

Maahs DM, et al. *Endocrinol Metab Clin North Am*. 2010;39:481-497.

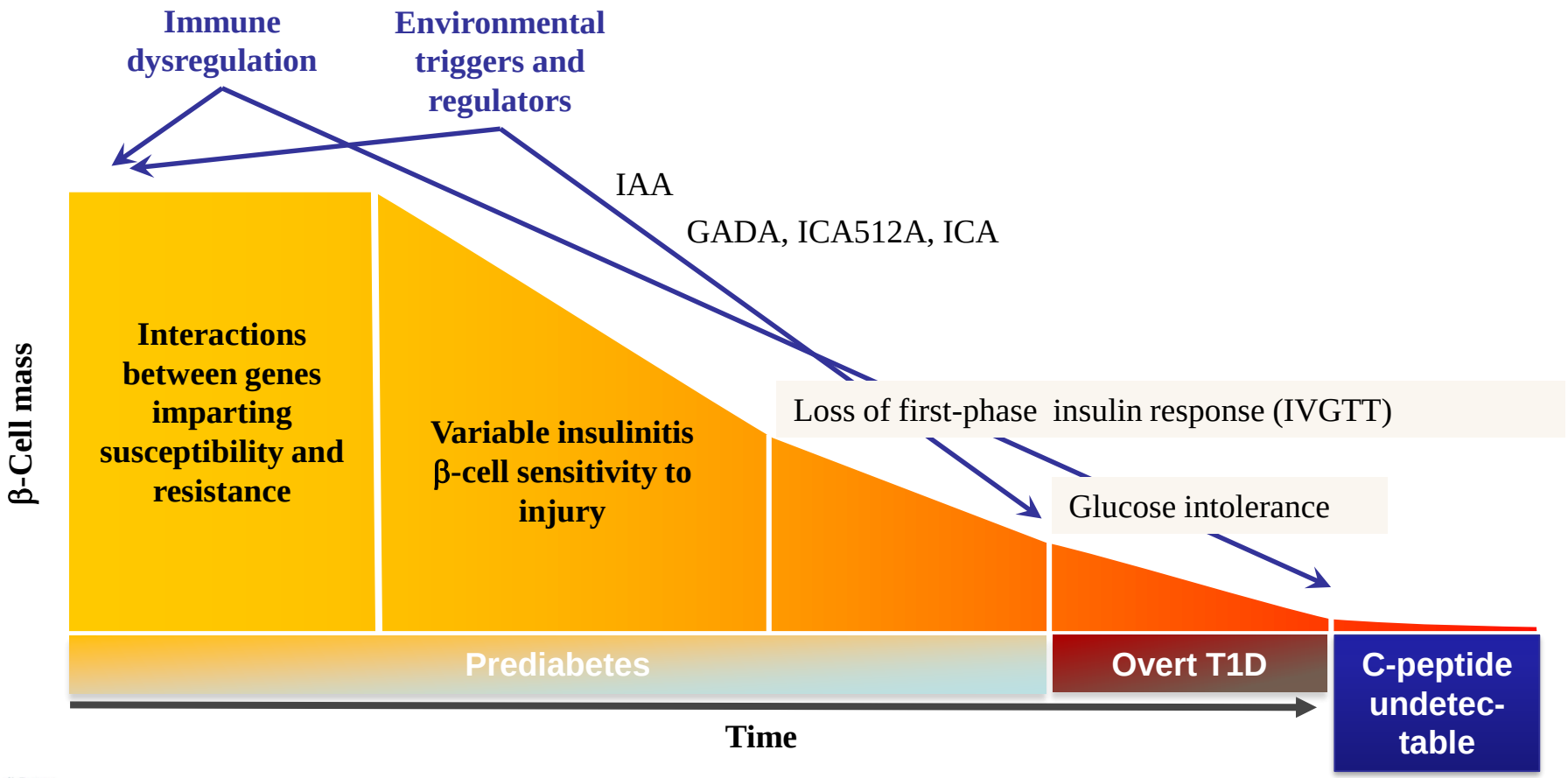
Pathophysiologic Features of Type 1 Diabetes

- Chronic autoimmune disorder
  - Occurs in genetically susceptible individuals
  - May be precipitated by environmental factors
- Autoimmune response against
  - Altered pancreatic β-cell antigens
  - Molecules in β-cells that resemble a viral protein
- Antibodies
  - Approximately 85% of patients: circulating islet cell antibodies
  - Majority: detectable anti-insulin antibodies
  - Most islet cell antibodies directed against GAD within pancreatic β-cells

GAD, glutamic acid decarboxylase.

Maahs DM, et al. *Endocrinol Metab Clin North Am.* 2010;39:481-497.

Autoimmune Basis for Type 1 Diabetes



Atkinson MA. *Diabetes*. 2005;54:1253-1263. Adapted from Atkinson MA, Eisenbarth GS. *Lancet*. 2001;358:221-229.

Diagnostic Elements

- ✓ **Symptoms of diabetes and a casual plasma glucose ≥ 200 mg/dl**
- ✓ **Fasting Plasma Glucose (FPG) ≥ 126 mg/dl**
- ✓ **Impaired Fasting Glucose (IFG):**

- **2-h plasma glucose ≥ 200 mg/dl after an OGTT**
- **These criteria should be confirmed by repeat testing on a different day**

Clinical features of Type 1 diabetes.

- Presents acutely. Symptoms due to hyperglycaemia (thirst, polyuria, tiredness,weight loss).
- Ketone production - abdominal pain, nausea and vomiting.
- Other symptoms: blurred vision, repeated infections.
- No chronic complications at diagnosis, may only be apparent 5-10 years post diagnosis.

Pharmacotherapeutic Goals

Glycemic Controls	
HbA1c	<7 – 6.5%
Pre-prandial capillary plasma	90 – 130 mg/dL
Post prandial capillary plasma	<180 mg/dL

Desired Outcomes

- ✓ Reduce risk for microvascular and macrovascular complications
- ✓ Reduce mortality
- ✓ Achieve glycemic control
- ✓ Improved quality of life

Medical Nutrition Therapy

Nutrient	Recommended Intake
Carbohydrate	50-60% of total calories
Protein	15-20%
Totale fat	25-35%
Saturated fat	< 10 (<7 % in dyslipidemia)
Polyunsaturated fat	10 %
Mono unsaturrated fat	up to 20%
Cholesterol	< 300 mg/dL (<200 mg/dl in dyslipidemia)
Total calories	Asjust based on age, weight and height

Pharmacotherapy in Type 1 DM

The primary therapy for type 1 DM is insulin therapy

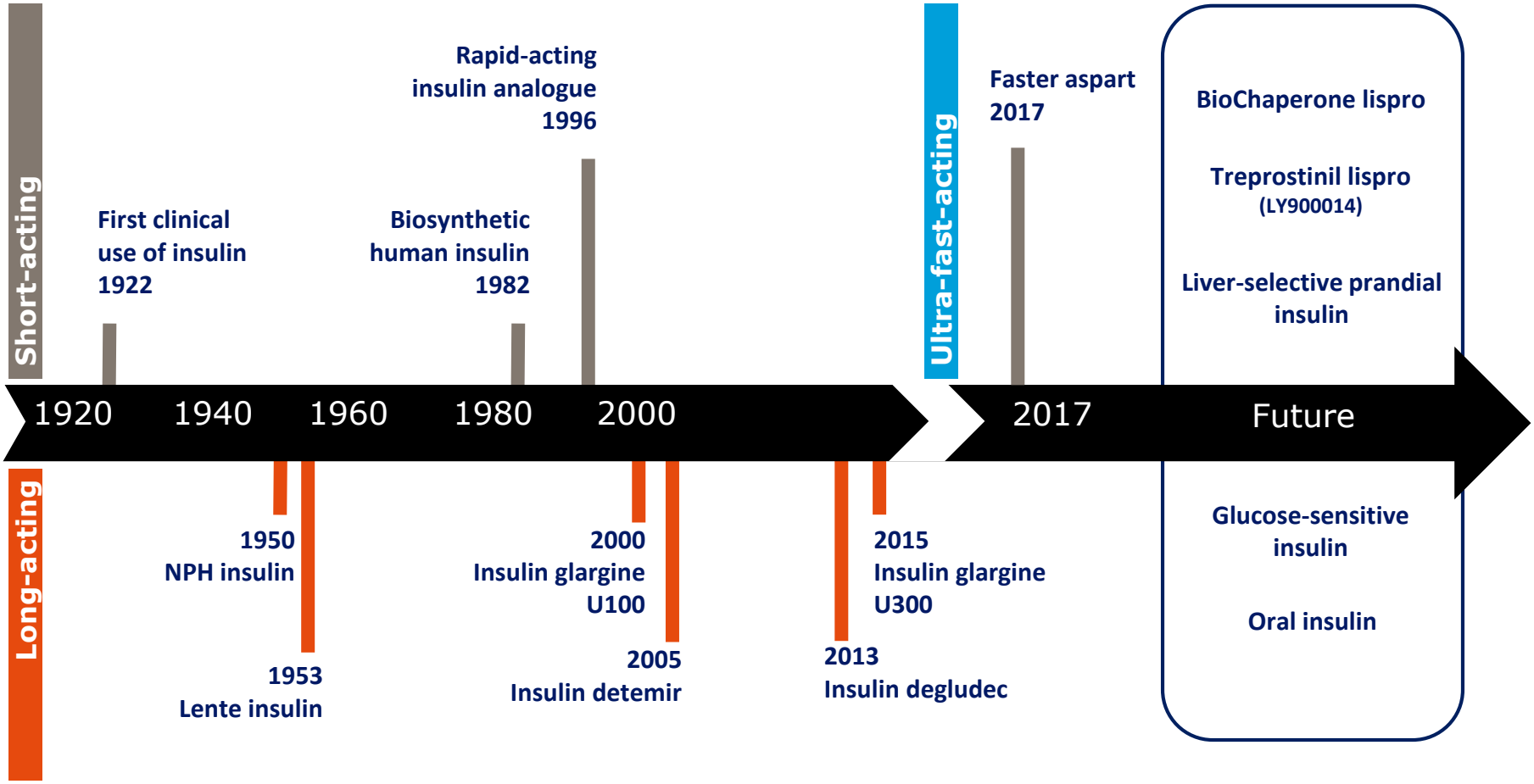
Four basic forms of insulin:

