
بسم الله الرحمن الرحيم


دیابت
DIABETES
10.2
BLOOD SUGAR

پیشگیری و کنترل دیابت

Presenter

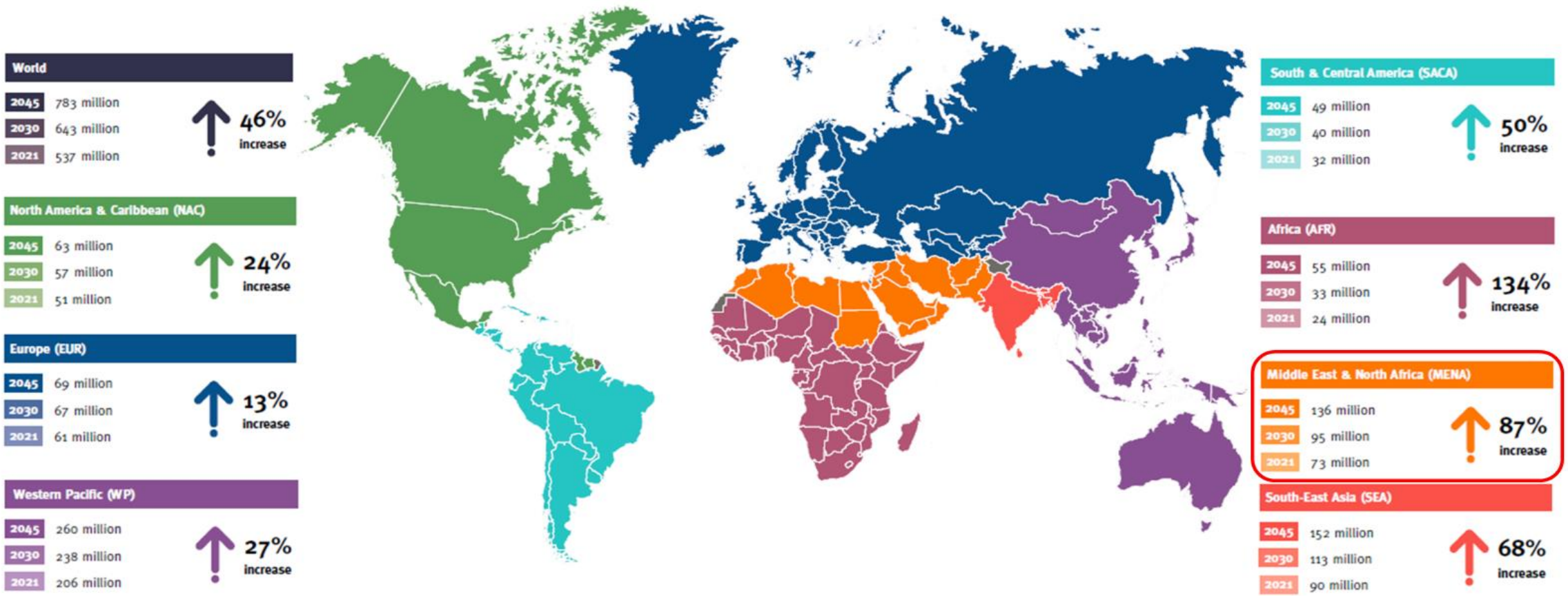
Soheila Borji, M.D.

ENDOCRINOLOGIST

تعریف

- یک بیماری متابولیک که در آن ناتوانی بدن در تولید انسولین کافی یا به “ مقدار کافی باعث افزایش سطح گلوکز در خون می شود.

Number of people with diabetes worldwide and per IDF Region in 2021–2045 (20–79 years) [1]



Estimated total number of adults (20–79 years) with diabetes in 2021, 2030 and 2045 [1]

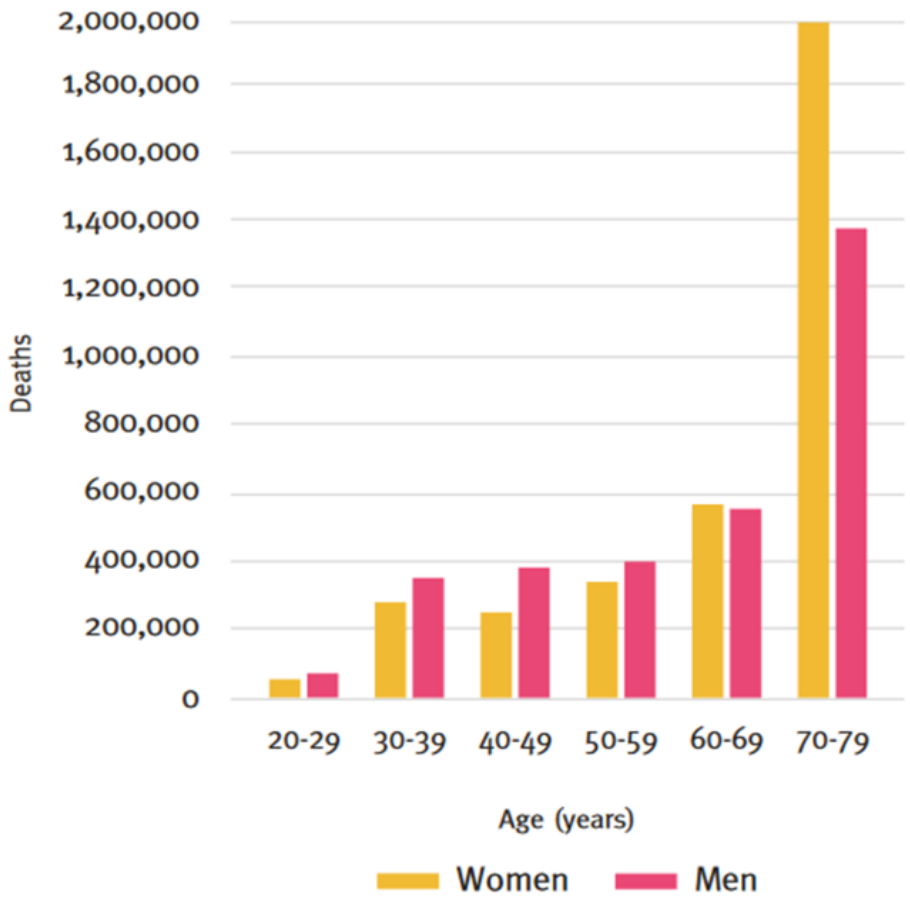
At a glance	2021	2030	2045
Total world population	7.9 billion	8.6 billion	9.5 billion
Adult population (20–79 years)	5.1 billion	5.7 billion	6.4 billion
Diabetes (20–79 years)			
Prevalence[i]	10.5%	11.3%	12.2%
Number of people with diabetes	536.6 million	642.7 million	783.2 million
Number of deaths due to diabetes	6.7 million	–	–
Total health expenditure due to diabetes[ii] (2021 USD)	USD 966 billion	USD 1,028 billion	USD 1,054 billion
Hyperglycaemia in pregnancy (20–49 years)			
Proportion of live births affected[iii]	16.7%	–	–
Number of live births affected	21.1 million	–	–
Impaired glucose tolerance (20–79 years)			
Prevalence[i]	10.6%	11.0%	11.4%
Number of people with impaired glucose tolerance	541.0 million	622.7 million	730.3 million
Impaired fasting glucose (20–79 years)			
Prevalence[i]	6.2%	6.5%	6.9%
Number of people with impaired glucose tolerance	319.0 million	369.7 million	440.8 million
Type 1 diabetes (0–19 years)			
Number of children and adolescents with type 1 diabetes	1.2 million	–	–
Number of newly diagnosed cases each year	184,100	–	–

If current trend continue 783 million adults will have diabetes by 2045.

IDF Diabetes Atlas 2021 – 10th edition | www.diabetesatlas.org


International Diabetes Federation
537 million
people worldwide
have diabetes
IDF Diabetes Atlas
10TH edition
2021

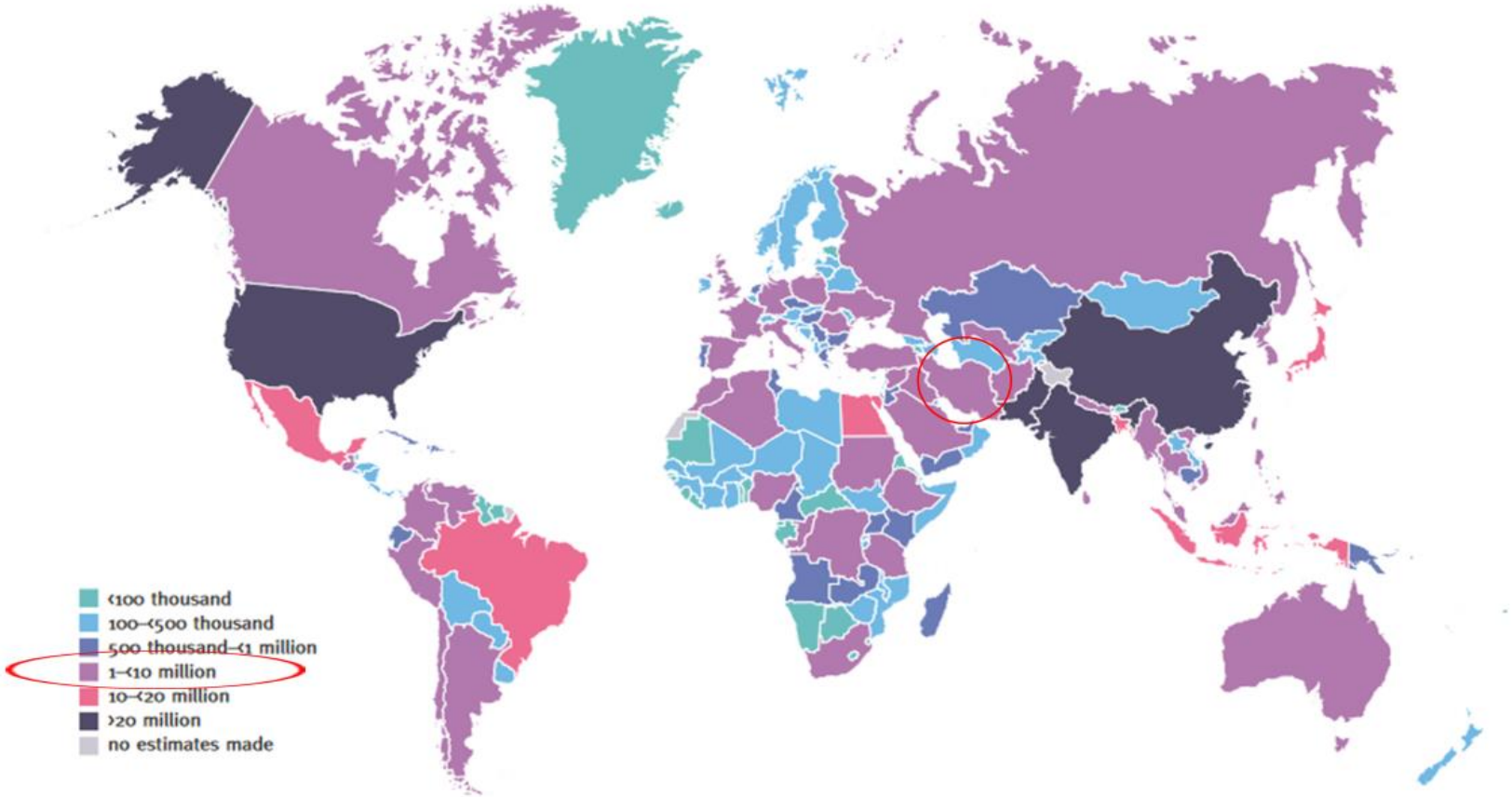
Number of deaths due to diabetes in adults (20–79 years) by age and sex in 2021 [1]



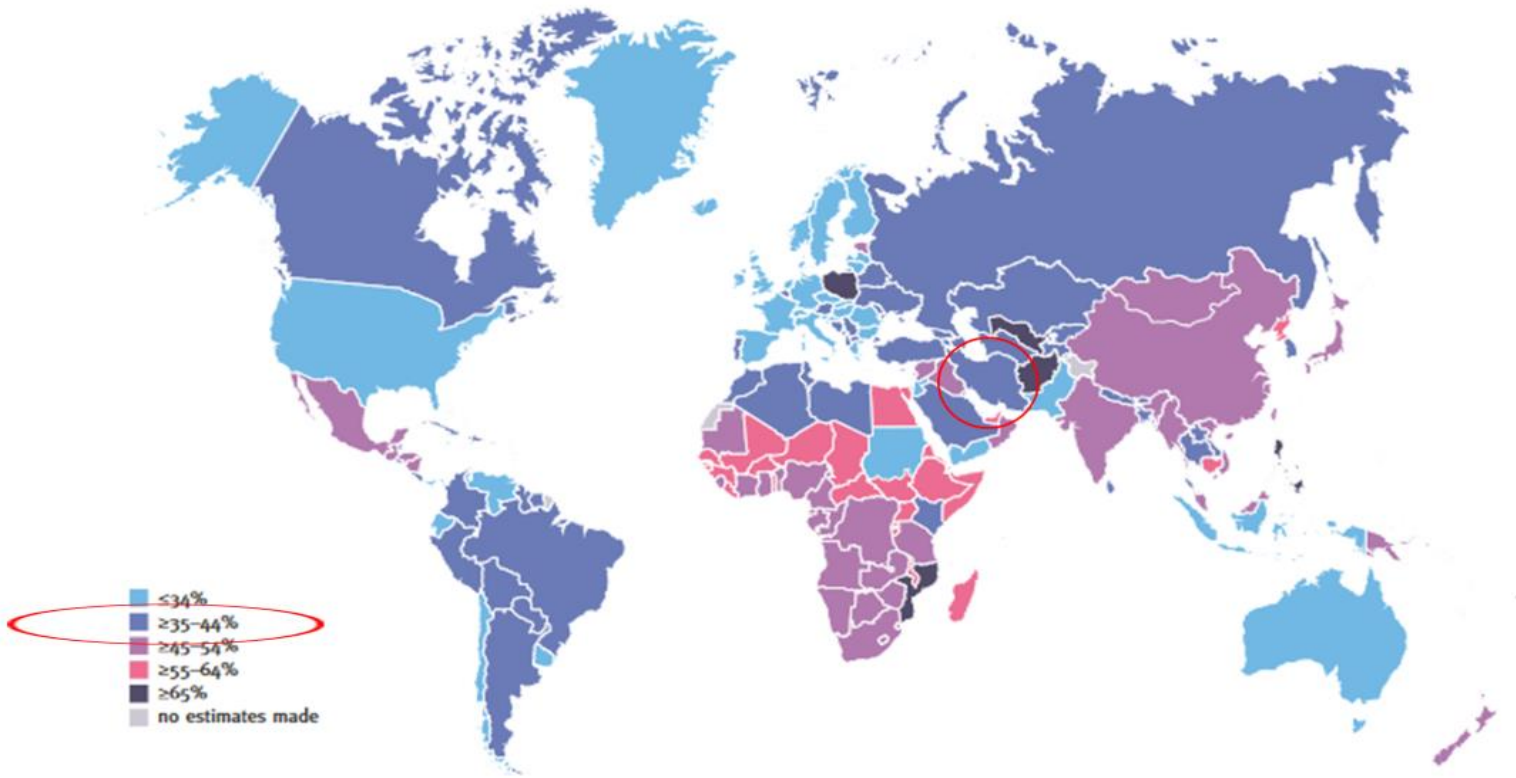
Every **8 seconds** a person dies from diabetes