– Rapid-acting

– Short-acting

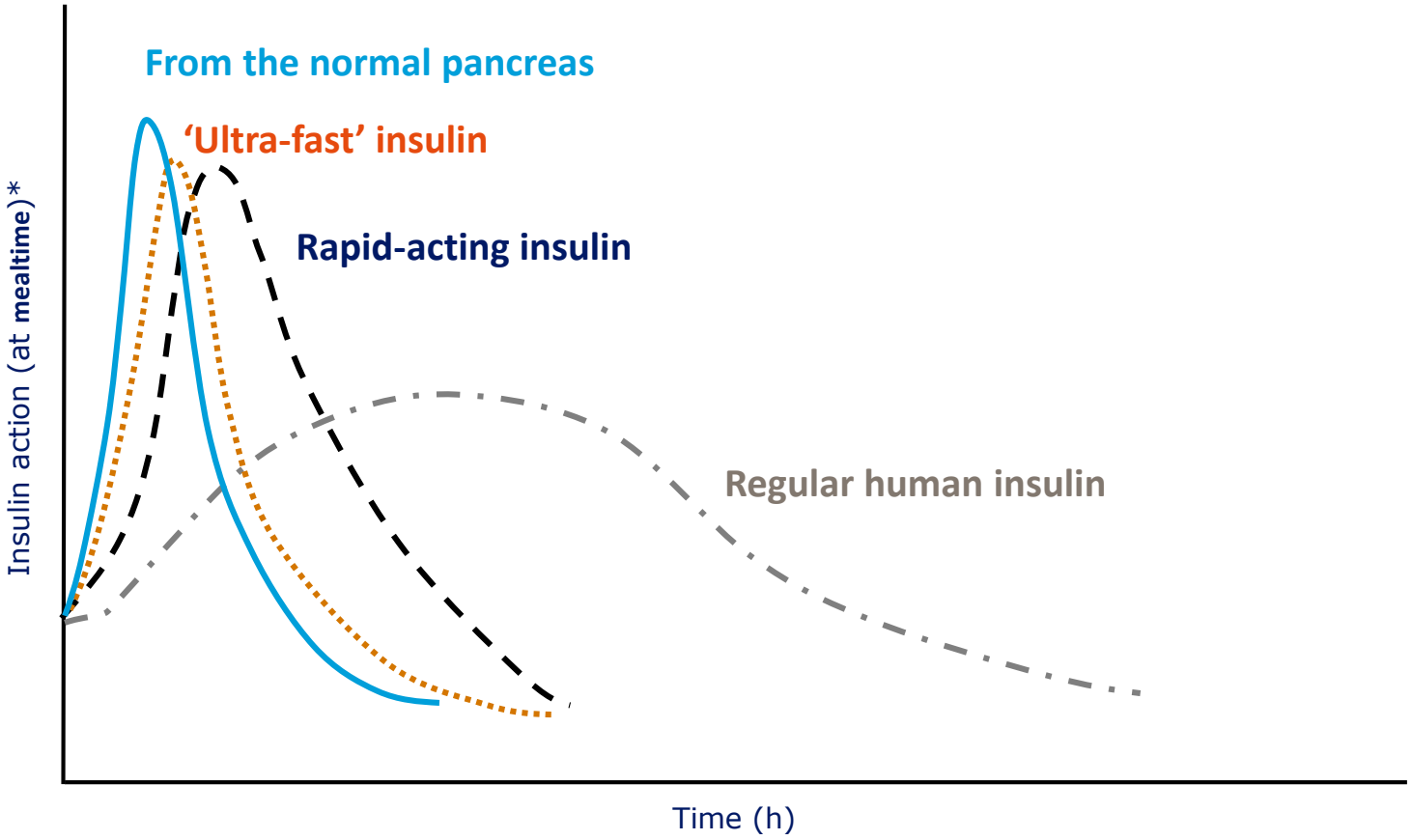
– Intermediate-acting

– Long-acting

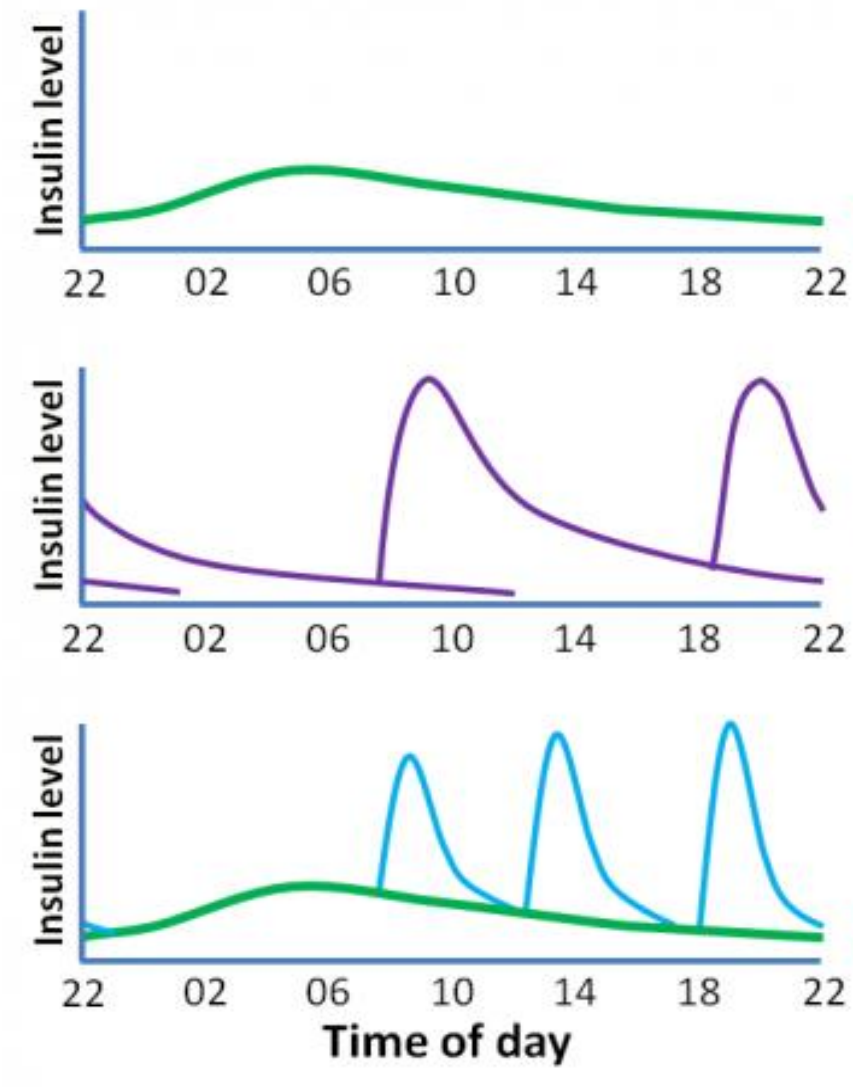


Faster aspart, fast-acting insulin aspart; NPH, neutral protamine Hagedorn

Adapted from Cahn *et al. Lancet Diabetes Endocrinol* 2015;3:638–52; Kazda *et al*. ADA 2017 (poster, P-959); Kim & Plosker. *Drugs* 2015;75:1679–86; Novo Nordisk. Capital Markets Day R&D update, 19 November 2015



*Schematic representation
T1D, type 1 diabetes; T2D, type 2 diabetes
Adapted from Home. *Diabetes Obes Metab* 2015;17:1011–20

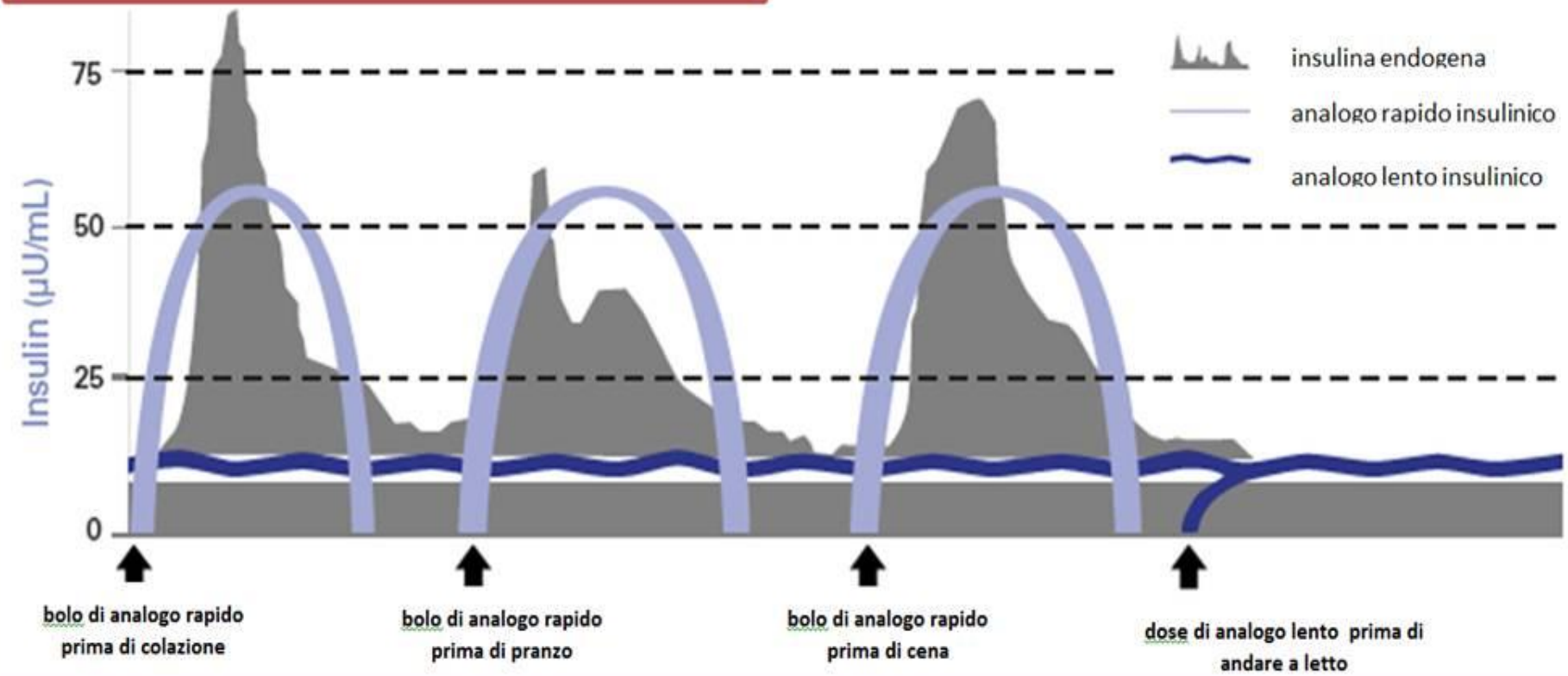


Once-daily basal insulin

Twice-daily mix-insulin

Basal-bolus therapy

schema basal-bolus



Insulin Adverse Reactions

- **Lipoatrophy: loss of fat at injection site due to antibody formation leading to breakdown of fat in the area of injection (need to rotate sites!)**
- **Hypertrophy: increase in fat mass at the site, the area is anesthetized, however leads to erratic insulin absorption**
- **Resistance: require large amounts of insulin to get desired effect, due to antibody formation**

Insulin Adverse Reactions

- **Foods that will provide 10g of carbs:**

– **Cup of orange juice or soda**
– **Sugar: 2 teaspoons or 2 cubes**
– **Glucose tablets: 2-4 tablets**
– **Apple juice: 1/3 cup**

- **Foods to avoid**

– **Ice cream, candy bars, cookies, cakes**
– **Complex carbs slowly absorbed**

- **If unconscious: Glucagon 1mg SQ, IM, or IV and Dextrose 50% 50ml infusion**

Hormonal Responses to Exercise (non-diabetic)

Insulin Secretion
↓↓

Counterregulatory Hormone Secretion
↑ (Epi/Nepi • Glucagon • GH, Cortisol)

Substrate Breakdown
- Glycogenolysis
- Lipolysis

BG Holds *Steady* Despite
↑ Glucose Utilization by Muscle

Hormonal Responses to Exercise (diabetic using insulin)

Insulin Levels
⇗ or ⇔

Counterregulatory Hormone Action Suppressed

Substrate Breakdown Blocked
Glucose Uptake Accelerated

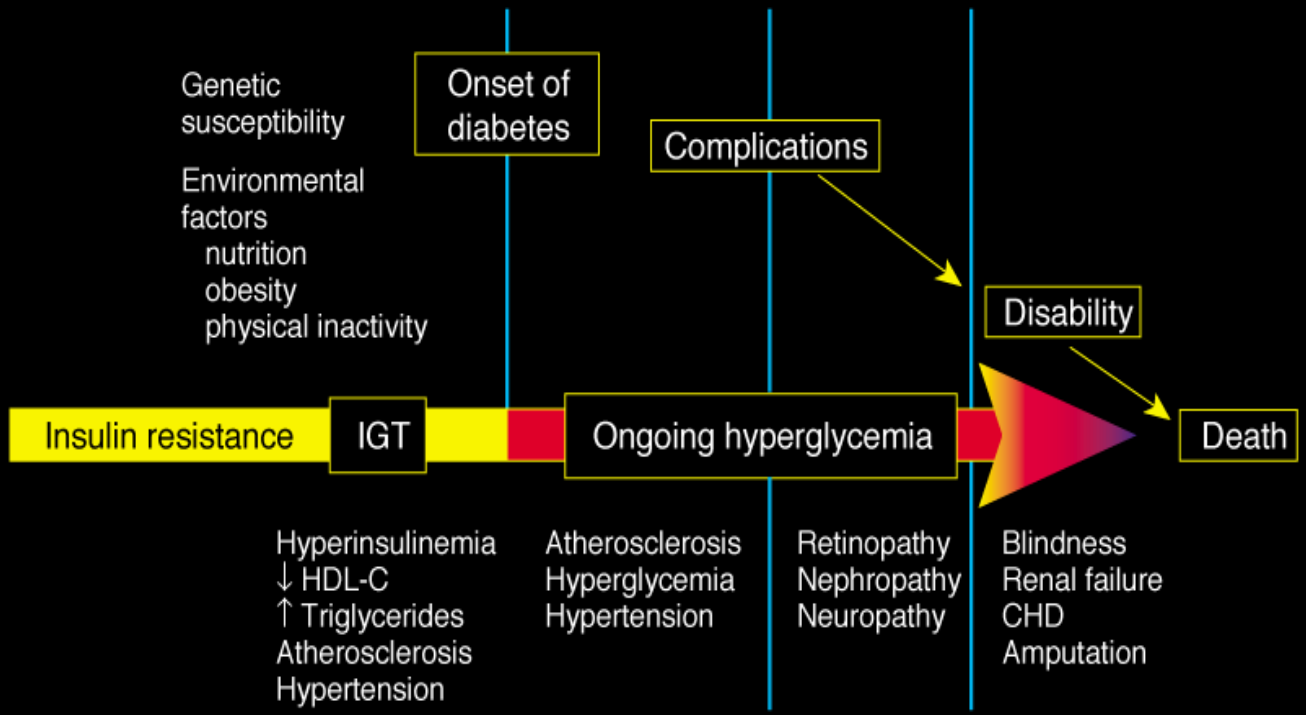
Hypoglycemia May Result

INSULIN TYPE	ONSET/DURATION OF ACTION	USES	NOTES
Rapid acting: ■ Lispro ■ Glulisine ■ Aspart	20 min/4 h	Type 1 DM Type 2 DM Gestational DM for postprandial glucose control	Can cause hypoglycemia; rare hypersensitivity reactions
Short acting: ■ Regular	1 h/6–8 h	Type 1 DM Type 2 DM Gestational DM DKA (IV) Hyperkalemia (+glucose) Stress hyperglycemia	The only insulin given IV
Intermediate-acting: ■ NPH	2–4 h/10–18 h	Type 1 DM Type 2 DM Gestational DM	Most commonly used insulin type
Long-acting: ■ Glargine ■ Detemir	1 h/12–24 h 1 h/8–24 h	Type 1 DM Type 2 DM Gestational DM for basal glucose control	Establishes basal insulin level

Type 2 Diabetes

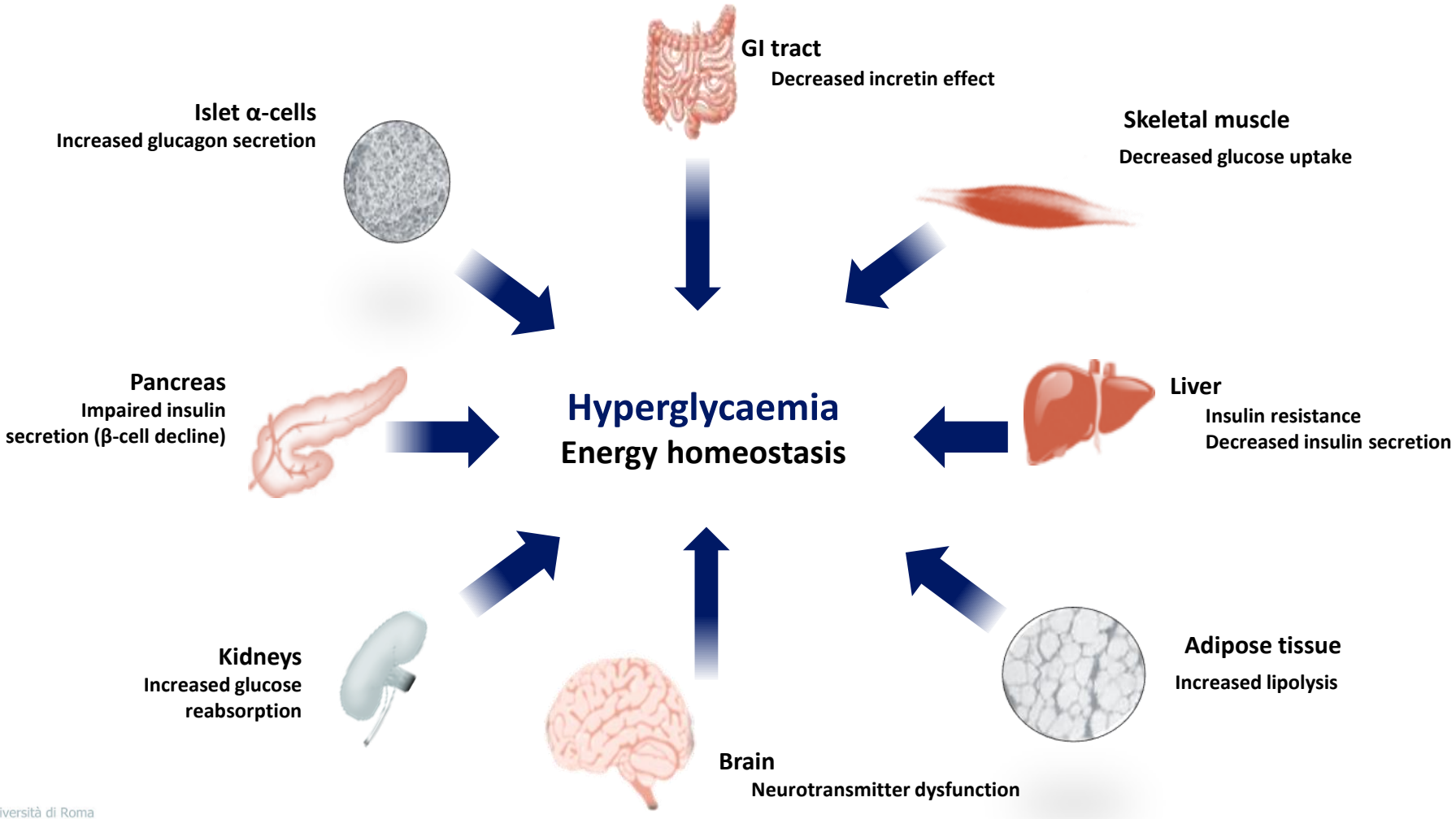
VBWG

Natural history of patients with type 2 diabetes . . . Problems before you see them



Pathogenesis of type 2 diabetes

The ominous octet



GI, gastrointestinal 1. DeFronzo. *Diabetes* 2009;58:773–95

Type 2 diabetes

- ✓ Patients frequently undiagnosed for many years.
- ✓ May present with hyperglycaemia symptoms.
- ✓ Coma is rare in type 2 diabetes.
- ✓ May progress to an absolute state of insulin deficiency.

Pathogenesis of Type 2 diabetes

- **Cause:** a combination of impaired insulin secretion and insensitivity of target tissues to insulin.
- Impaired insulin secretion due to beta cell malfunction can be associated with:

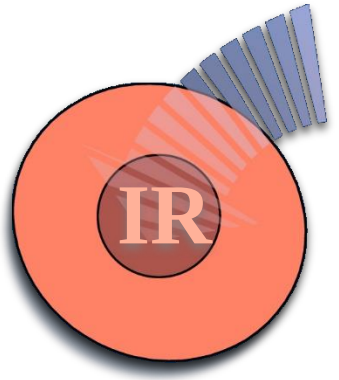
1. Incorrect secretion pattern.
2. Ratio of proinsulin to insulin.
3. Amyloid deposits.
4. Slow destruction of beta cells

Mechanisms for insulin resistance

1. Receptor numbers are decreased. (Often seen in obese and aged patients.)
2. Receptor structure is abnormal.
3. Insulin resistance at post receptor events.

What is insulin resistance?

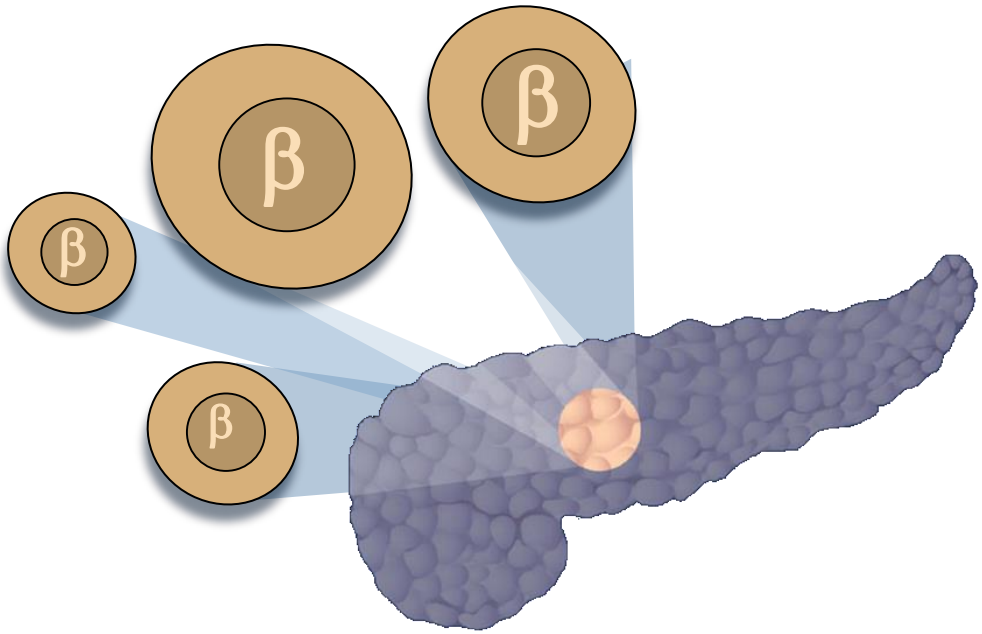
- Major defect in individuals with type 2 diabetes[1]
- Reduced biological response to insulin[1–3]
- Strong predictor of type 2 diabetes[4]
- Closely associated with obesity[5]



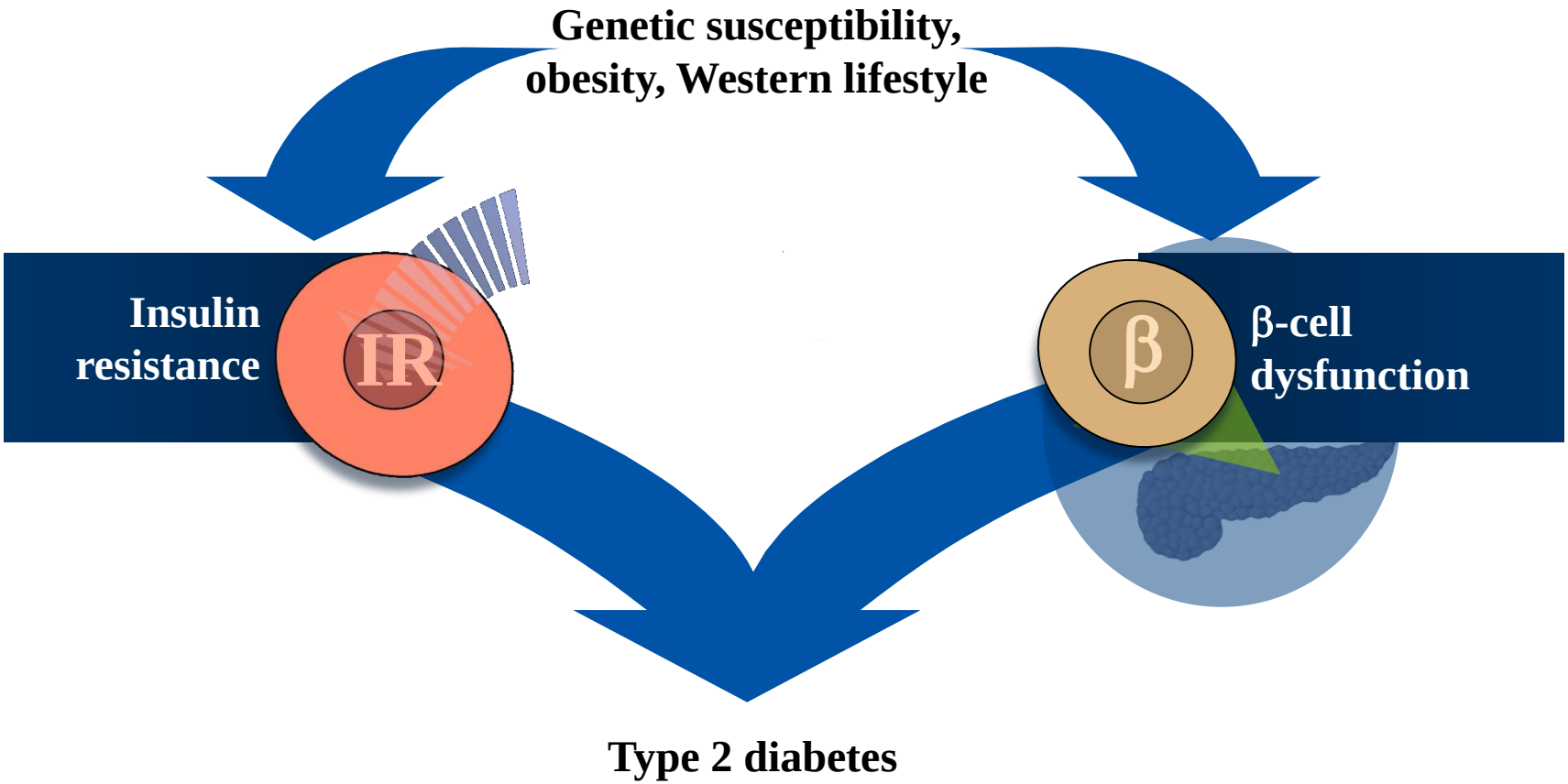
[1]American Diabetes Association. *Diabetes Care* 1998; 21:310–314.
[2]Beck-Nielsen H & Groop LC. *J Clin Invest* 1994; 94:1714–1721. [3]Bloomgarden ZT. *Clin Ther* 1998; 20:216–231.
[4]Haffner SM, *et al. Circulation* 2000; 101:975–980. [5]Boden G. *Diabetes* 1997; 46:3–10.

What is β-cell dysfunction?

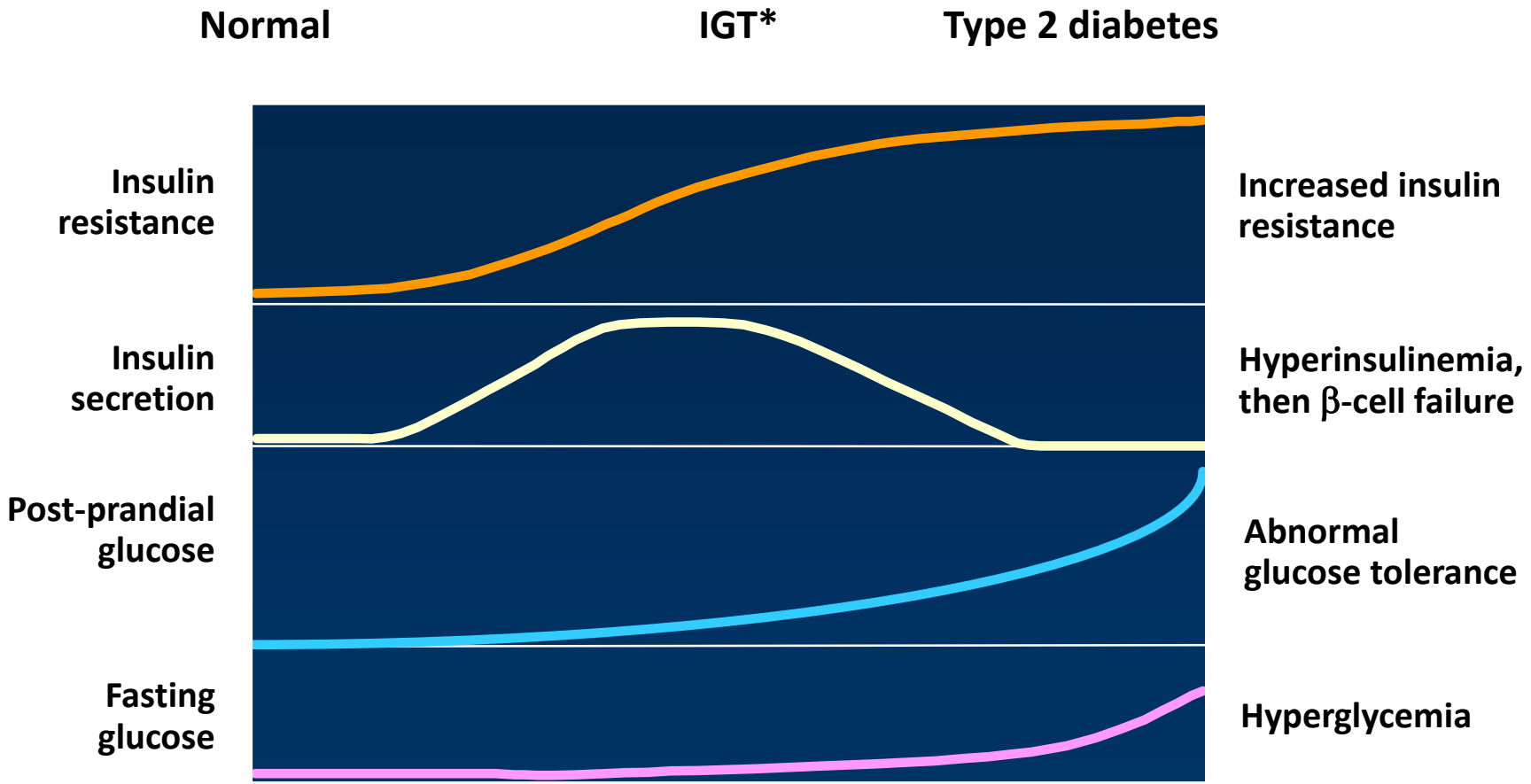
- Major defect in individuals with type 2 diabetes
- Reduced ability of β-cells to secrete insulin in response to hyperglycemia



Insulin resistance and β-cell dysfunction are core defects of type 2 diabetes



How do insulin resistance and β-cell dysfunction combine to cause type 2 diabetes?