(5 million annually)

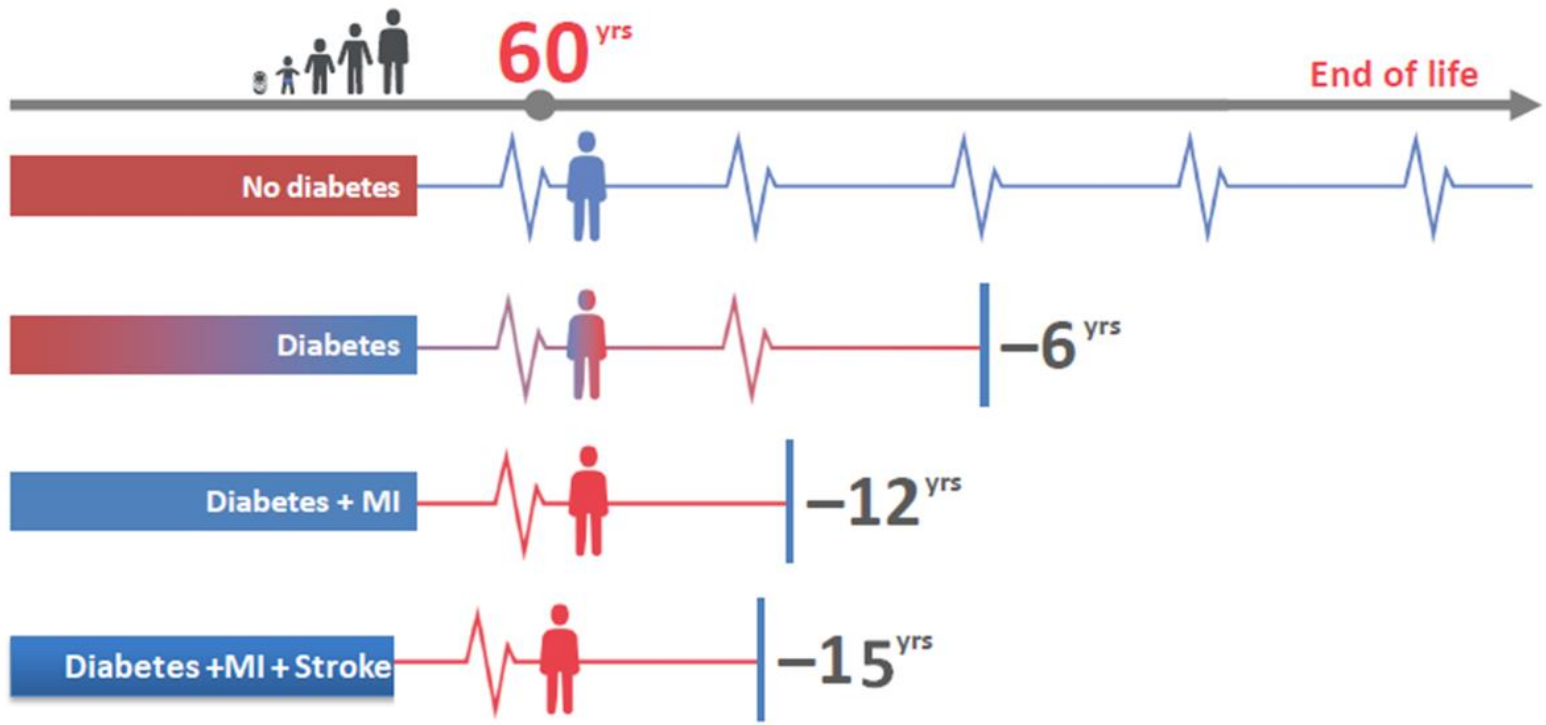
Estimated total number of adults (20–79 years) with diabetes in 2021 [1]



Proportion of adults (20–79 years) with undiagnosed diabetes by country in 2021 [1]



Life expectancy is reduced by ~ 15 years in diabetes patients with previous CVD [1]



1. Di Angelantonio, E.(2015). *JAMA*, 314(1), 52-60

The Problem

Diabetes is prevalent,

It hurts,

It Kills.

But we have not been able to stop it to date!

DIABETES RESEARCH AND CLINICAL PRACTICE XXX (2014) XXX–XXX

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Trends in the prevalence of diabetes and impaired fasting glucose in association with obesity in Ira 2005–2011

Alireza Esteghamati [a,], Koorosh Etemad [b], Jalil Koohpayehzadeh [b], Mehrshad Abbasi [a], Alipasha Meysamie [c], Sina Noshad [a], Fereshteh Asgari [b], Mostafa Mousavizadeh [a], Ali Rafei [b], Elias Khajeh [a], Mohamadreza Neishaboury [a], Sara Sheikhbahaei [a], Manouchehr Nakhjavani [a]*

- 11.4% (95% CI, 9.9-12.9) of Iranian adults aged 25-70 yrs had diabetes.
- In about one-fourth, diabetes, was undiagnosed.
- The prevalence of diabetes was higher in:
  - *Women (12.8%) than in men (9.9%)*
  - *Urban (12.6%) than in rural (7.6%) residents*
- 2005 to 2011: 35% increase in the diabetes prevalence rate
- The prevalence of IFG: 14.6 %

Esteghamati A, et al.Diabetes Res Clin Pract 2014;103:319-27.

Primary Care Diabetes 15 (2021) 472–479

Contents lists available at ScienceDirect

Primary Care Diabetes

journal homepage: http://www.elsevier.com/locate/pcd

Original research

Warning signals of elevated prediabetes prevalence in the modern Iranian urban population

Somayyeh Barati[a], Parham Sadeghipour[b], Zahra Ghaemmaghami[b], Bahram Mohebbi[b,c], Mohammadreza Baay[a], Mohammad Javad Alemzadeh-Ansari[b,c], Zahra Hosseini[b], Yeganeh Karimi[a], Mojtaba Malek[d], Majid Maleki[b], Feridoun Noohi[b], Yasaman Khalili[a], Azin Alizadehasl[c,d], Nasim Naderi[a], Maedeh Arabian[a], Hamidreza Pouraliakbar[a], Shiva Khaleghparast[a], Behshid Ghadrdoost[a], Shabnam Boudagh[e], Hooman Bakhshandeh[a,d,*]

Objective: Estimation of prevalence of diabetes mellitus (DM) and pre-DM and their associated factors among a sample of the Iranian urban population between 2017 and 2019.

- The estimated overall prevalence of DM was 14.1% .


انواع دیابت
نوع ۱ (جوانان)
نوع ۲ (بزرگسالان)
دیابت بارداری
عدم تحمل گلوکز

دیابت نوع 1

In adults, type 1 diabetes accounts for approximately

5%

of all diagnosed cases of diabetes

- همچنین به عنوان دیابت نوجوانان شناخته می شود
- معمولا در کودکان و بزرگسالان جوان تشخیص داده می شود
- هنگامی که سیستم ایمنی بدن خود سلول های تولید کننده انسولین پانکراس - سلول های بتا - که انسولین تولید می کنند را از بین می برد.
- تنها 5 درصد از مردم به این بیماری مبتلا هستند
- بدن انسولین تولید نمی کند
- قابل پیشگیری نیست

- علل؟

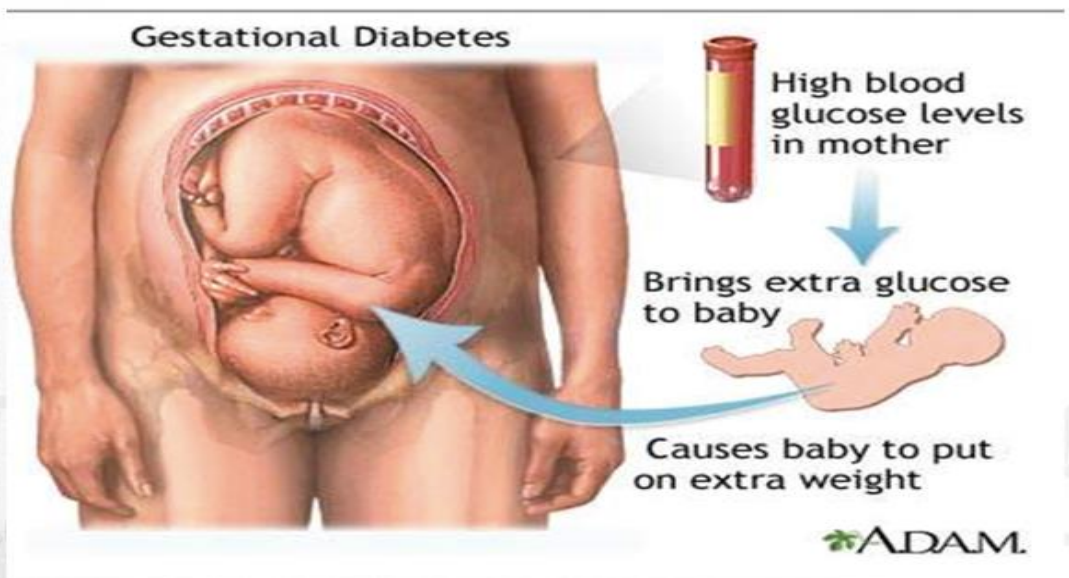
- استعداد ابتلا به دیابت - ژنتیک - وعواملی(مانند آب و هوا، ویروس و غیره) در محیط باعث ایجاد بیماری می شود.

دیابت نوع 2

- شایع ترین شکل دیابت
- حدود 90٪ موارد
- قبلاً به عنوان دیابت شروع بزرگسالان، دیابت غیر وابسته به انسولین نامیده می شد
- بدن انسولین تولید می کند، اما از آن به درستی استفاده نمی کند
- گلوکز به داخل سلول ها حرکت نمی کند، و در جریان خون انباشته می شوند
- علائم ،اغلب نادیده گرفته می شوند زیرا ممکن است جدی به نظر نرسند.

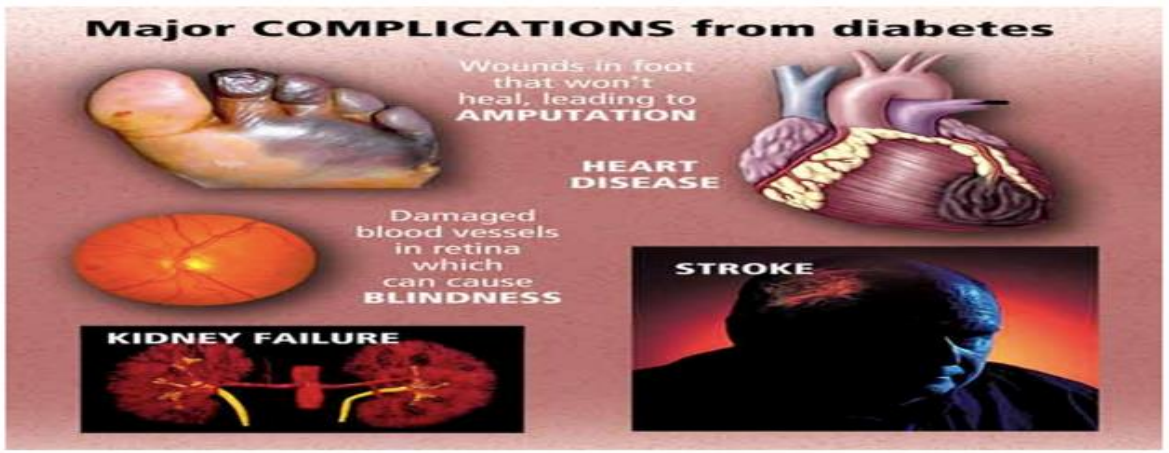
دیابت بارداری(GDM)

- ابتلا به دیابت در دوران بارداری
- خانواده Hxدیابت، اضافه وزن قبل از بارداری؟
- ابتلا به دیابت بارداری فرد را در معرض خطر ابتلا به دیابت نوع 2 قرار میدهد
- به دنیا آوردن نوزاد بیش از 9 پوند نیز فرد را در معرض خطر ابتلا به نوع 2 قرار می دهد
- از هر 100 زن باردار 18 نفر به دیابت بارداری مبتلا می شوند



عوارض مزمن دیابت کنترل نشده:

- گرفتگی عروق مغزی و قلبی
- نارسایی کلیه
- رتینوپاتی و اختلال در خونرسانی به شبکیه چشم
- نابینایی
- اختلا ل در عروق و اعصاب محیطی
- زخم پا و قطع عضو