*IGT = impaired glucose tolerance

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Adapted from *Type 2 Diabetes BASICS*. International Diabetes Center (IDC), Minneapolis, 2000.

Clinical features of Type 2 diabetes

- Diagnosis due to presence of complications.(At least 30% patients have complications at diagnosis).
- Symptoms are mild, gradual onset. Classic diabetic symptoms may be present.
- Type 2 diabetics are usually:

  over 40 years, fat (“apple obesity”) and no ketones are present.

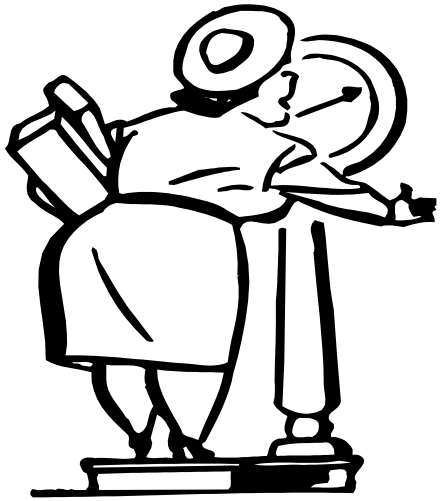
Those at Risk of developing Type 2 Diabetes

- Gestational Diabetes
- Family History
- Ethnicity
- Obesity
- Physical Inactivity
- Age
- IGT/IFG
- Polycystic Ovary Syndrome

Risk factors for type 2 diabetes

- Hypertension
- Dyslipidaemia
- Abdominal obesity
- Overweight
- Insulin Resistance

Metabolic Syndrome/ Syndrome X



Prevention of type 2 diabetes

Lifestyle modification

- Diabetes Prevention Program
- Finnish Diabetes Prevention Study

Diagnosis of Diabetes

Diagnosis cannot be made from:

- Blood glucose strips read visu

or by a meter.

- Glycosalated Haemoglobin - HbA1c

Glucose Tolerance Test

- 3 days of unrestricted diet and exercise
- Evening meal as normal the night before
- Overnight fast of 8-14 hours

TEST

- Fasting blood on the morning
- Drink 75g of anhydrous glucose in 250-300ml water over 5 mins
- Blood sample 2 hours later
- No smoking during the test

DIAGNOSIS AFTER AN OGTT

	Impaired Fasting Glucose (IFG)	**Impaired Glucose Tolerance (IGT)**	**Diabetes**
Fasting Venous Plasma Glucose	6.1 mmol/l to 6.9 mmol/l	<7.0 mmol/l	≥ 7.0 mmol/l
2 hr post	< 7.8 mmo/l	≥7.8 mmol/l up to 11.1 mmol/l	≥11.1 mmol/l (WHO,2006)

Impaired Glucose Regulation

- Impaired Glucose Tolerance (IGT)

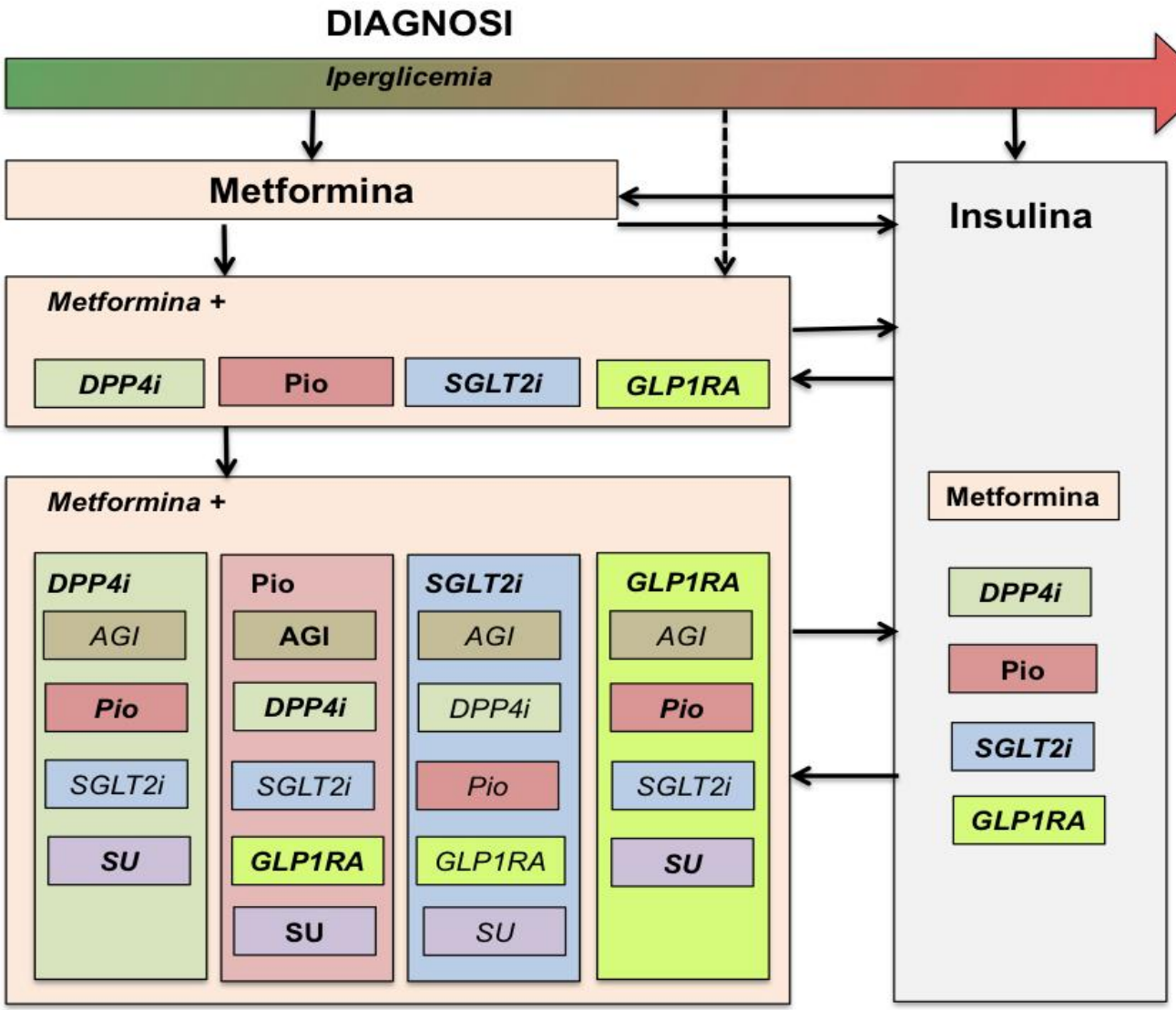
  - Abnormalities in glucose regulation in the post-prandial state.

  - More common in women

- Impaired Fasting Glucose (IFG)

  - Elevated fasting glucose concentrations, but lower than those required to diagnose diabetes

  - More common in men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SGLT2i
GLP1RA
Metformina +
DPP4i
AGI
Pio
SGLT2i
SU
Pio
AGI
DPP4i
SGLT2i
GLP1RA
SU
SGLT2i
AGI
DPP4i
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GLP1RA
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GLP1RA
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Insulina
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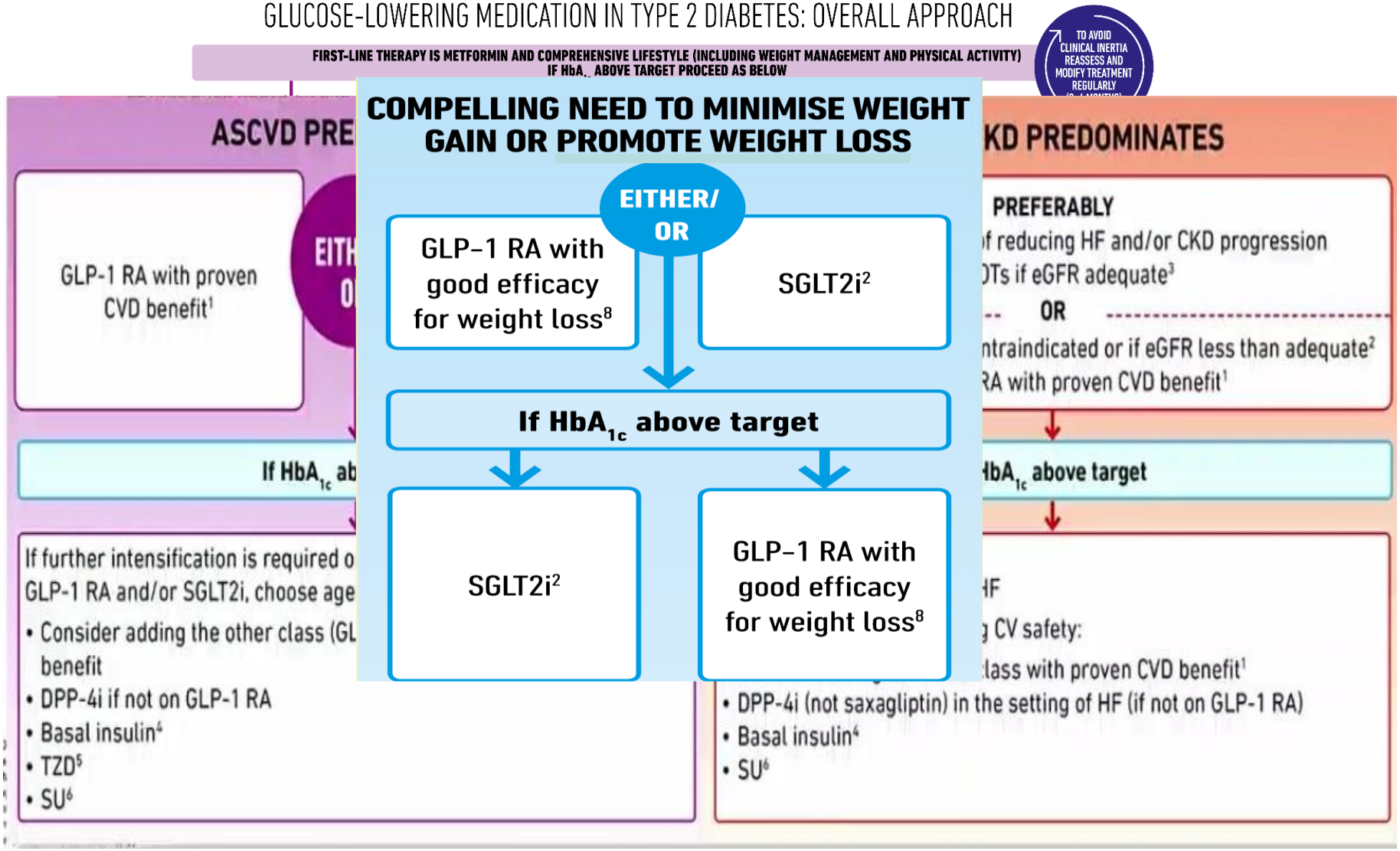
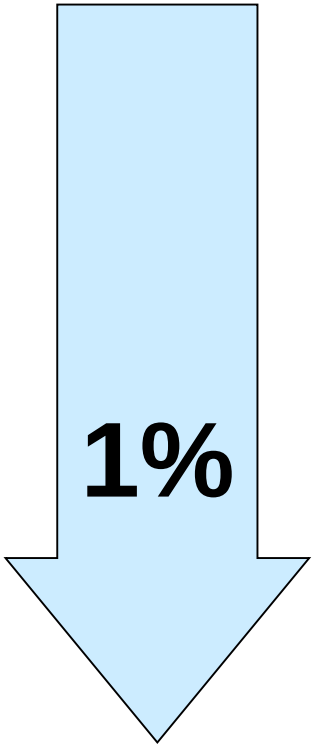
GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

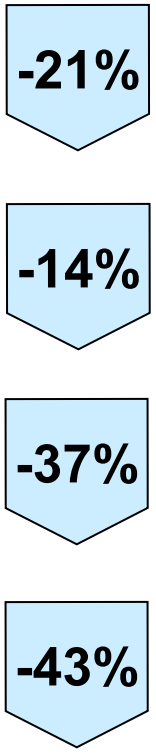


Lessons from UKPDS:
Better control means fewer complications

EVERY 1%
reduction in HBA_{1C}



REDUCED RISK*



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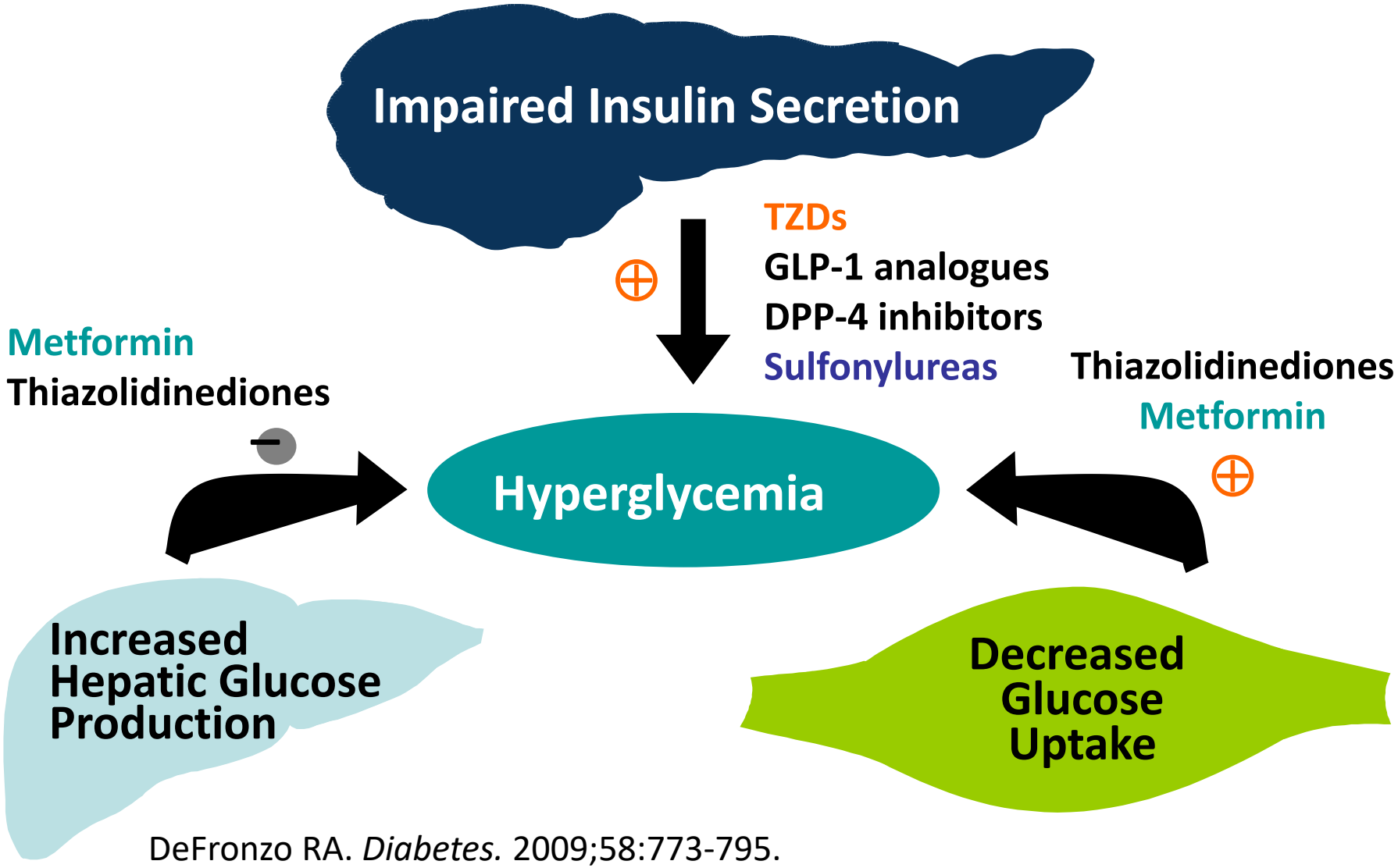
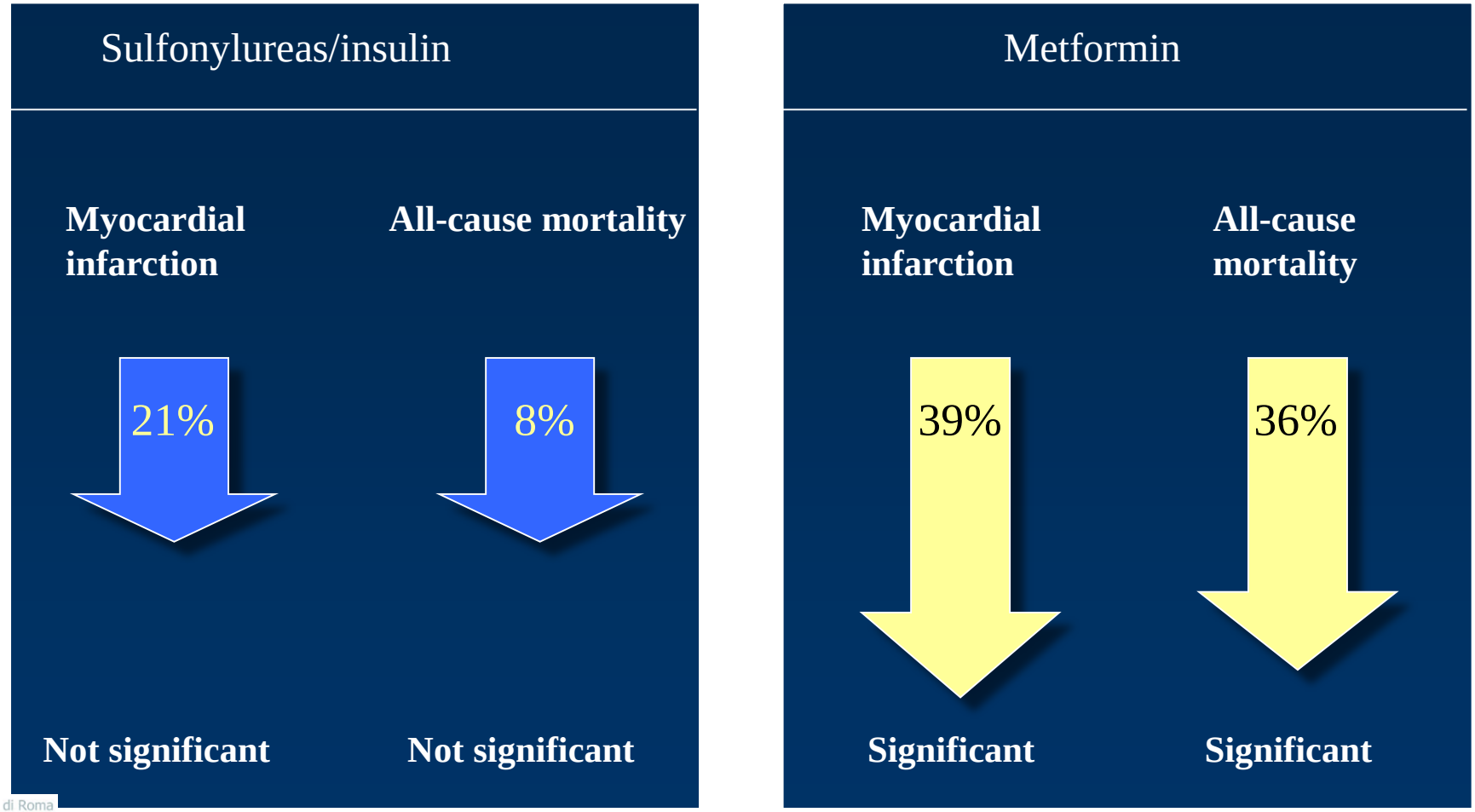
UKPDS 35. BMJ 2000; 321: 405-12

Pathophysiologic Approach to Treatment of T2DM

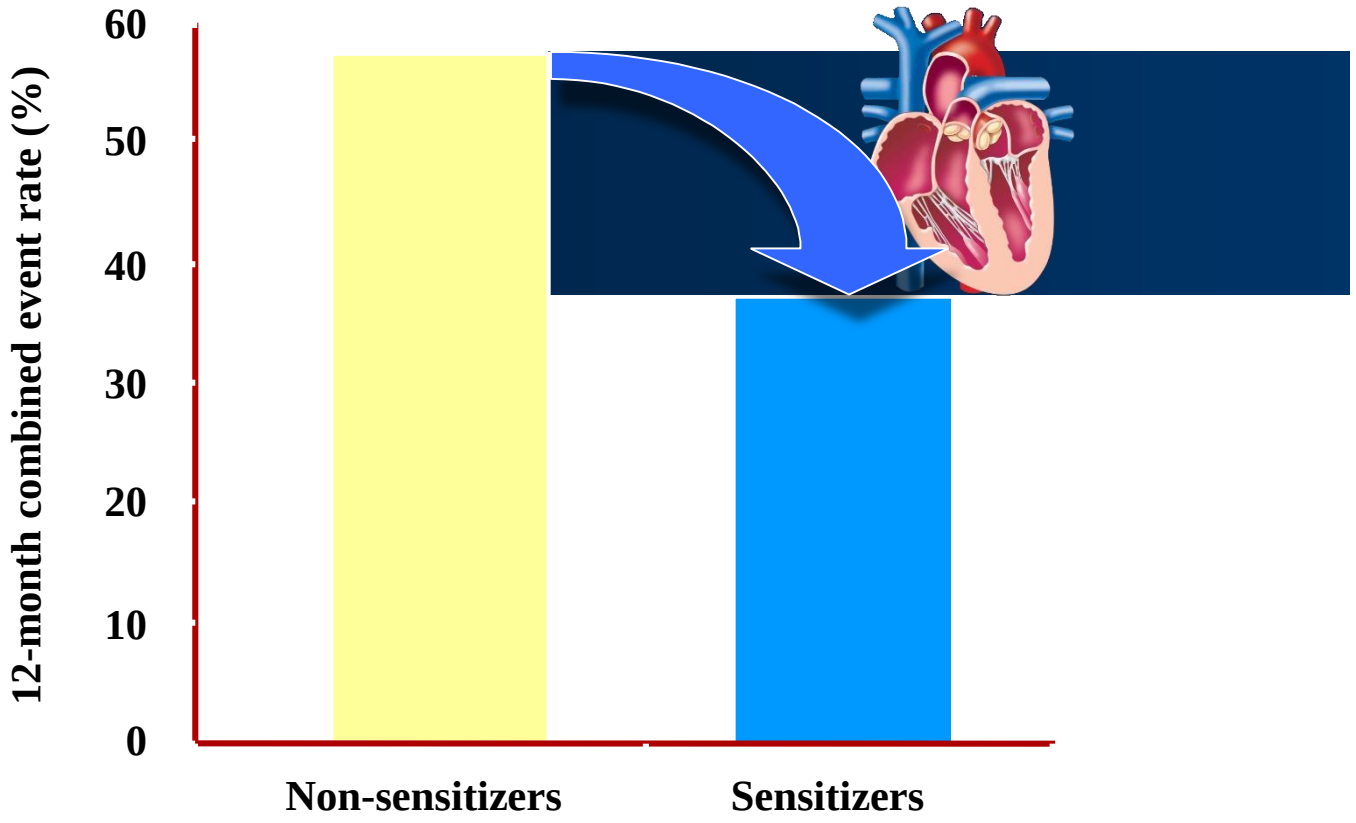


DeFronzo RA. *Diabetes.* 2009;58:773-795.

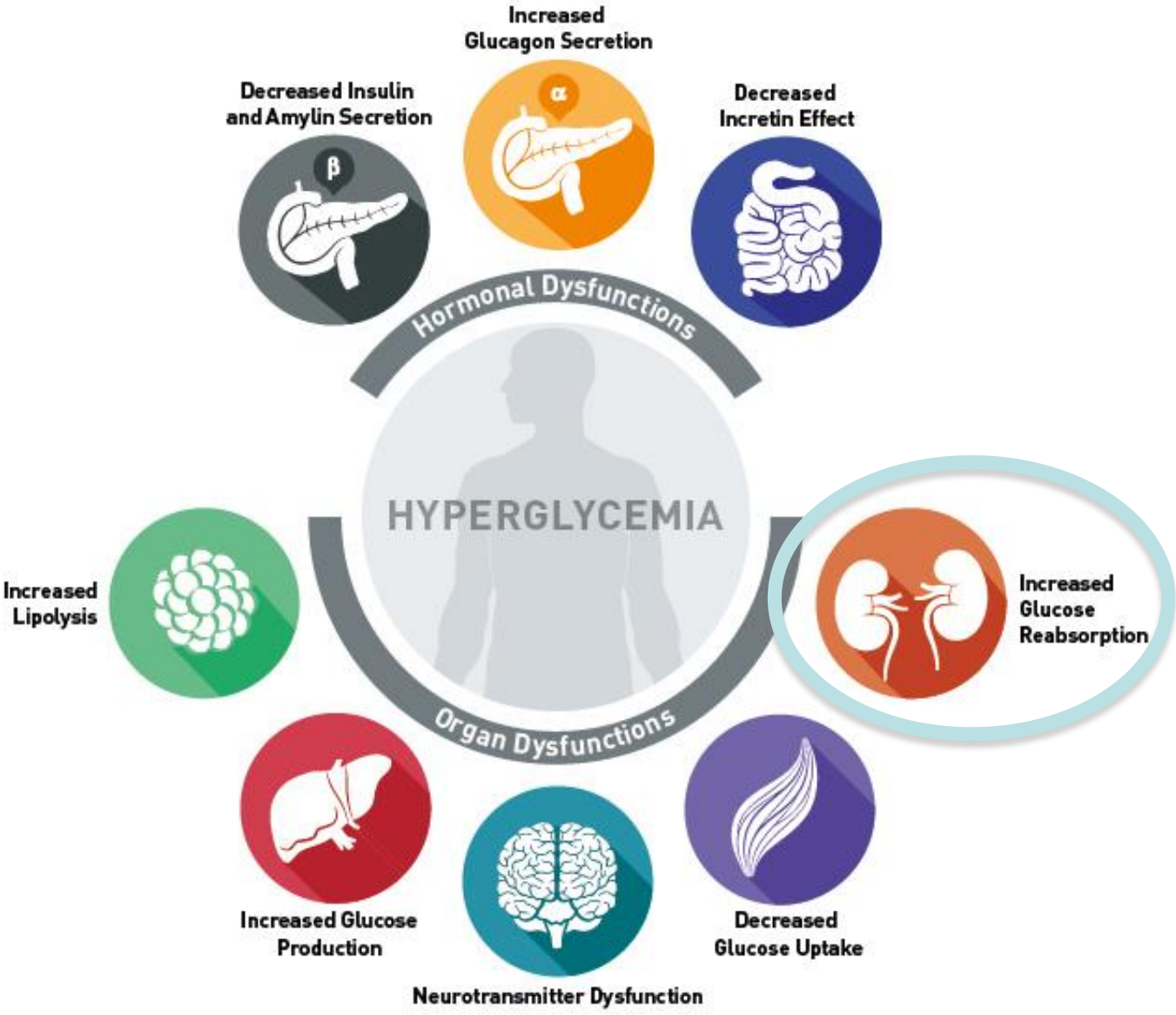
Does decreasing insulin resistance decrease macrovascular complications?