علائم دیابت

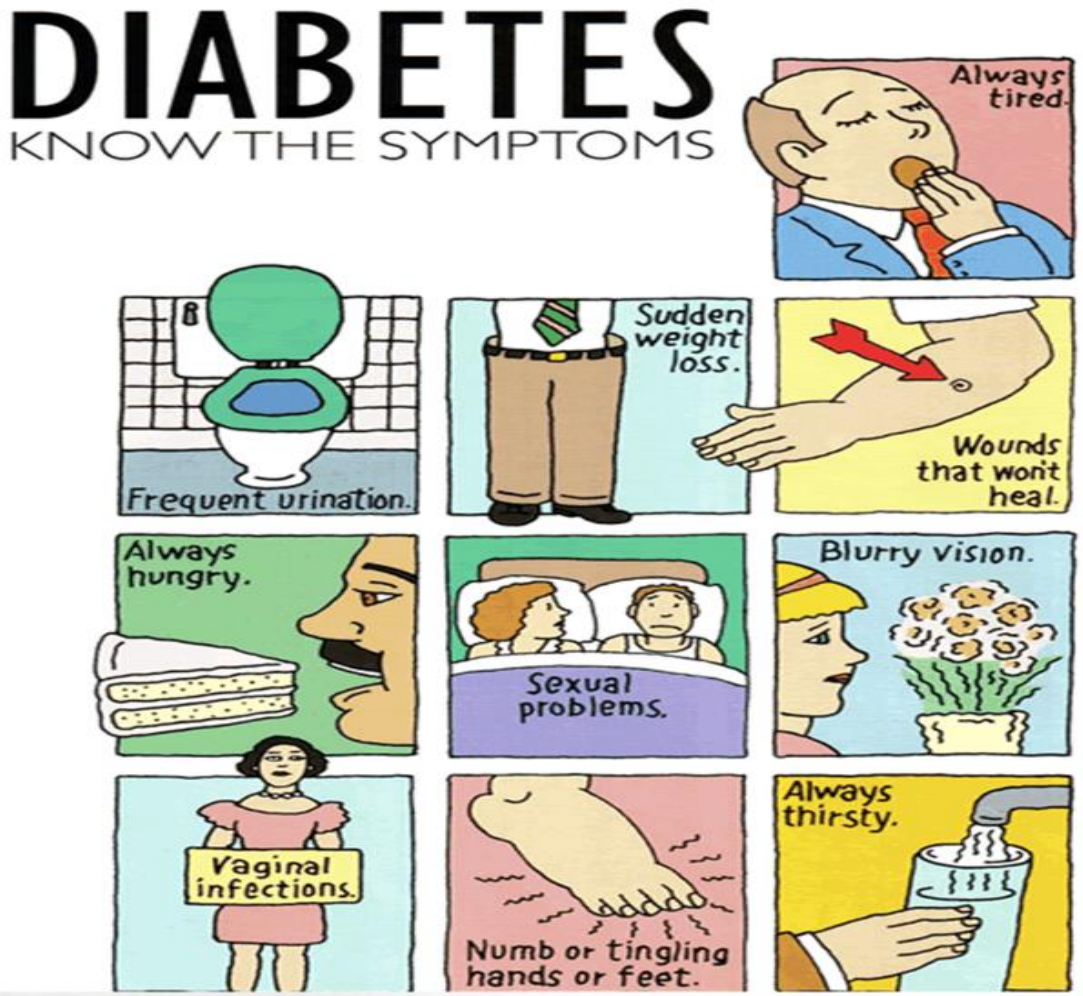
- نشانه های رایج دیابت:
- تشنگی و عطش
- تکرر ادرار و ادرار زیاد
- کاهش غیر طبیعی وزن
- خستگی
- تهوع و گاهی استفراغ
- تاری دید

عفونت مکرر ادراری در زنان

ابتلا به عفونتهای قارچی

خشکی دهان

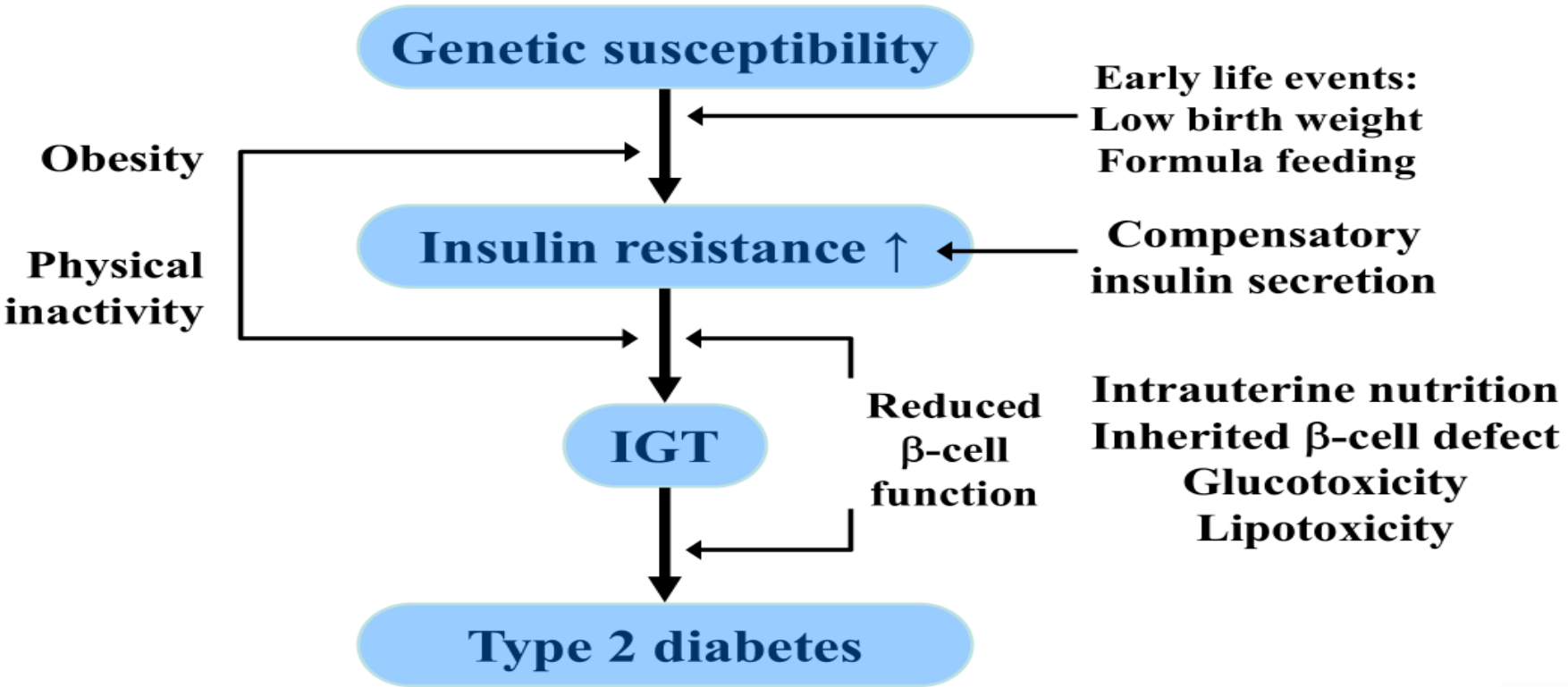
- دیر خوب شدن زخم
- خشکی پوست



تعاریف اختلالات متابولیسم کربوهیدرات ها

قند خون	طبیعي	IFG	IGT	دیابت
ناشتا (mg/dL)	<100	<126-≥100	-----	126≥
دو ساعت بعد از گلوکز (mg/dL)	<140	------	-≥140 <200	200≥
علایم دیابت با قند خون در هر زمان ≥200				

Natural history of type 2 diabetes



عوامل ابتلا به دیابت نوع ۲

۱- استعداد ژنتیکی

۲- عوامل محیطی

- عدم تحرک بدنی
- تغذیهٔ نامناسب
- چاقی و نمای بالای توده بدنی

نيمي از بيماران ديابتي از بيماري خود بي خبرند.

از شروع ديابت تا تشخيص آن اغلب 5-7 سال فاصله است.

بسياري از بيماران ديابتي هنگامي براي درمان مراجعه مي كنند كه عوارض وخيمي در چشم، قلب، كليه ها و سلسله اعصاب دارند.

پيشگيري اوليه

پيشگيري ثانويه

پيشگيري ثالثيه

پیشگیري اولیه

دیابت

Research Institute for Endocrine Sciences
F. Azizi

پیشگیری

- نوع 1:
  - در حال حاضر قابل پیشگیری نیست.
  - مطالعات در مورد راه های جلوگیری از تخریب بیشتر سلول های بتا
  - حفظ و کنترل سطح قند، تزریق انسولین
  - سبک زندگی سالم –
  - ورزش و رژیم غذایی
  - پیوند جزایرلانگرهانس لوزالمعده

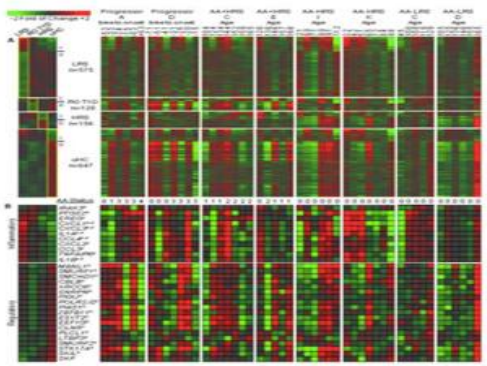
Identifying Type 1 Diabetes before Beta Cell Loss

Martin Hessner, PhD | Medical College of Wisconsin |Basic Science Award | Funded for 3 years at $345,000

Type 1 diabetes is thought to progress without symptoms for several years in most patients prior to diagnosis. During this critical time, while beta cells are destroyed, the disease is often not detected until beta cell loss is substantial enough for the patient to notice symptoms of advanced disease. By that time, it is typically too late to effectively intervene with therapies that may preserve beta cells.

Dr. Hessner is investigating so-called "biomarkers," which are components in blood or tissue samples that can be measured to predict which individuals are most likely to develop type 1 diabetes. His work is unique, because it aims to detect biomarkers that are present before beta cell destruction progresses to clinical symptoms, up to 5 years or more prior to disease onset.

One potential candidate biomarker may be related to inflammation. Dr. Hessner recently showed that family members of people with type 1 diabetes have an enhanced inflammatory state that is regulated



پیشگیری

- نوع 2:
- اولیه: حفظ یک سبک زندگی سالم
- ثانویه:اندازه گیری HgA1c(قند سه ماهه)
- رژیم غذایی سالم
- HgA1c میانگین قند خون در طول 3 ماه اندازه گیری می کند که چه درصدی از هموگلوبین خون با گلوکز ترکیب شده است و بر حسب درصد اندازه گیری میشود.
- طبیعی: 4%- 5.6٪، پیش دیابت = 5.7٪ -6.4٪ و دیابت = 6.5٪ به بالا
- ورزش و فعالیت بدنی منظم
- معاینه و مراقبت از پا

پیشگیری

- دیابت بارداری:
- فعالیت بدنی محققان دریافتند که فعالیت بدنی قبل و بعد از بارداری، خطر ابتلا به GDMرا تا حدود 70 درصد یا بیشتر کاهش می دهد
- رژیم غذایی یک مطالعه نشان داد که هر 10 گرم افزایش فیبر در روز خطر ابتلا به GDMرا تا 26 درصد کاهش می دهد.

Risk factor for diabetes

Type 2

- Overweight and obesity
- Physical inactivity
- High-fat and low-fibre diet
- Family history
- Low birth weight
- Previously identified IFG or IGT
- Low HDL or high triglyceride
- History of GDM or big baby
- Polycystic ovary
- Hypertension
- Age
- Ethnicity

Research Institute for Endocrine Sciences
F. Azizi

عوامل خطر اصلاح پذير براي پيشگيري از ديابت

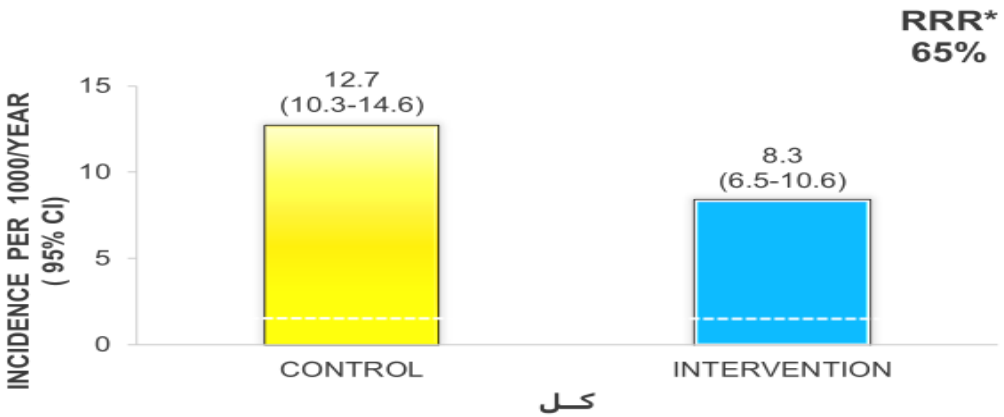
1. اضافه وزن و چاقي
2. چاقي شكمي
3. نداشتن فعاليت بدني
4. مرحله قبل از ديابتي

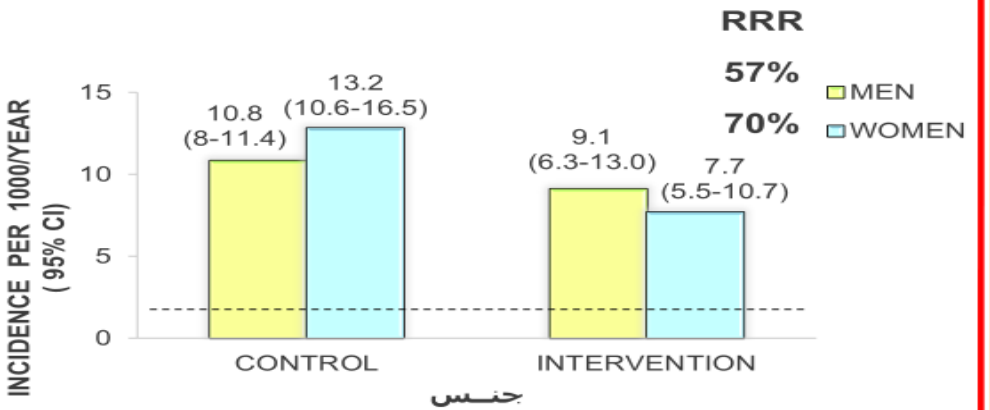
   بالا بودن قند خون ناشتا يا 2 ساعت
5. غيرطبيعي بودن چربيهاي خون