Insulin sensitizers reduce cardiovascular events in type 2 diabetes

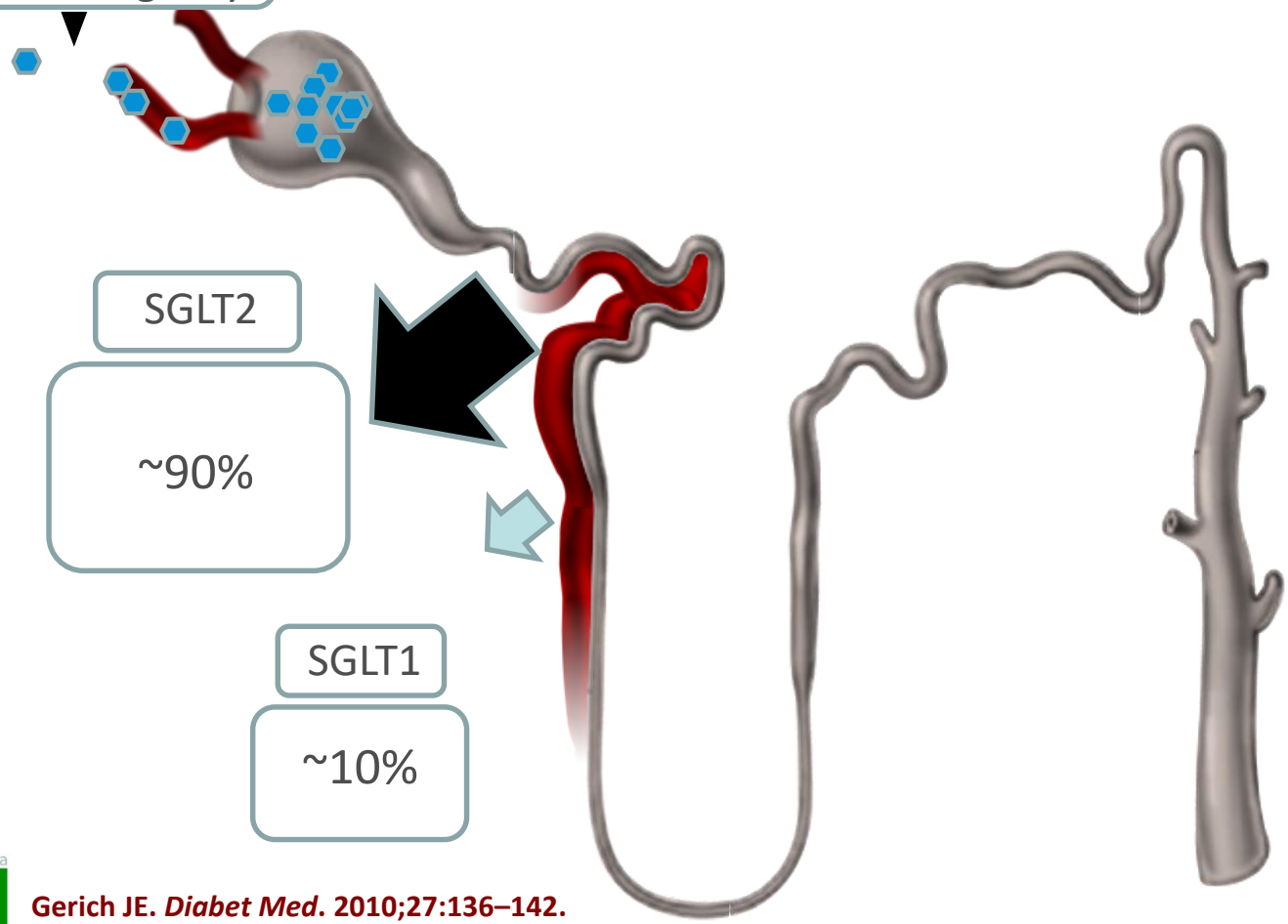


Kao JA, *et al. J Am Coll Cardiol* 2004; 43:37A.



Riassrbomineto del glucosio a livello renale in pazienti con iperglicemia

Glucosio filtrato180 g/day



SGLT2

~90%

SGLT1

~10%

Quando la concentrazione di glucosio aumenta al di sopra della soglia renale (~180 mg/dL), the capacity of the transporters is exceeded, con conseguente escrezione urinaria di glucosio

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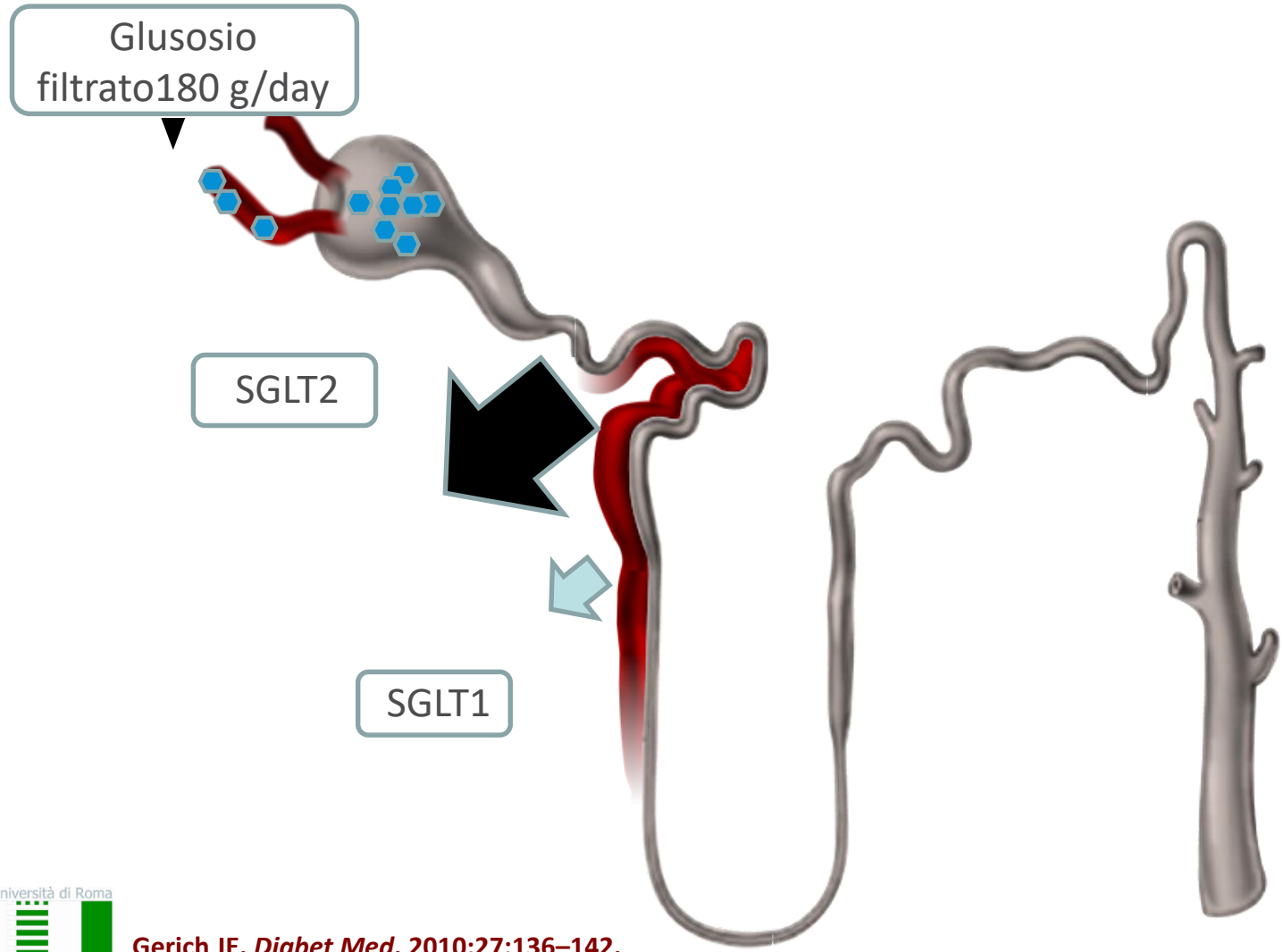
Gerich JE. *Diabet Med*. 2010;27:136–142.

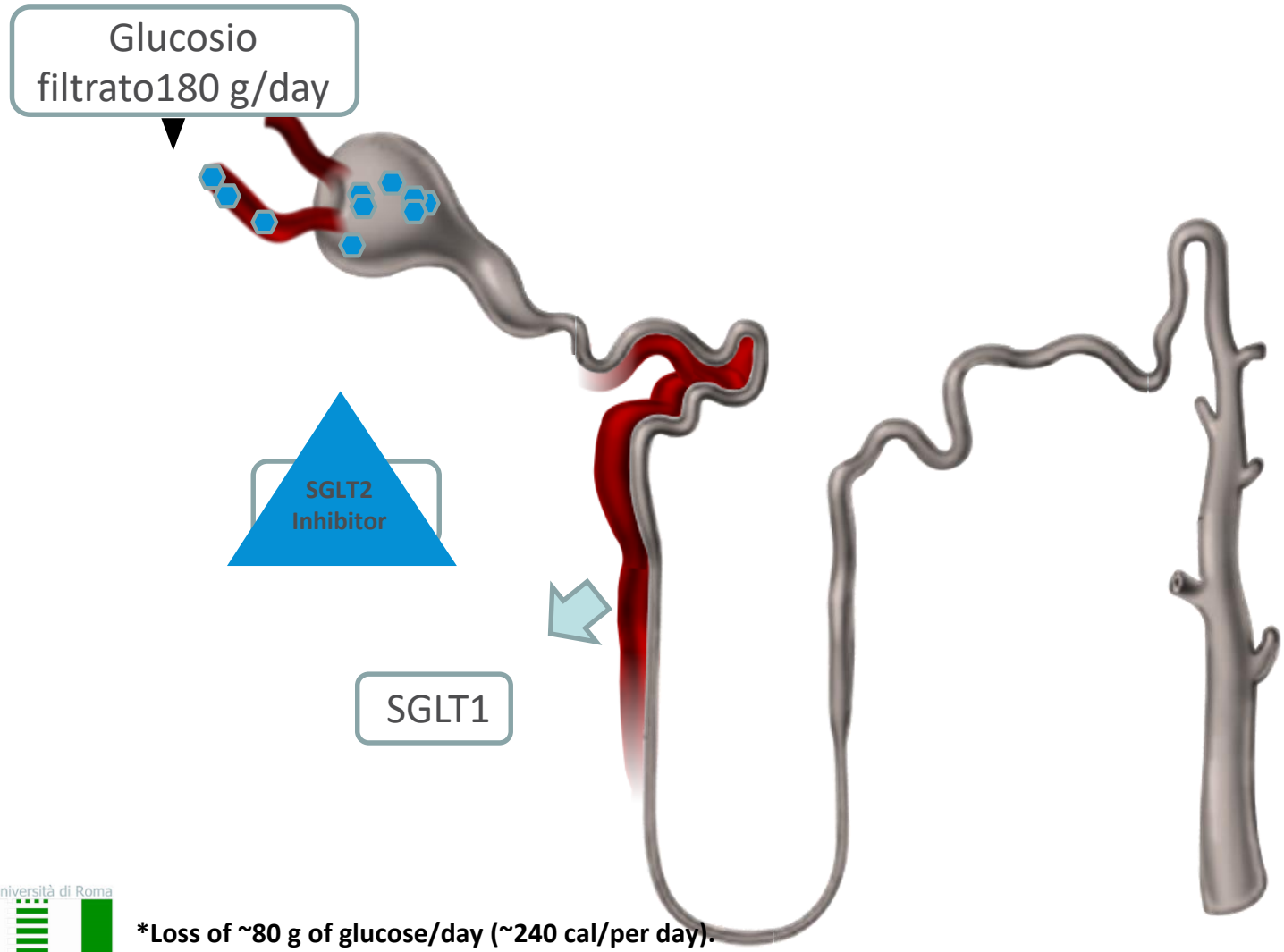
Upregulation del SGLT2 in pazienti diabetici con iperglicemia



Nel diabete di tipo 2, il SGLT2 è upregulated, incrementando cosi l'assorbimento di glucosio a livello del tubulo renale e diminuendo la sua escrezione urinaria

Gerich JE. *Diabet Med*. 2010;27:136–142.

Urinary glucose excretion via SGLT2 inhibition



SGLT2i inibiscono il riassorbimento di glucosio a livello del tubulo controrno prossimale, provacando la sua escrezione urinaria

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

Gerich JE. *Diabet Med*. 2010;27:136–142.