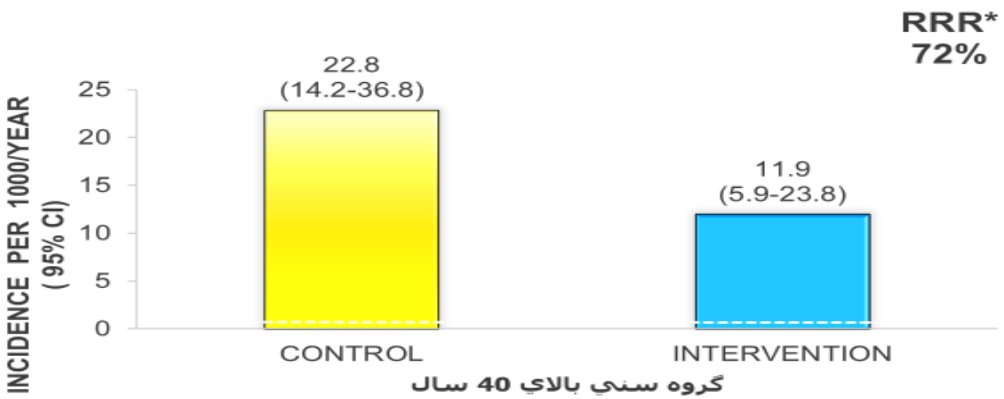
   HDL پايين

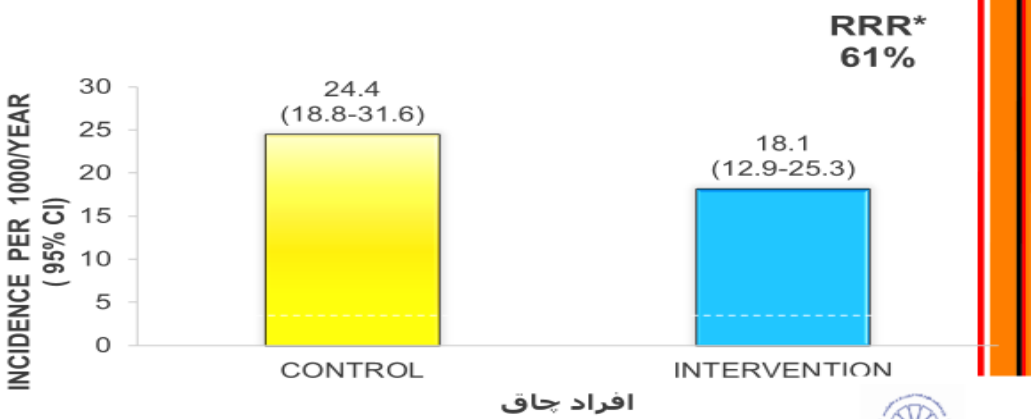
   تري گليسريد بالا

اثر اصلاح شيوه زندگي در كاهش بروز ديابت
(مطالعه قند و ليپيد تهران)









•RRR: Relative Risk Reduction

Harati et al. Am J Prev Med 2010; 38: 628

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برنامه کشوری پیشگیری و کنترل دیابت نوع ۲

۱- پیشگیری اولیه

کاهش بروز و شیوع دیابت نوع ۲ در افراد پره دیابتی(مبتلایان به IFG , IGT)

۲- پیشگیری ثانویه

پیشگیری، کاهش و تأخیر در بروز عوارض کوتاه مدت و دراز مدت دیابت

۳- پیشگیری ثالثیه

کاهش یا تأخیر در بروز معلولیت، ناتوانیها، مرگ ناشی از عوارض دیابت و کاهش سالهای از دست رفته عمرافراد مبتلا به دیابت

۱- کاهش هزینه های اقتصادی

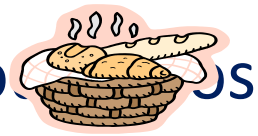
۲- کاهش ناتوانی ها

۳- کاهش مرگ ومیر

۴- افزایش طول عمر مفید

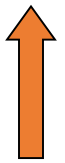
Factors affecting blood glucose

- Food (carbohydrate) intake increases blood glucose



- Exercise lowers blood glucose

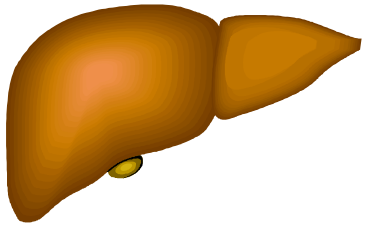
- Stress may increase blood glucose



Where insulin acts?

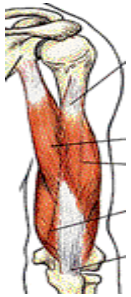
Insulin

Liver



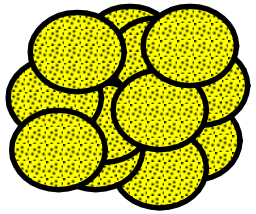
- Inhibits glucose production
- Promotes formation of glycogen & its storage

Muscle



- Promotes uptake & utilization of glucose

Adipose tissue



- Promotes uptake of glucose
- Suppresses lipolysis

Diabetes Mellitus

- ١٠% of diabetes is Type ١ [١]
    - Genetic link
    - Presence of islet cell autoantibodies
    - Autoimmune destruction of the beta cells
- ٩٠% of diabetes is Type ٢ [٢]
    - Genetic predisposition
    - Obesity
    - Impairment of insulin secretion and defects in insulin action in Type ٢ diabetes

١. Atkinson MA and Eisenbarth GS. *Lancet.* ٢٠٠١;٣٥٨:٢٢١–٢٢٩.
٢. CDCP. December ٢٠٠٣. Atlanta, GA: US Dept. of Health and Human Services, CDCP,٢٠٠٣.

Type 1 Diabetes

- Beta cell destruction
  - Usually leading to absolute insulin deficiency
- Immune mediated
- Idiopathic
- Environmental factors
  - Destruction of beta cells is triggered by environmental factors like
  - Viruses: coxsackie, mumps & rubella

Features of type ١ diabetes

- ٥% -١٠% of diabetic population
- Younger (<٣٥yrs) & lean patients
- Progressive autoimmune (self) destruction of beta cells
- Absolute insulin deficiency
- Prone to ketosis
- Exogenous insulin -necessary for survival

Treatment for type ١ diabetes

- Only insulin
- No role for Oral drugs
- Diet & exercise-as adjuvants only
- Various insulin regimens are used
- Devices are preferred

Consequences of the absolute insulin deficiency in Type 1 diabetes

No insulin secretion

↓

Alternative use of fat as a fuel

↓

Production of acidic waste products – ketones

↓

Ketoacidosis

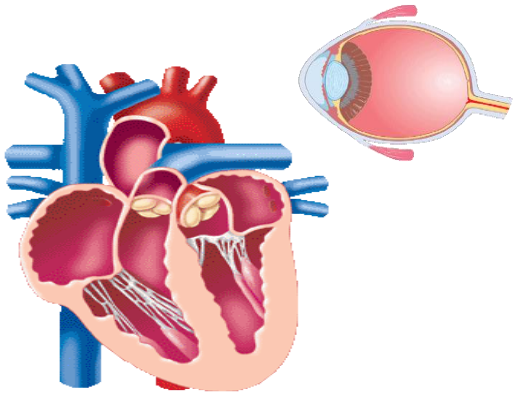
No insulin secretion

↓

Hyperglycaemia

Type ۲ diabetes

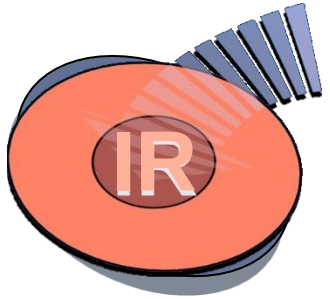
- Characterized by chronic hyperglycemia
- Associated with microvascular and macrovascular complications
- Generally arises from a combination of insulin resistance and β-cell dysfunction



Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Department of Noncommunicable Disease Surveillance, World Health Organization, Geneva ۱۹۹۹. Available at: http://www.diabetes.org.uk/infocentre/carerec/diagnosi.doc

Insulin resistance

- Major defect in individuals with type ۲ diabetes[۱]
- Reduced biological response to insulin[۱–۳]
- Strong predictor of type ۲ diabetes[۴]
- Closely associated with obesity[۵]



۱.American Diabetes Association. Diabetes Care ۱۹۹۸; ۲۱:۳۱۰–۳۱۴.

۲. Beck-Nielsen H & Groop LC. J Clin Invest ۱۹۹۴; ۹۴:۱۷۱۴–۱۷۲۱.

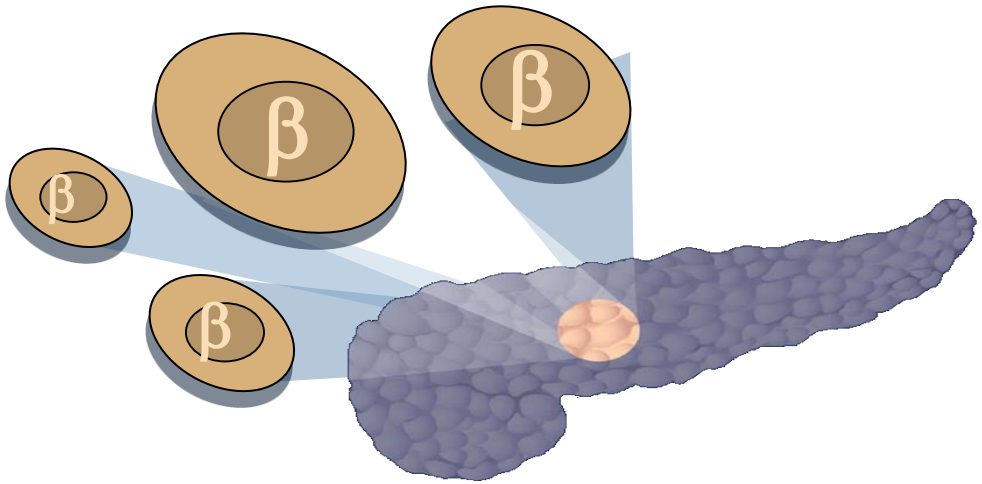
۳. Bloomgarden ZT. Clin Ther ۱۹۹۸; ۲۰:۲۱۶–۲۳۱.

۴. Haffner SM, et al. Circulation ۲۰۰۰; ۱۰۱:۹۷۵–۹۸۰.

۵. Boden G. Diabetes ۱۹۹۷; ۴۶:۳–۱۰.

β-cell dysfunction

- Major defect in individuals with type ۲ diabetes
- Reduced ability of β-cells to secrete insulin in response to hyperglycemia

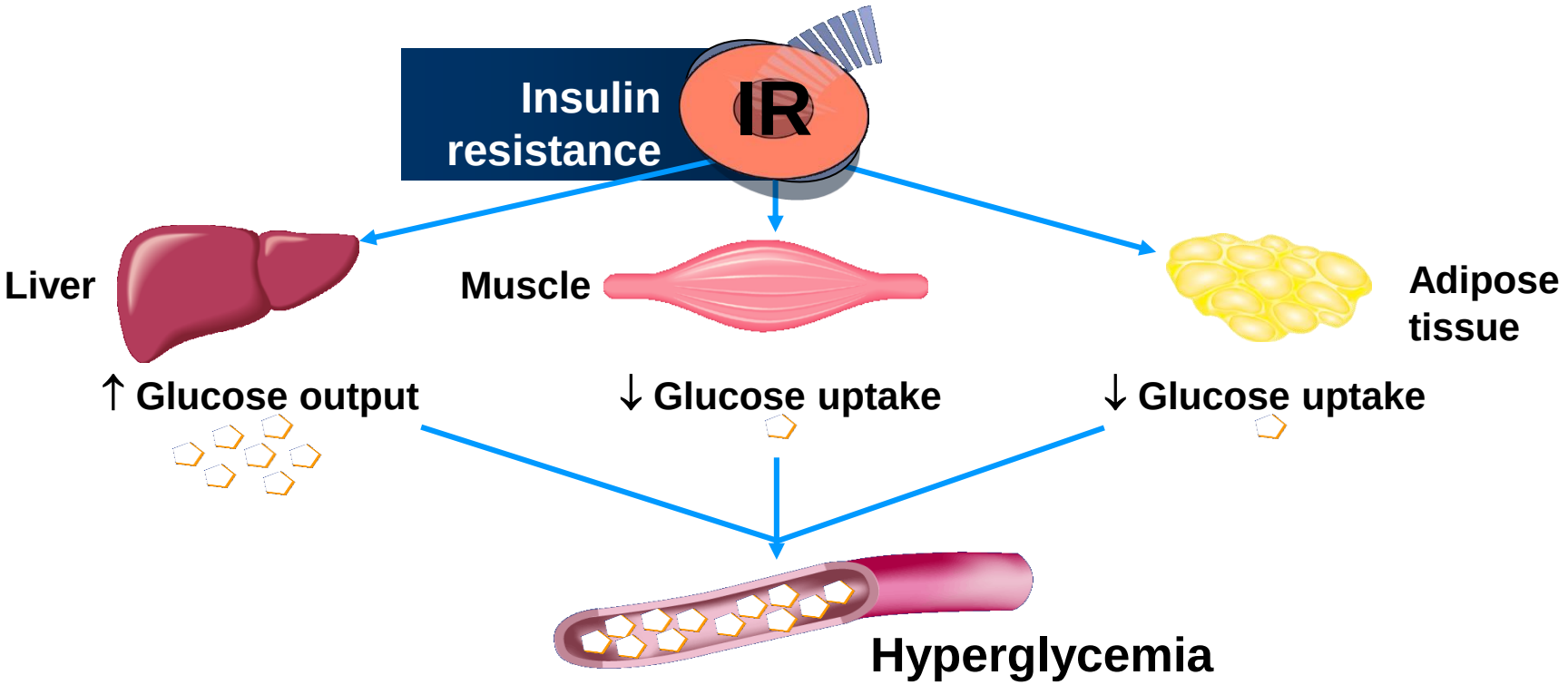


DeFronzo RA, et al. Diabetes Care ۱۹۹۲; ۱۵:۳۱۸–۳۵۴.

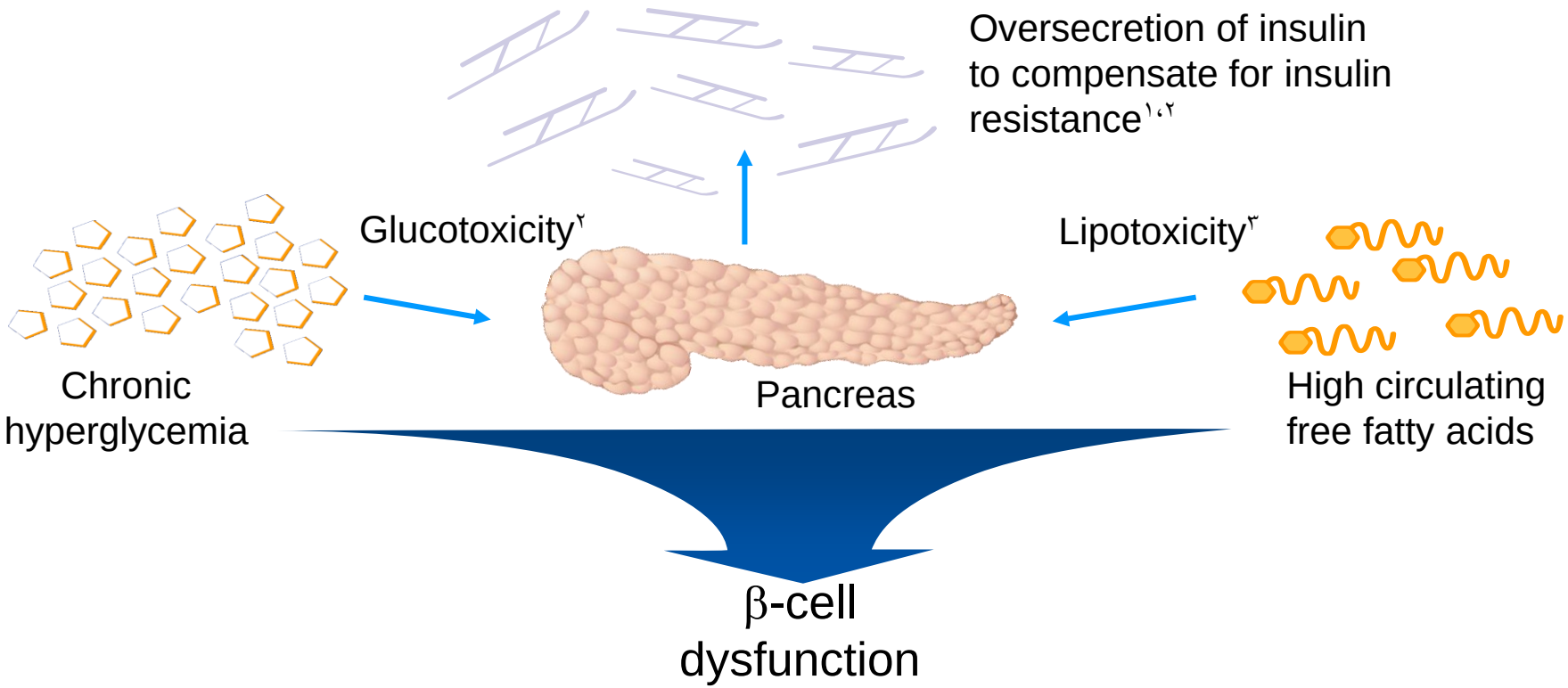
Insulin resistance and β-cell dysfunction are core defects of type ٢ diabetes

Rhodes CJ & White MF. Eur J Clin Invest ٢٠٠٢; ٣٢ (Suppl. ٣):٣–١٣.

Insulin resistance – reduced response to circulating insulin



Why does the β-cell fail?

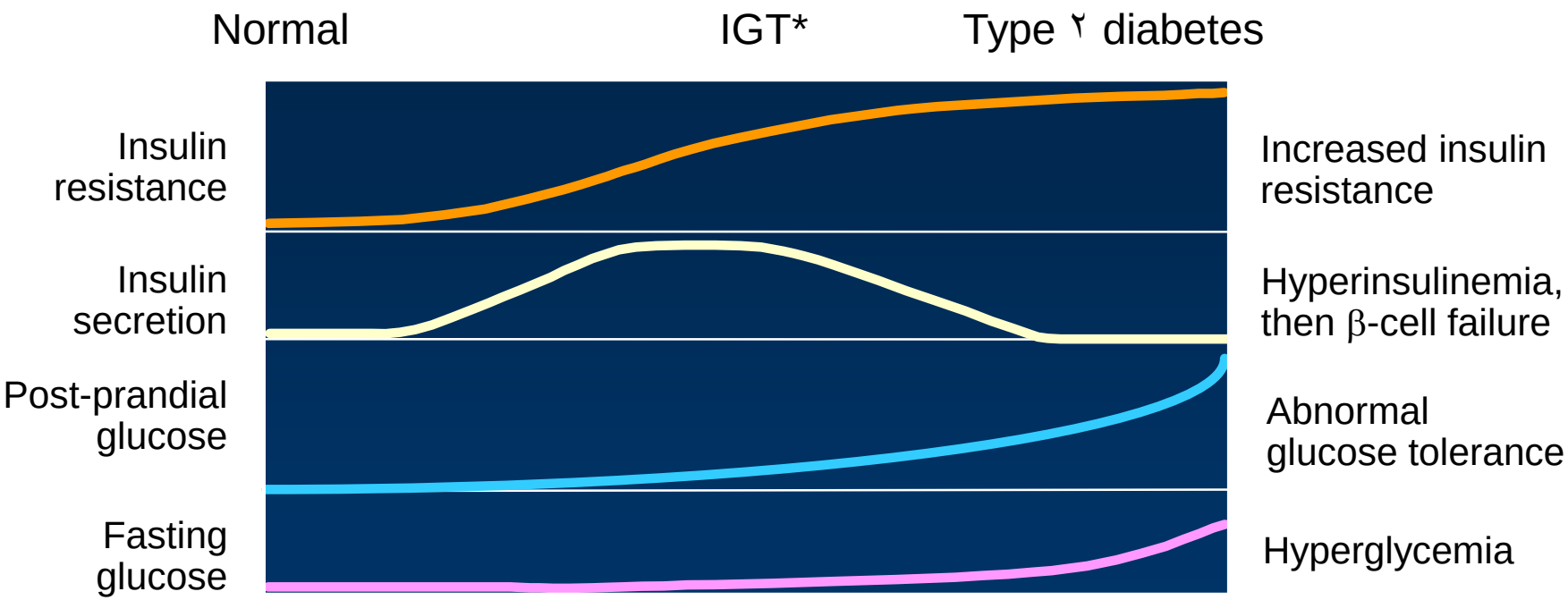


[1]Boden G & Shulman GI. *Eur J Clin Invest* ۲۰۰۲; ۳۲:۱۴–۲۳.

[2]Kaiser N, *et al. J Pediatr Endocrinol Metab* ۲۰۰۳; ۱۶:۵–۲۲.

[3]Finegood DT & Topp B. *Diabetes Obes Metab* ۲۰۰۱; ۳ (Suppl. ۱):S۲۰–S۲۷.

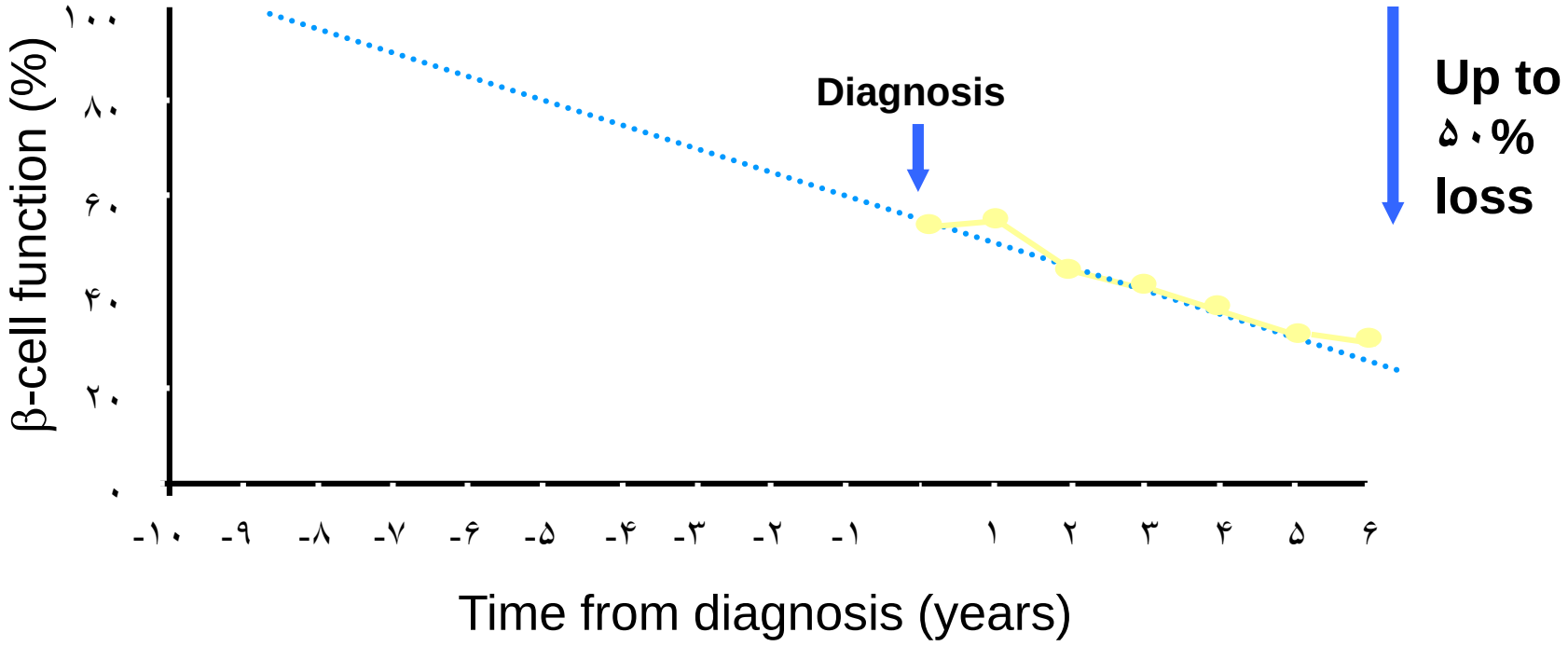
How do insulin resistance and β-cell dysfunction combine to cause type ٢ diabetes?



*IGT = impaired glucose tolerance

Adapted from *Type ٢ Diabetes BASICS*. International Diabetes Center (IDC), Minneapolis, ٢٠٠٠.

Loss of β-cell function occurs before diagnosis



Holman RR. *Diabetes Res Clin Prac* ۱۹۹۸; ۴۰ (Suppl.):S۲۱–S۲۵.

What is OGTT?

OGTT= Oral Glucose Tolerance Test

- Overnight fasting, check FPG
- ٧٥/١٠٠ gm glucose in water is given (Glucose load)
- Glucose testing at ١ & ٢hrs
- confirm diagnosis
- detect IGT (Pre diabetes)

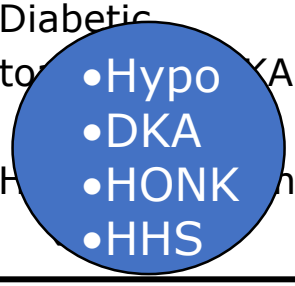
Result (mg/dl)	<١٤٠	>١٤٠ but <١٩٩	≥٢٠٠
Interpretation	NGT	IGT	DM

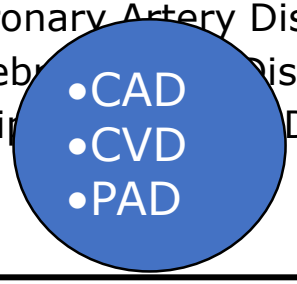
NGT=Normal Glucose Tolerance; IGT= Impaired Glucose Tolerance (Pre diabetes); DM= Diabetes Mellitus

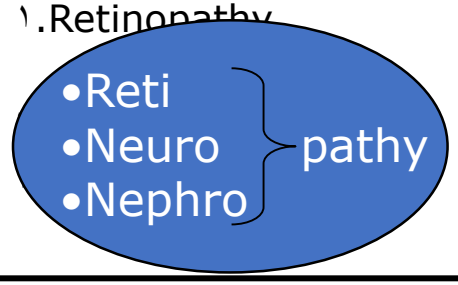
٢٥-٤٠% with IGT progress to DM

Diabetic Complications: Classification

Acute complications	Chronic complications	
١. Hypoglycemia	Macrovascular	Microvascular
٢. Diabetic Keto… (DKA) ٣. H… non ketotic state	١. Coronary Artery Disease ٢.Cereb… isease ٣. Perip… Disease	١.Retinopathy







Complications:

Hypoglycemia

Low BG (<٧٠ or ٥٦ mg/dl); Both Type ١ & Type ٢

Potential risk with [illegible] & sulphonylureas

Severe hypo[illegible]

With insulin - [illegible]

Hypoglycemia- a potential risk with all blood glucose lowering agents in Type ٢ diabetes

٣-٤% of diabetes-related deaths

Hypoglycemia: grading

Mild hypoglycaemia:

- Mild symptomatic episodes are usually self-treated

Severe hypoglycemia:

- Confusion and loss of cognitive ability, with the patient needing assistance from another person
- More common in type ١ diabetes patients with long disease duration
- Much more likely during intensive glucose control
- Can occur in type ٢ diabetes treated with insulin and insulin secretagogues
- Asymptomatic hypoglycemia increases the risk of severe episodes

Watkins et al. Diabetes and its Management, Ed. ٦. Blackwell Publishing, ٢٠٠٣; Pickup & Williams. Slide Atlas of Diabetes. Blackwell Publishing, ٢٠٠٤

Hypoglycemia: treatment

Mild hypoglycemia:

- oral treatment with readily available carbohydrates such as glucose tablets, fresh orange juice, non-diet drink
- complex carbohydrates, such as biscuits, to maintain glucose levels until the next meal
- check blood glucose levels

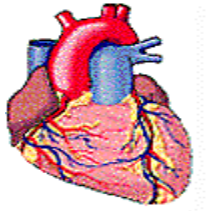
Severe hypoglycemia:

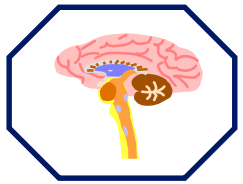
- if conscious, use oral carbohydrates as above
- if already unconscious:
- intramuscular glucagon ١ mg
- intravenous glucose ٧٥ ml ٢٠% glucose

Watkins et al. Diabetes and its Management, Ed. ٦. Blackwell Publishing, ٢٠٠٣; Pickup & Williams. Slide Atlas of Diabetes. Blackwell Publishing, ٢٠٠٤

What are the Macrovascular complications?