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The NEW ENGLAND JOURNAL of MEDICINE

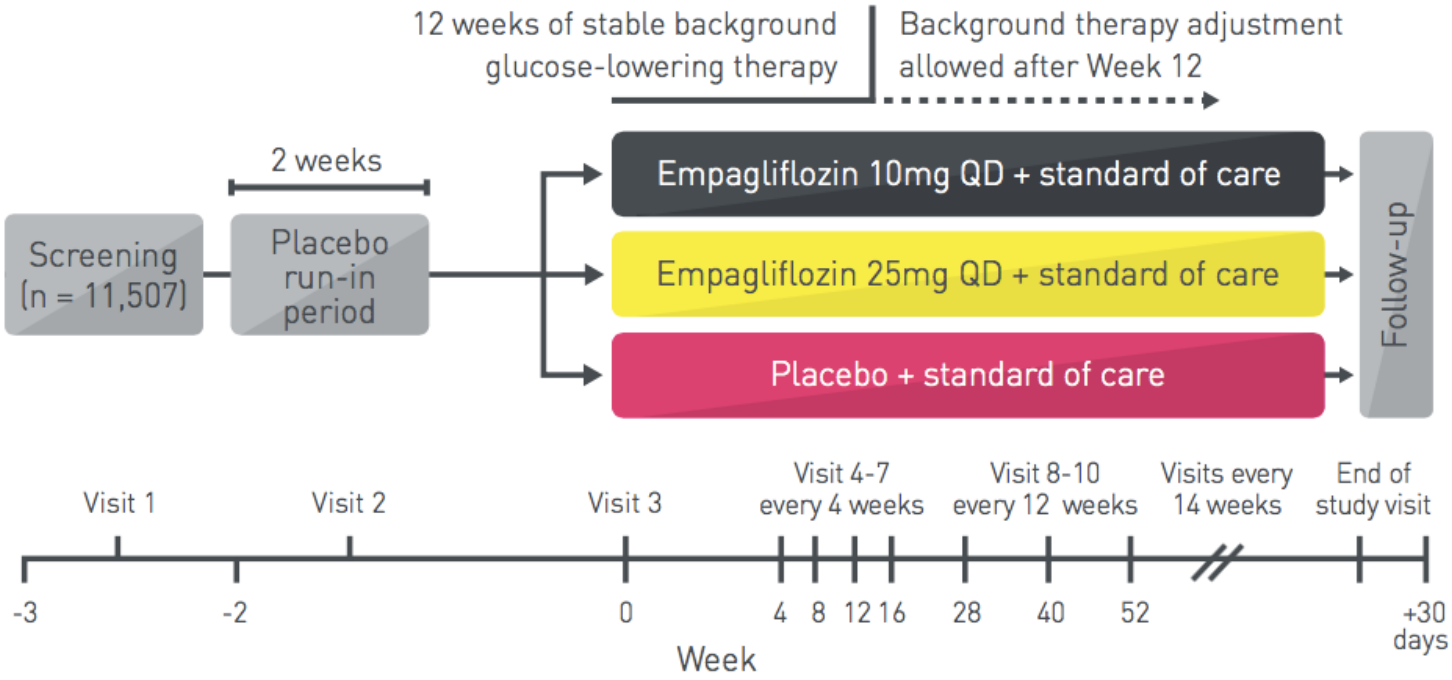
ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

Zinman B et al, NEJM, 17 September 2015

EMPA-REG OUTCOME® Trial Design

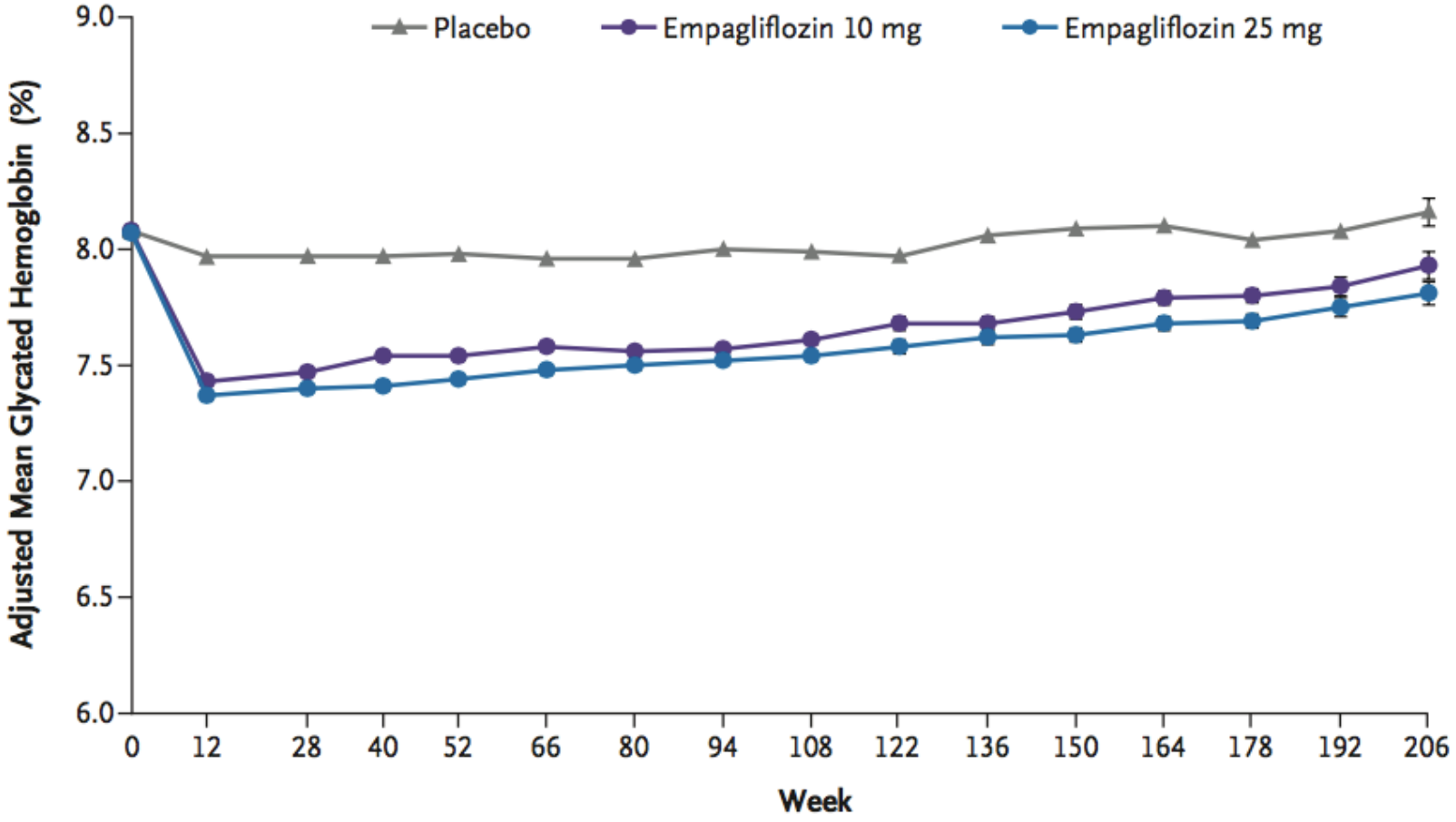


Key inclusion criteria[3]

- High risk of CV events due to previous CV event or established CVD
- Insufficient glycemic control

Zinman B et al, NEJM, 17 September 2015

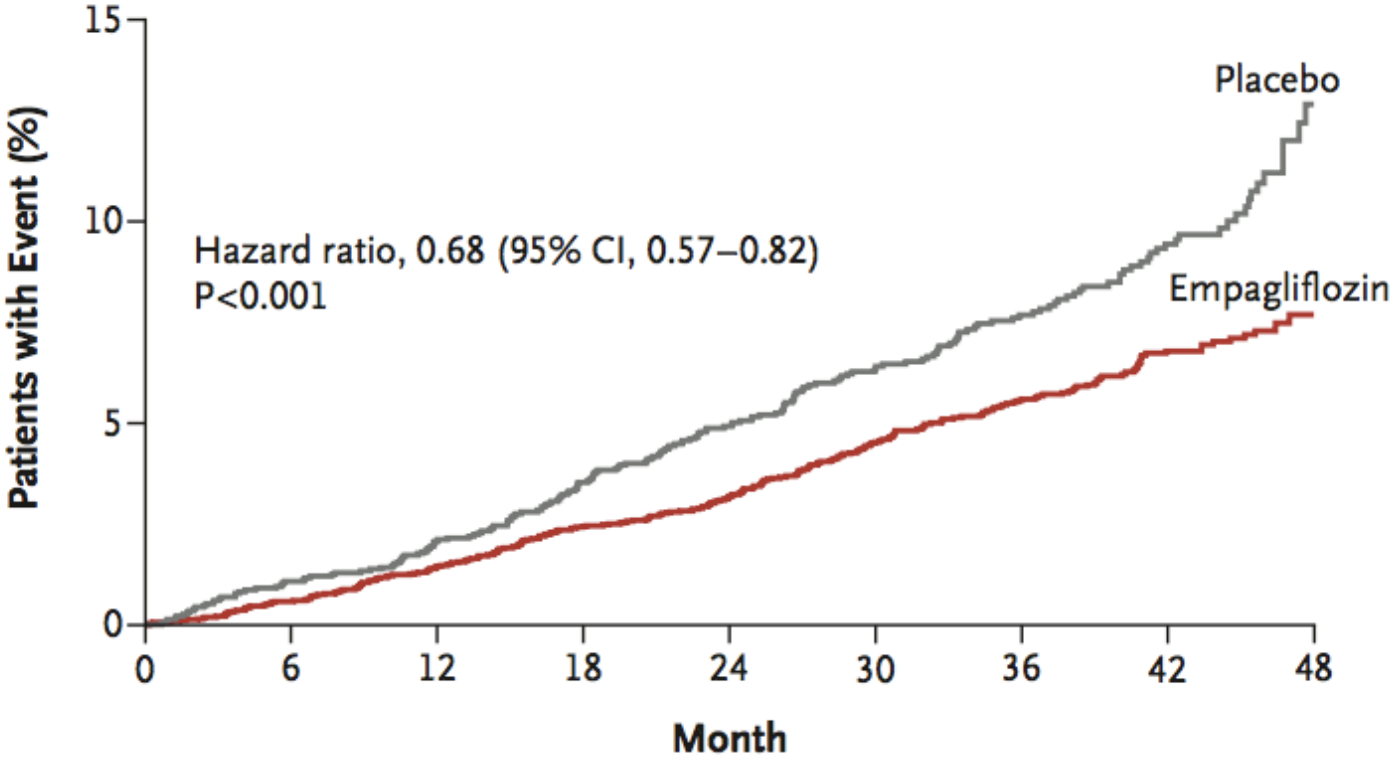
Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes



Zinman B et al, NEJM, 17 September 2015

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Death from Any Cause



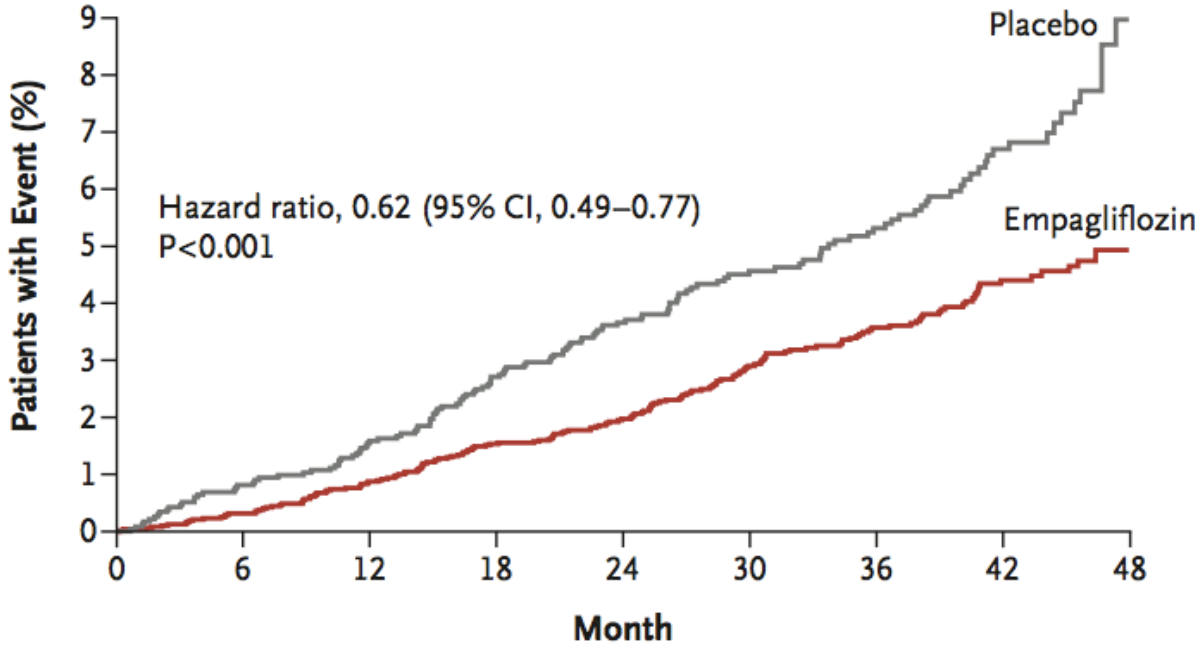
No. at Risk

Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

Zinman B et al, NEJM, 17 September 2015

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Death from Cardiovascular Causes