- **CAD/IHD**
  - Angina (typical type of chest pain)
  - Myocardial infarction (heart attack)
  - Heart failure- LVF & CCF
- **CVA**
  - Stroke (paralysis)
- **PAD**
  - Intermittent claudication, Ischemic feet, amputation
- **Diabetic Cardiomyopathy**





Pharmacotherapy in diabetes

- Non pharmacological treatment
- Pharmacological treatment

Non-pharmacologic treatment

١. Patient education & motivation

٢. Dietary modification

٣. Exercise

٤. Stress management

٥. Monitoring blood glucose levels

Types of OADs

Secretagogues

- Sulfonylureas
- Meglitinides

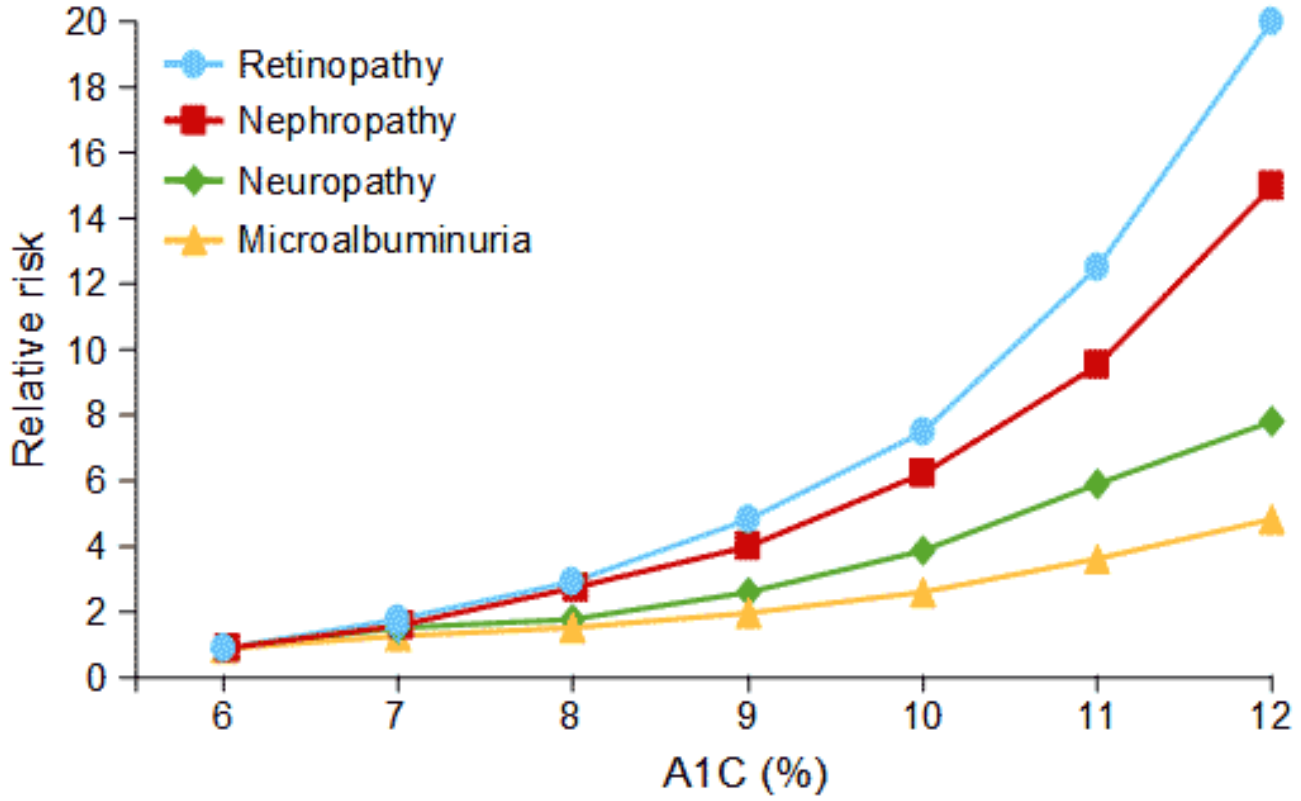
Sensitizers

- Thizolidinediones
- Biguanides

Miscellaneous

- Alpha Glucosidase inhibitors (AGIs)
- DPP-۴ inhibitors
- SGLT۲ inhibitors

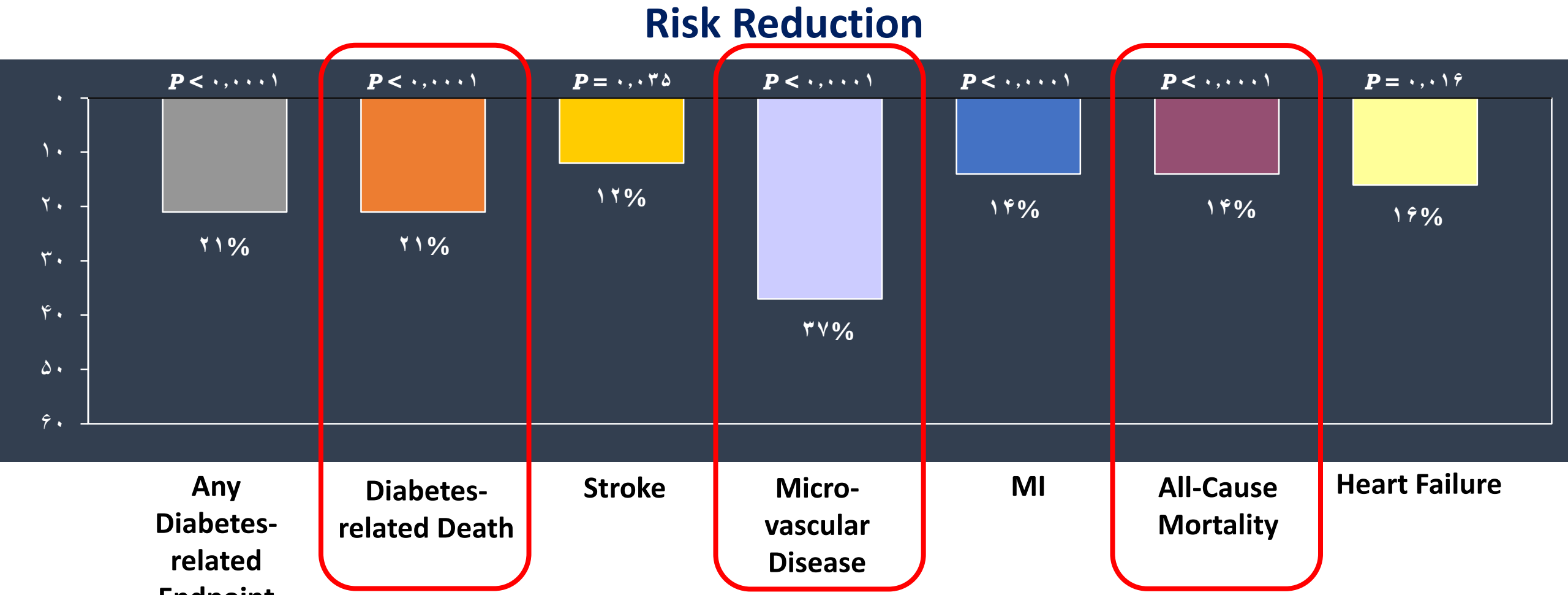
Relative Risk of Progression of Diabetic Complications[۱]



۱. Adapted from DCCT. Diabetes ۱۹۹۵;۴۴:۹۶۸-۴۳.

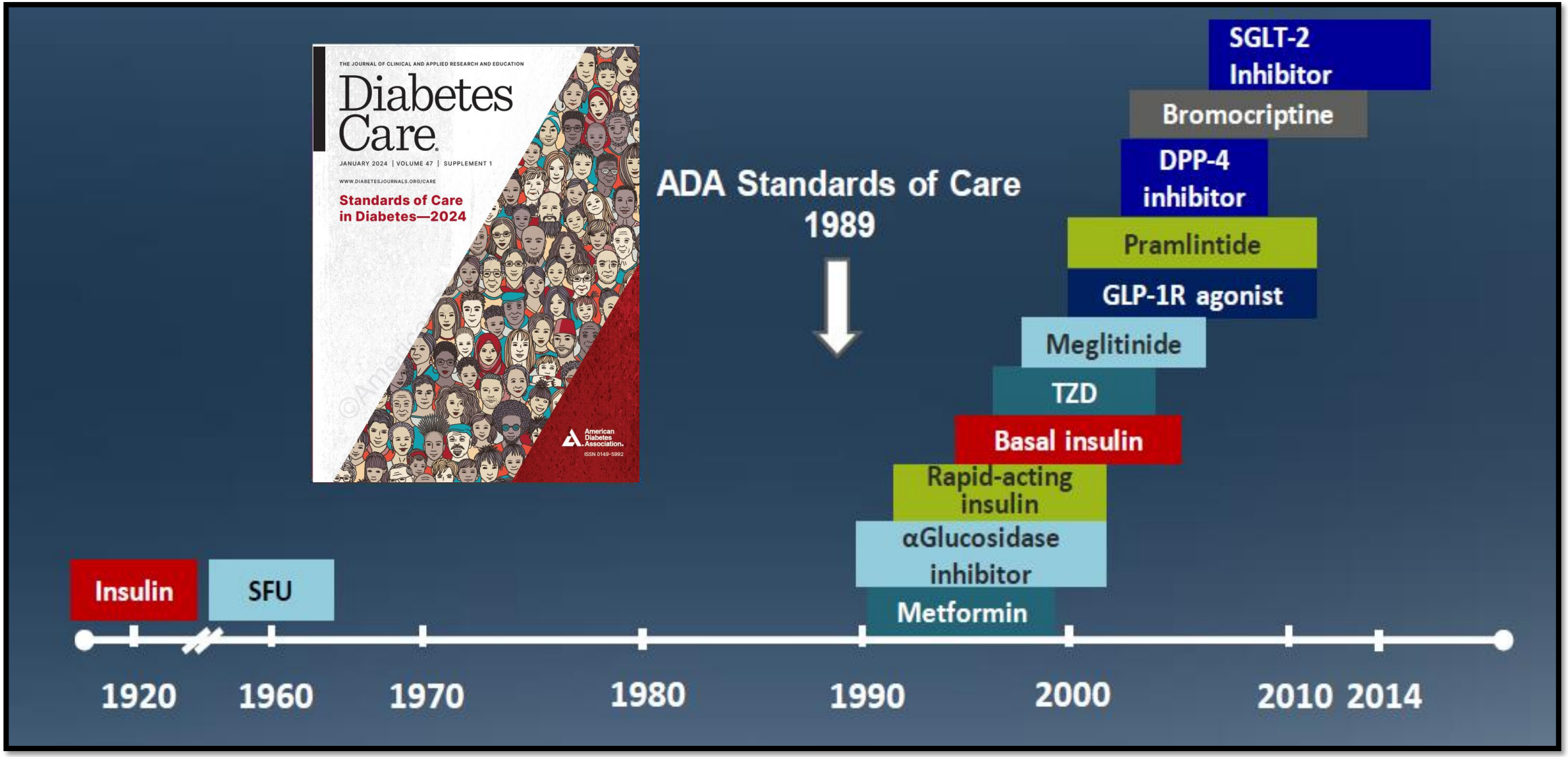
UKPDS ۳۵

Each ۱% Reduction in A۱c Reduces the Complication Risk[۱]

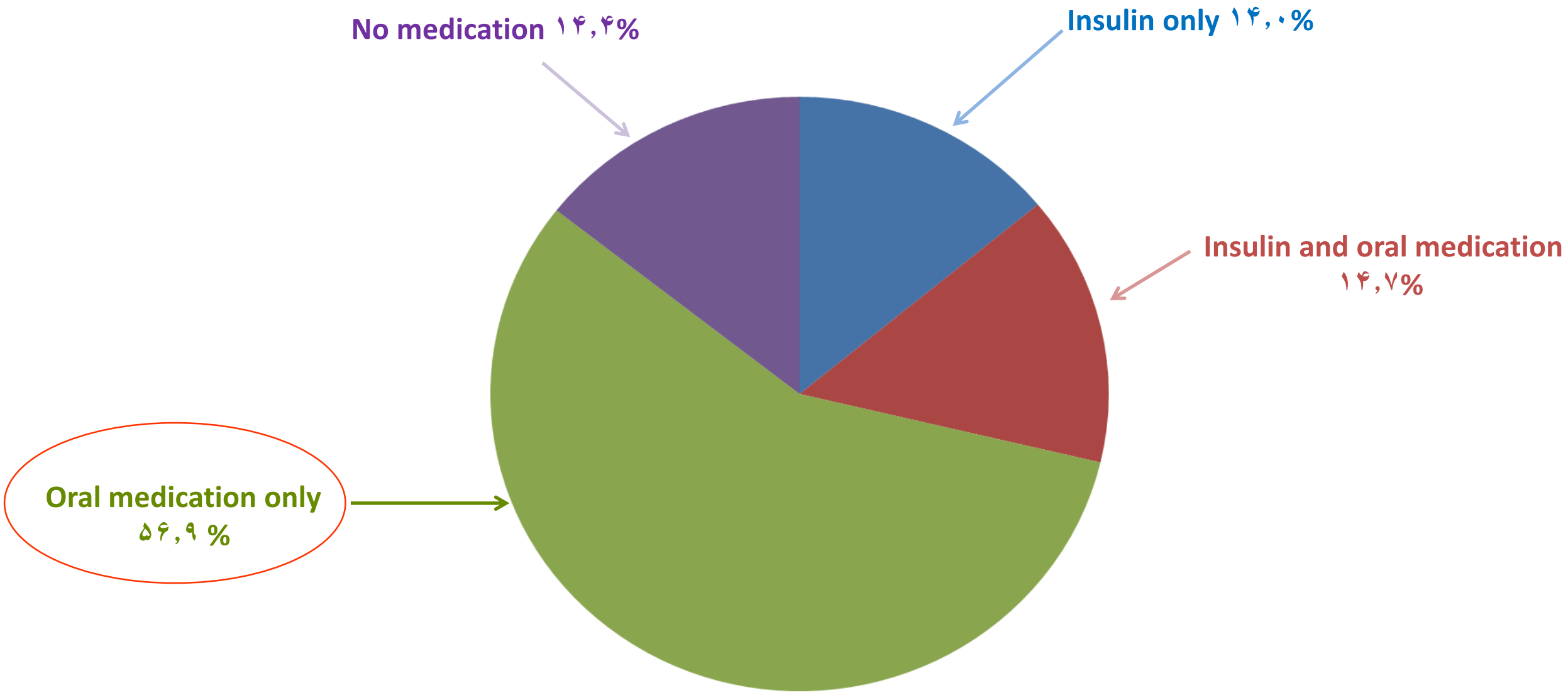


۱. Stratton IM, et al. BMJ. ۲۰۰۰;۳۲۱:۴۰۵-۴۱۲.

Significant Therapeutic Advances in Diabetes Care Over Past ٢٠ Years ١



Treatment of Diabetes [1]