No. at Risk

Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
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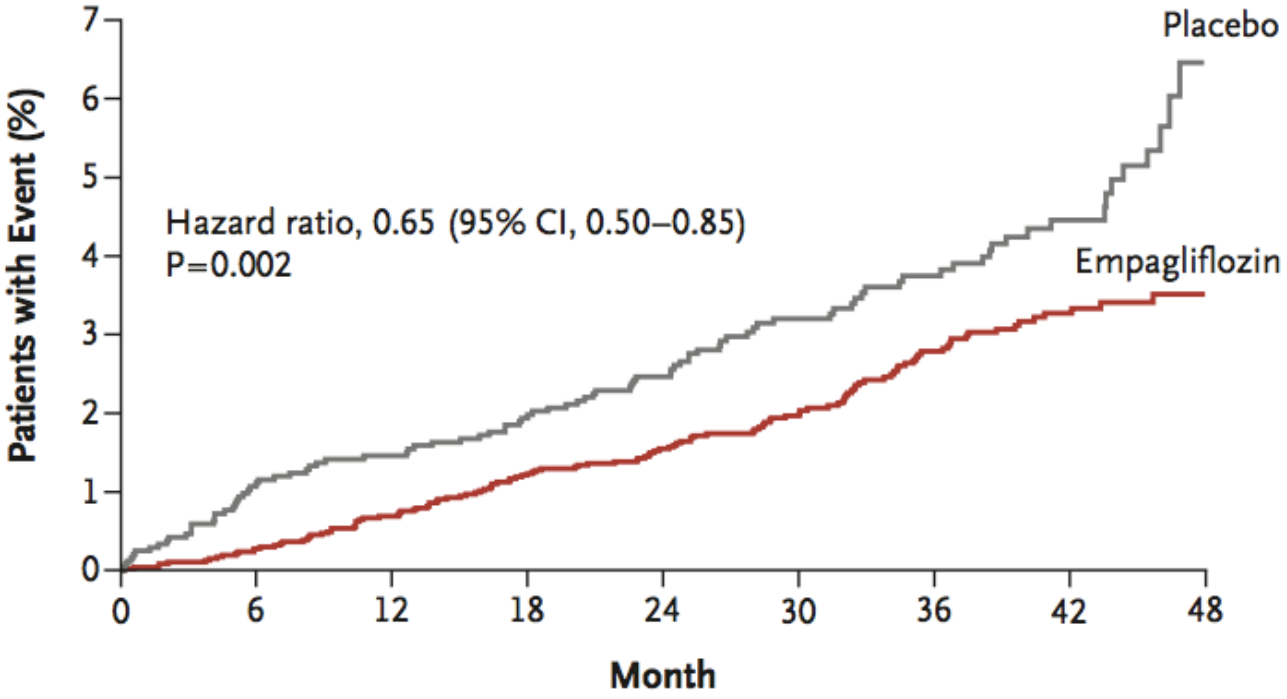
Zinman B et al, NEJM, 17 September 2015

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Hospitalization for Heart Failure

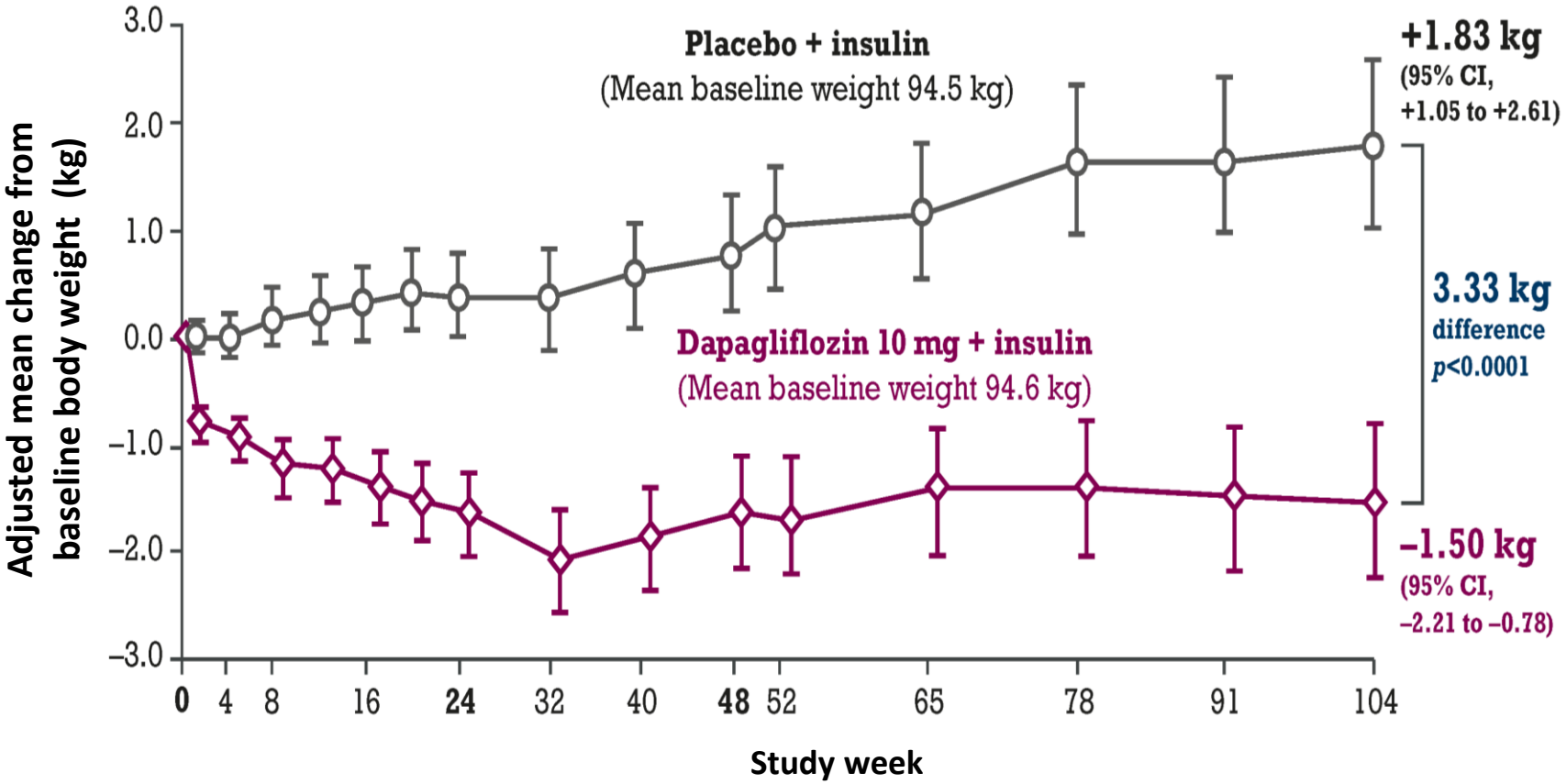


No. at Risk									
Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

Zinman B et al, NEJM, 17 September 2015

Dapagliflozin in patients with type 2 diabetes receiving high doses of insulin: efficacy and safety over 2 years

J. P. H. Wilding[1], V. Woo[2], K. Rohwedder[3], J. Sugg[4] & S. Parikh[4] for the Dapagliflozin 006 Study Group[†]



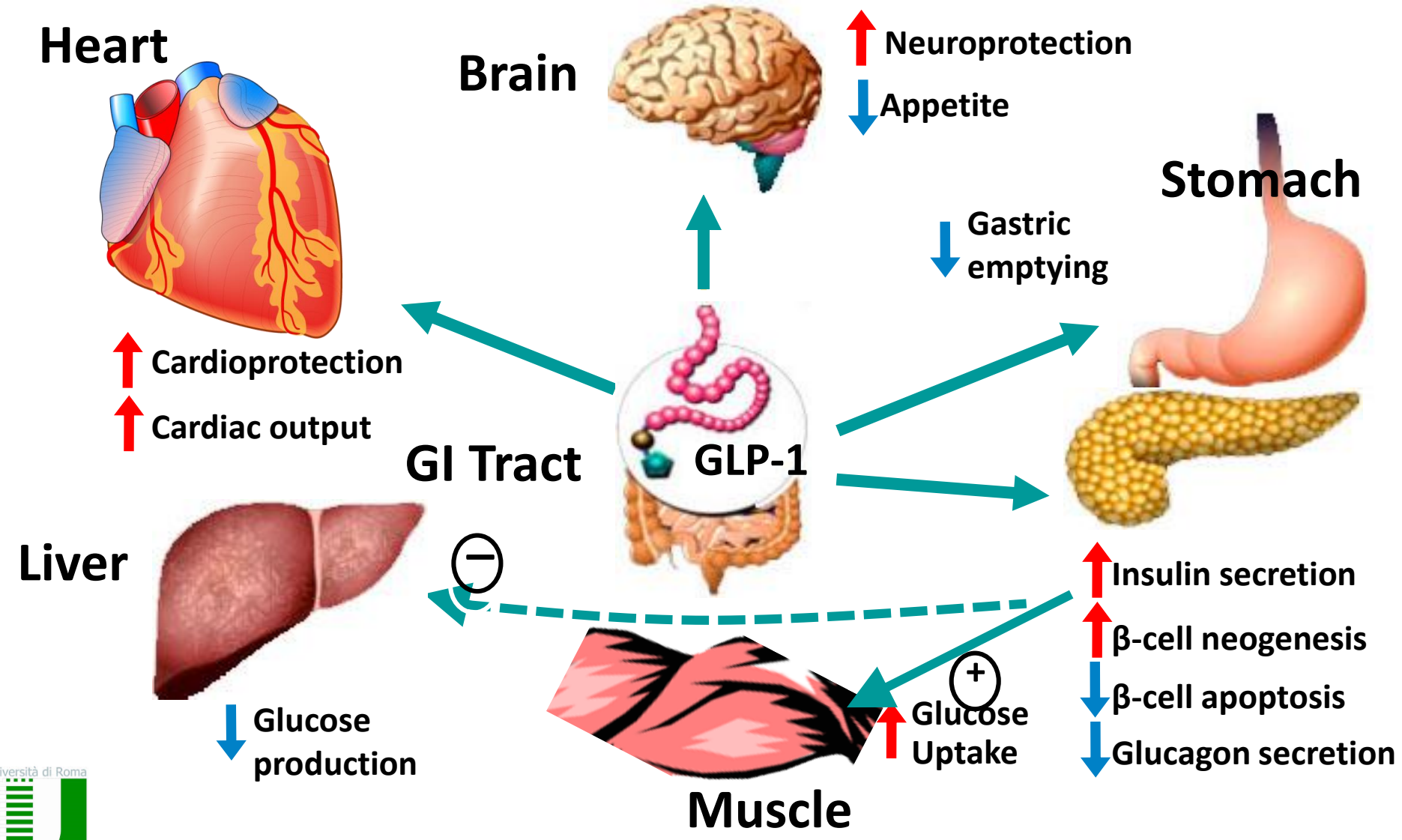
Wilding JP, *et al. Diabetes Obes Metab* 2014;16:124–136

GLP-1 Receptor Agonists

- First-in-class exenatide approved in 2005
- Augment insulin secretion
- Inhibit glucagon secretion
- Lower fasting glucose and improve postprandial glucose profile

Schnabel CA, et al. *Vasc Health Risk Manag*. 2006;2:69-77.

GLP-1 Actions in Peripheral Tissue



Drucker DJ. *Cell Metab*. 2006;3:153-165.

Incretin-based Therapies

GLP-1 RAs

Drug	Starting dose
Exenatide	INITIAL: 5 mcg SC twice daily
Liraglutide	INITIAL: 0.6 mg SC once daily x 1 week, then increase to 1.2 mg SC once daily
Exenatide extended-release	INITIAL: 2 mg SC once weekly
Albiglutide	INTIAL: 30 mg SC once weekly
Dulaglutide	INITIAL: 0.75 mg SC once weekly

DPP-4 Inhibitors

Drug	Starting dose
Alogliptin	INITIAL: 25 mg PO once daily
Linagliptin	INITIAL: 5 mg PO once daily
Saxagliptin	INITIAL: 2.5 mg or 5 mg PO once daily
Sitagliptin	INITIAL: 100 mg PO once daily

Beneficial Effects of Incretin-based Therapies

Effect	GLP-1 RAs*	DPP-4 Inhibitors**
Reduction in A1c	0.5%-1.5%	0.5%-0.9%
Reduction in FPG	7-74 mg/dL	11-29 mg/dL
Reduction in PPG	41-47 mg/dL	49-68 mg/dL
Effect on weight	↓1-4 kg	↓0.9-↑1.4 kg
Improvement in markers of pancreatic beta cell function?	Yes	Yes

*Exenatide 5-10 mcg SC twice daily, Liraglutide 1.2-1.8 mg once daily
**Sitagliptin 100 mg PO once daily, Saxagliptin 2.5-5 mg PO once daily, Linagliptin 5 mg PO once daily

Cobble M. *Diabetol Metab Synd*. 2012;4(1):8.

Side Effects: GLP-1 Receptor Agonists and DPP-4 Inhibitors

	GLP-1 Receptor Agonists	DPP-4 Inhibitors
Side effects	Gastrointestinal	Well tolerated
Weight	> 85% patients lose weight	Weight neutral
Administration	Once, twice-daily or weekly injection	Oral, once daily
Other cardiac risk factors	↓ Triglycerides ↑ HDL ↓ Blood pressure	Unknown

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Davidson JA. *Cleve Clin J Med*. 2009;76(suppl5):S28-S38.

Side Effects: Metformin and Thiazolidinediones

	Metformin	Thiazolidinediones
Side effects	Gastrointestinal	Fluid retention, congestive heart failure, bone fractures
Weight	Weight neutral	Weight gain
Renal impairment	Restricted > 1.4 mg/dL	

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Seufert J, et al. *Clin Ther*. 2004;26:805-818.

How much exercise?

Exercises should be done according to FITT principle.

- **FREQUENCY:** Exercising 4 to 6 times a week.
- **INTENSITY:** 30-40 min of exercise at 50- 60 % of target heart rate.
- **TYPE:** SAFE exercises are recommended.
- **TIME:** Morning is ideal

Peripheral and autonomic neuropathy

Recommended:

- non-weight-bearing activities
- swimming
- bicycling
- chair and arm exercises

Contraindicated:

- treadmill
- prolonged walking
- jogging
- step exercises

Nephropathy

Recommended

- Low to moderate intensity forms of exercise

Contraindicated

- High intensity forms of exercise

Diabetic retinopathy

Recommended

- **Low-impact cardiovascular conditioning, such as swimming, walking, low-impact aerobics, stationary cycling, endurance exercises**

Contraindicated

- **Strenuous activities, pounding or jarring, such as weight lifting, jogging, high-impact aerobics, racquet sports.**

Summary

- Physical activity should be encouraged in all people with diabetes
- People need to be educated about prevention and treatment of hypoglycaemia
- People should be taught to plan for periods of physical activity

"Exercise is the best insulin sensitizer on the market; better than any medication we currently have available"