۱. National Diabetes Information Clearinghouse. National Diabetes Statistics, ۲۰۱۴. Available at: http://diabetes.niddk.nih.gov/dm/pubs/statistics/

ADA ۲۰۲۴

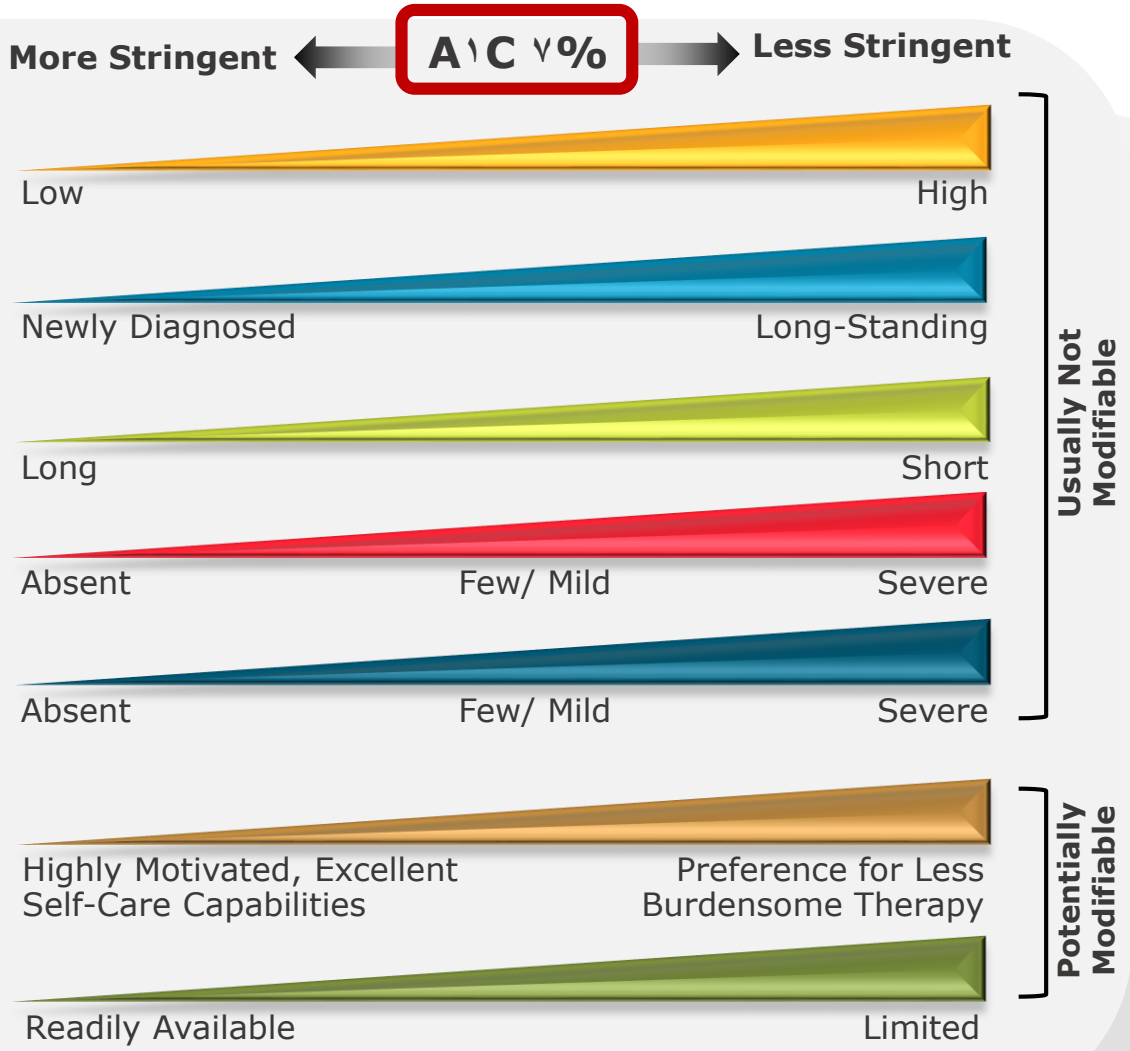
Diabetes Care

Standard of Care in Diabetes

Approach to Individualization of Glycemic Control[1]

Patient/Disease Features

- Risks Associated with Hypoglycemia & Other Drug Adverse Effects
- Disease Duration
- Life Expectancy
- Important Comorbidities
- Established Vascular Complications
- Individual Needs and Preferences
- Resources & Support System



١. Diabetes Care ٢٠٢٤; ٤٧(Suppl. ١): S١٥٨–S١٧٨.

Person – Centered Glycemic Management in Type ٢ Diabetes[١]

١. Diabetes Care ٢٠٢٤;٤٧(Suppl. ١):S٥٢–S٧٦

Healthy Lifestyle behaviors; Diabetes self-Management education and Support (DSMES); Social Determinants of health (SDOH)

To avoid clinical inertia, reassess and modify treatment regularly (٣-٦ months)

Goal: Cardiorenal Risk Reduction in High-risk Patients with Type ٢ Diabetes (In addition to Comprehensive CV RISK Management)

+ASCVD
Defined differently across CVOTs but all included individuals with established CVD (e.g. MI, stroke any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk
While definitions vary, most comprise≥ ٥٥ years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia or albuminuria

+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF

+CKD
eGFR < ٣٠ ml/min per ١,٧٣m² OR albuminuria (ACR ≥ ٣٠,٠ mg/mmol (٣٠٠mg/g)). These measurements may vary over time; thus, a repeat measure is requires to document CKD

+ASCVD/INDICATORS OF HIGH RISK
- GLP-١ RA with proven CVD benefit
- Either/ or
- SGLT٢i with proven CVD benefit

If A١C above target

- For patients on a GLP-١ RA, consider adding SGLT٢i with proven CVD benefit and vice versa
- TZD

+HF
SGLT٢i with proven benefit in this population

+CKD (on maximally tolerated dose of ACEi/ARB
Preferably
SGLT٢i with primary evidence of reducing CKD progression
Use SGLT٢i in people with an eGFR ≥ ٢٠ ml/min per ١,٧٣ m²; once initiated should be continued until initiation of dialysis or transplant

OR

GLP-١ RA with proven CVD benefit if SGKT٢i not tolerated or contraindicated

If A١C above target, for patients SGLT٢i, consider incorporating a GLP-١ RA and vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management:
Choose approaches that Provide the efficacy to achieve goals:
Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
Prioritize avoidance of hypoglycemia in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals
Efficacy for glucose lowering

Very high:
Dulaglutide (high dose), Semaglutide, Tirzepatide
Insulin
Combination Oral, Combination Injectable
(GLP-١ RA/Insulin)

High:
GLP-١ RA (not listed above), Metformin, SGLT٢i, Sulfonylurea, TZD

Intermediate:
DPP-٤i

Achievement and Maintenance of Weight Management Goal
Set individualized weight management goals

- **General lifestyle advice: medical nutrition therapy/eating patterns/physical activity**
- **Intensive evidence-based structured weight management programme**
- **Consider medication for weight loss**
- **Consider metabolic surgery**

When choosing glucose-lowering therapies:
Consider regimen high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very high:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-١ RA (not listed above), SGLT٢i

Neutral:
DPP-٤i, Metformin

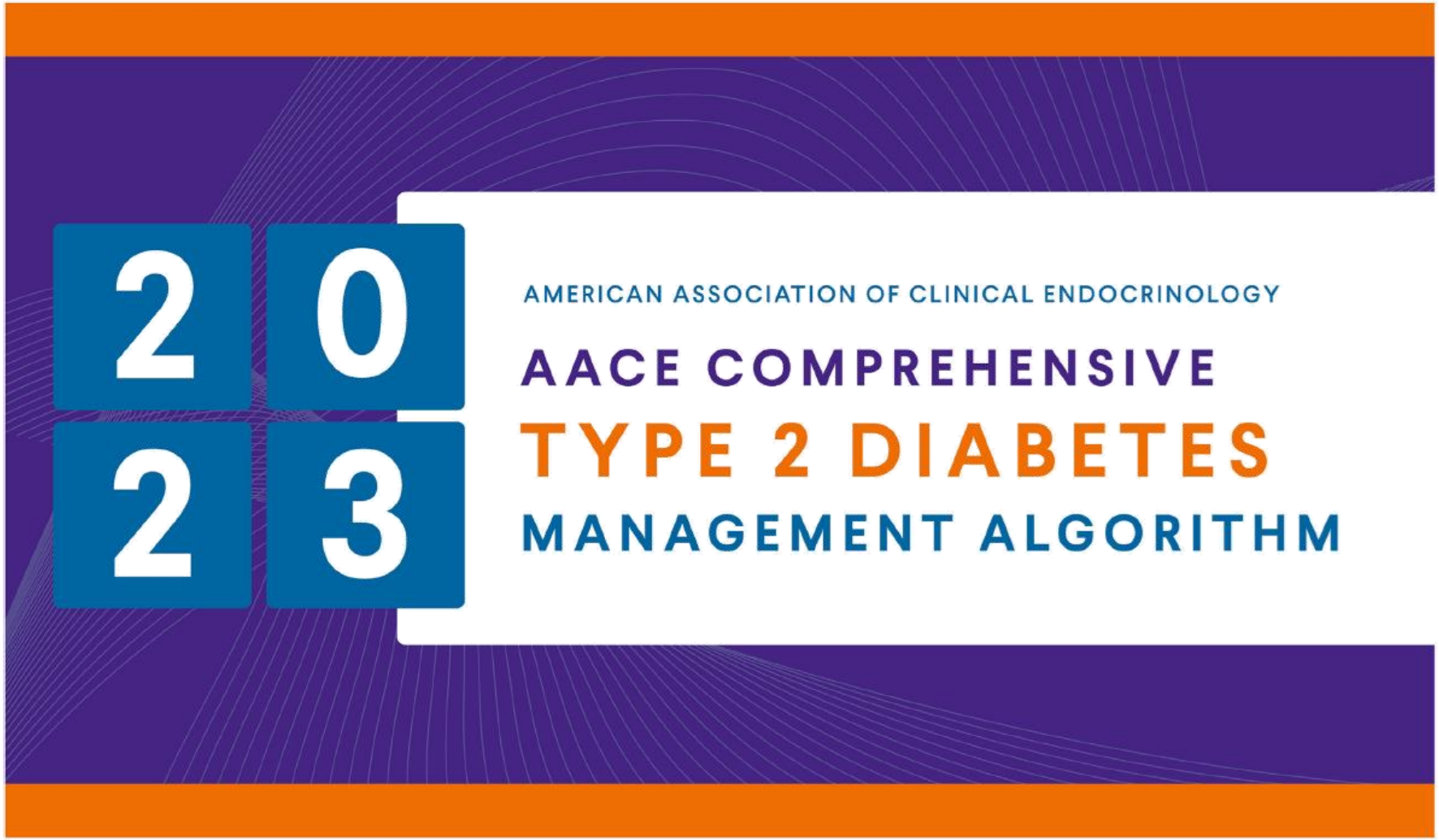
If HbA١C above target

Identify barriers to goals:
- Consider DSMES referral to self-efficacy to achievement of goal
- Consider technology (e.g. diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact on achievement of goals

AACE ٢٠٢٣

American Association of Clinical Endocrinology

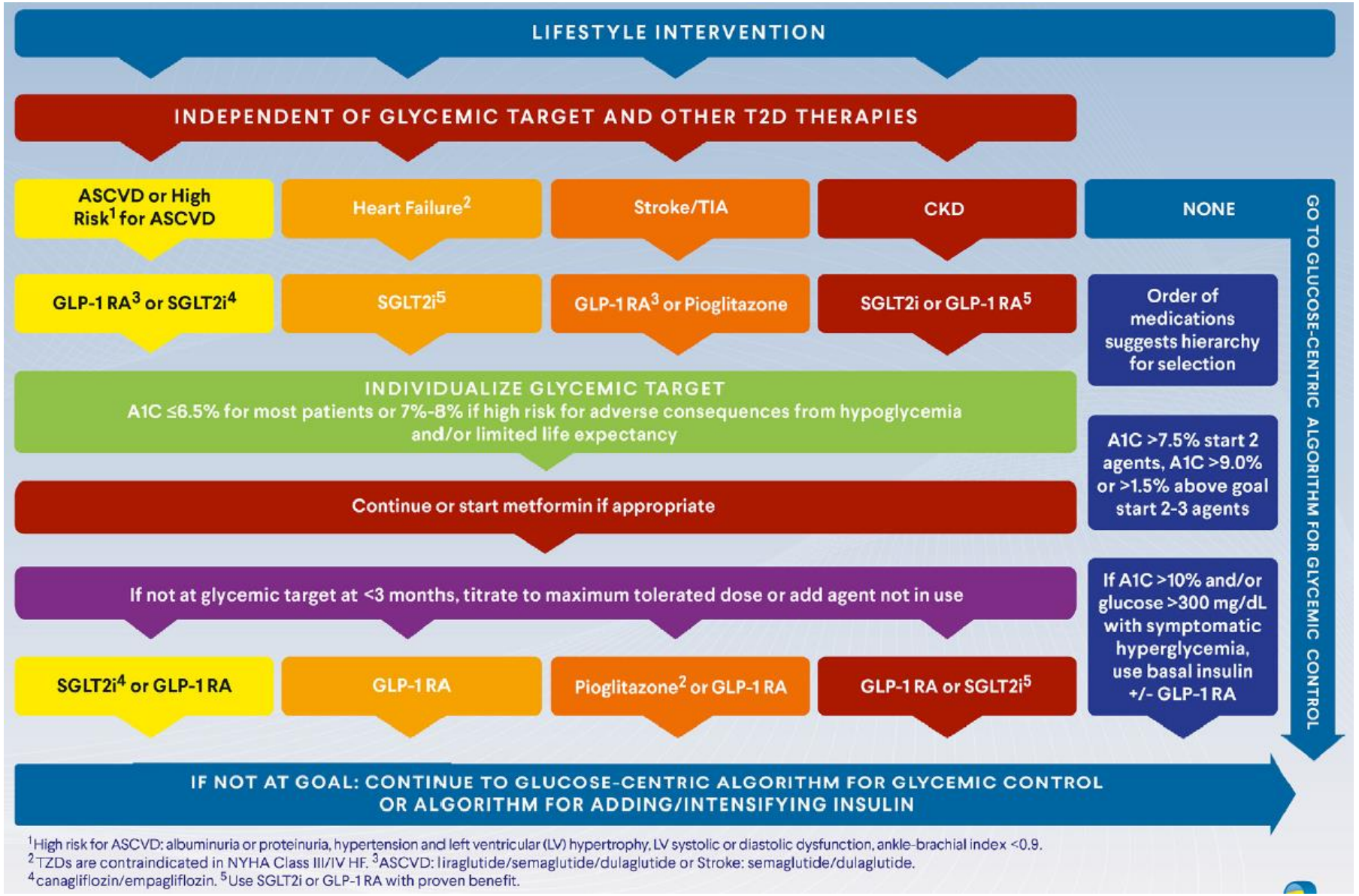
AACE Comprehensive Type ٢ Diabetes Management Algorithm



Algorithm Title Page

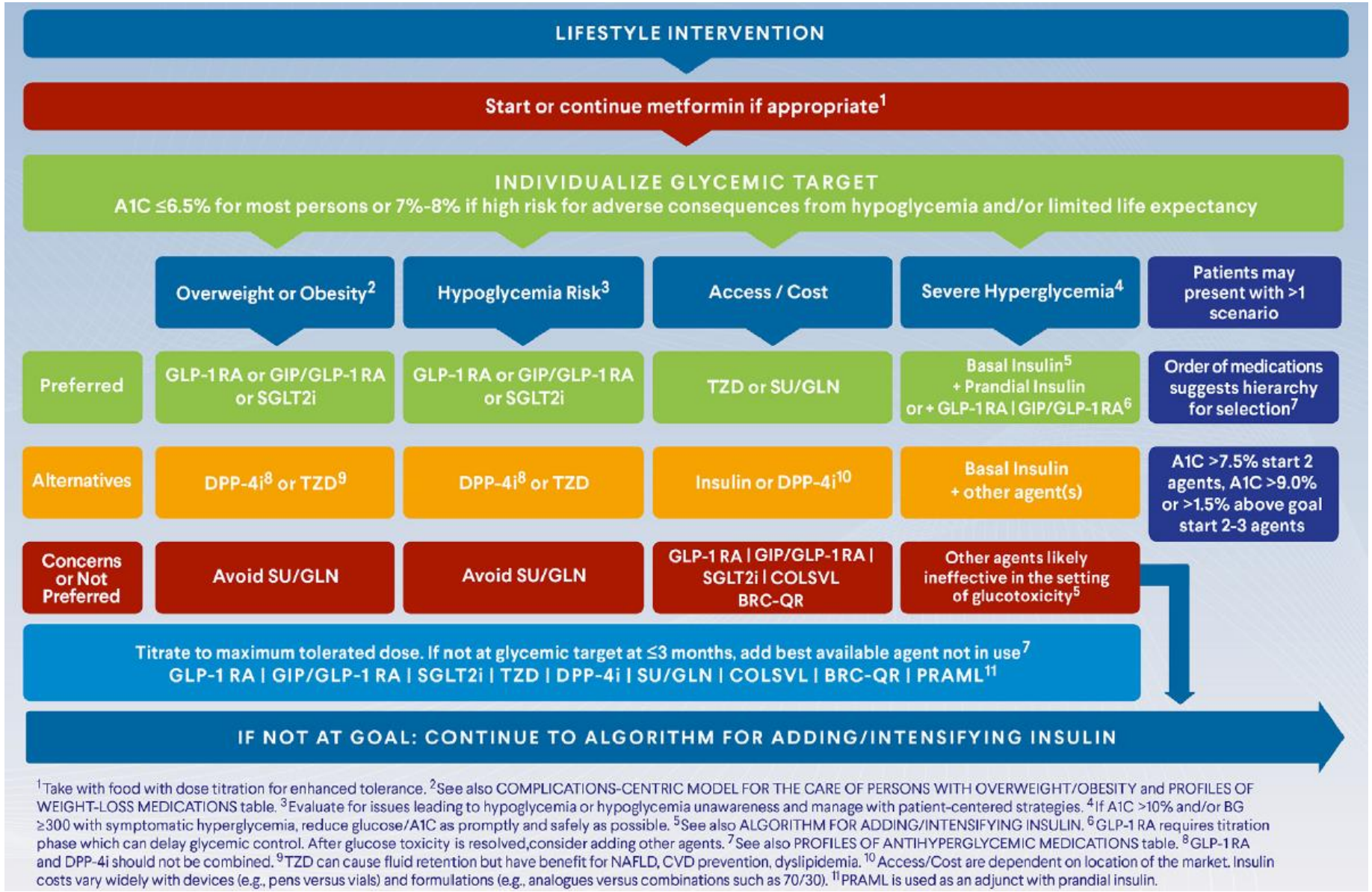
2023 AACE Type 2 Diabetes Algorithm Title Page. *AACE* = American Association of Endocrinology.

Complication-Centric Algorithm for Glycemic Control



١-Endocrine Practice ٢٩ (٢٠٢٣) ٣٠٥-٣٤٠

Glucose-Centric Algorithm for Glycemic Control[1]



[1]Take with food with dose titration for enhanced tolerance. [2]See also COMPLICATIONS-CENTRIC MODEL FOR THE CARE OF PERSONS WITH OVERWEIGHT/OBESITY and PROFILES OF WEIGHT-LOSS MEDICATIONS table. [3]Evaluate for issues leading to hypoglycemia or hypoglycemia unawareness and manage with patient-centered strategies. [4]If A1C >10% and/or BG ≥300 with symptomatic hyperglycemia, reduce glucose/A1C as promptly and safely as possible. [5]See also ALGORITHM FOR ADDING/INTENSIFYING INSULIN. [6]GLP-1 RA requires titration phase which can delay glycemic control. After glucose toxicity is resolved,consider adding other agents. [7]See also PROFILES OF ANTIHYPERGLYCEMIC MEDICATIONS table. [8]GLP-1 RA and DPP-4i should not be combined. [9]TZD can cause fluid retention but have benefit for NAFLD, CVD prevention, dyslipidemia. [10]Access/Cost are dependent on location of the market. Insulin costs vary widely with devices (e.g., pens versus vials) and formulations (e.g., analogues versus combinations such as 70/30). [11]PRAML is used as an adjunct with prandial insulin.

١-Endocrine Practice ٢٩ (٢٠٢٣) ٣٠٥-٣٤٠

	MET	GLP-1 RA	DUAL GIP/ GLP-1 RA	SGLT2i	TZD	INSULIN (basal & basal bolus)	DPP-4i	SU	GLN	AGi	COLSVL	BRC	PRAML
EFFICACY FOR GLUCOSE LOWERING	++	+++	+++	++	++	+++/++++	+	++	+	+	+	+	+
ASCVD MACE	Neutral	Benefit[1,3]	Safe	Benefit[2]	Neutral[3]	Neutral	Neutral	Possible Increased Risk	Neutral	Insufficient Evidence	Neutral[3]	Safe	Insufficient Evidence
ASCVD CHF		Unclear		Reduced Risk	Moderate to Severe[4]	Moderate	Moderate[4]						
ASCVD STROKE		Benefit[5]		Possible Benefit[2]	Benefit	Neutral	Neutral						
CKD	CKD3a/3b[6]	Benefit[7]	Insufficient Evidence	Benefit	Neutral	Increased hypoglycemia risk with impaired renal function	Neutral	Increased hypoglycemia risk with impaired renal function		Not recommended SCR >2 mg/dL or CrCl <25	Neutral	Neutral	Neutral
RENAL ADJUSTMENT	Not with CKD4 eGFR <30[6]	Exenatide not recommended eGFR <45		Check medication-specific eGFR thresholds[8]			Adjust Dose[9]						
HYPOGLYCEMIA RISK[14]	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate to Severe	Neutral	Moderate to Severe	Mild	Neutral	Neutral	Neutral	Neutral
WEIGHT	Slight loss	Loss	Loss	Loss	Gain[4]	Gain	Neutral	Gain	Neutral	Neutral	Neutral	Neutral	Loss
NAFLD	Neutral	Benefit	Benefit	Potential Benefit	Benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Benefit
GI ADVERSE SYMPTOMS	Mild to Moderate	Moderate[10]	Moderate[10]	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate	Mild	Moderate	Moderate
OTHER CONSIDERATIONS		Medullary Thyroid Carcinoma/ MEN2	Medullary Thyroid Carcinoma/ MEN2	GU infections DKA[11] Fracture Risk[12]	Fracture Risk		Rare Arthralgias/ Myalgias						
ACCESS/COST	$	$$$	$$$	$$$	$	$ - $$$[13]	$-$$	$	$-$$	$-$$	$$$	$$$	$$$

■ Possible benefits ■ Use with caution ■ Likelihood of adverse events ■ Neutral, not studied, insufficient evidence

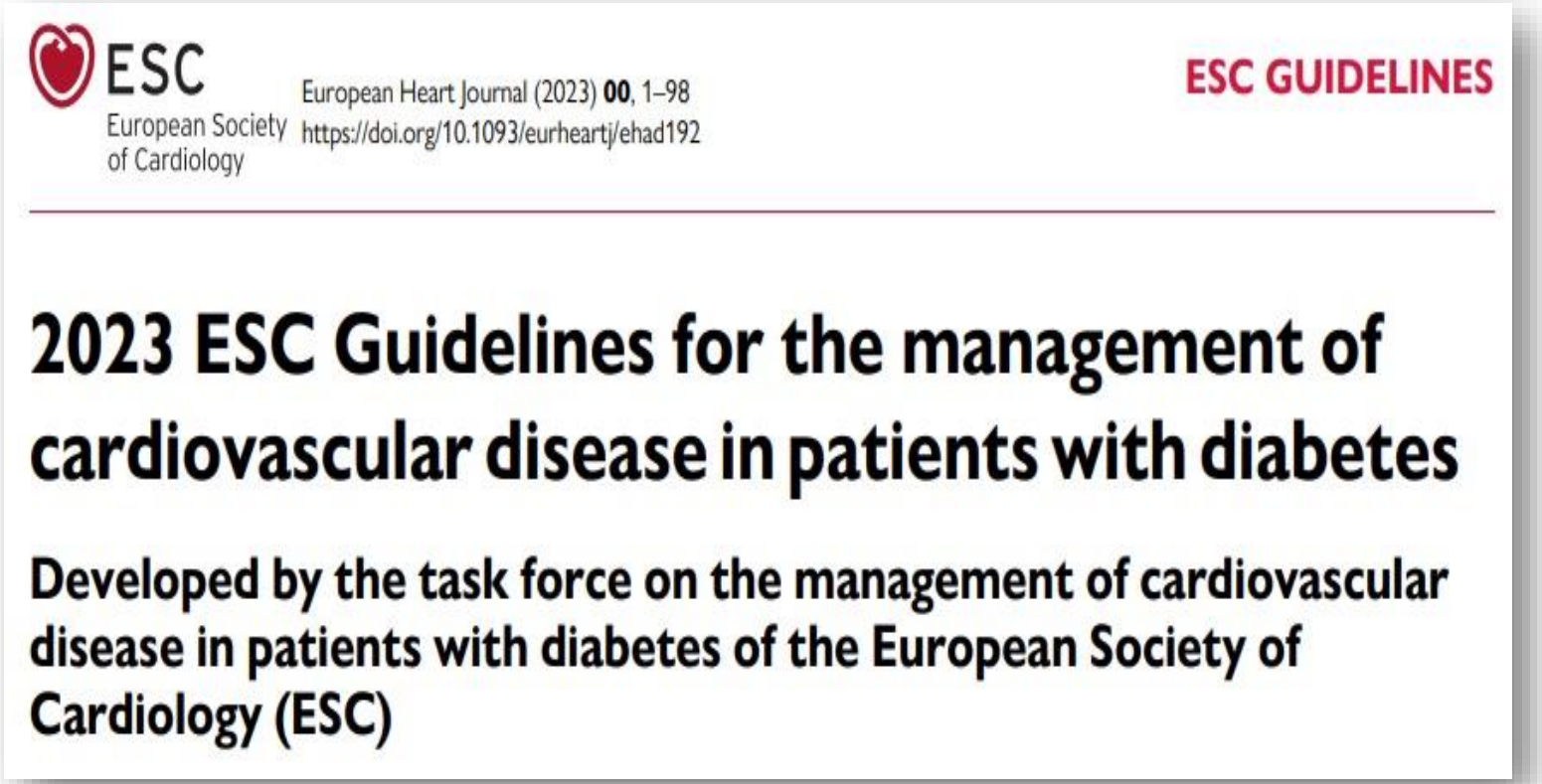
[1]GLP-1 RA MACE benefits with liraglutide, semaglutide, dulaglutide. [2]SGLT2i MACE benefits with empagliflozin, canagliflozin. Possible benefit for hemorrhagic stroke. [3]GLP-1 RA, TZD, COLSVL can lower LDL. [4]TZDs increase fluid retention and edema and are contraindicated in persons with NYHA Class III/IV CHF. There is Increased risk of hospitalization for CHF with saxagliptin, and limited experience for persons with NYHA Class II/IV CHF with alogliptin [5]GLP-1 RA stroke benefits observed with semaglutide and dulaglutide. [6]CKD3a no adjustment with monitoring, CKD3b decrease dose and do not initiate, CKD4 contraindicated. Hold for acute kidney injury, IV contrast. [7]Dulaglutide, semaglutide decrease CKD progression. [8]The eGFR thresholds for initiation and/or continuation of therapy in CKD vary among SGLT2i. Check medication-specific eGFR levels. [9]Only linagliptin does not require adjustment. [10]Slow titration, portion control, and consider reducing to prior tolerated dose. [11]Precipitants

ESC ۲۰۲۳

۲۰۲۳ ESC Guideline for the Management of Cardiovascular Disease in Patient with Diabetes

Developed by the Task Force on the Management of Cardiovascular Disease in Patients with Diabetes of the European Society of Cardiology (ESC)

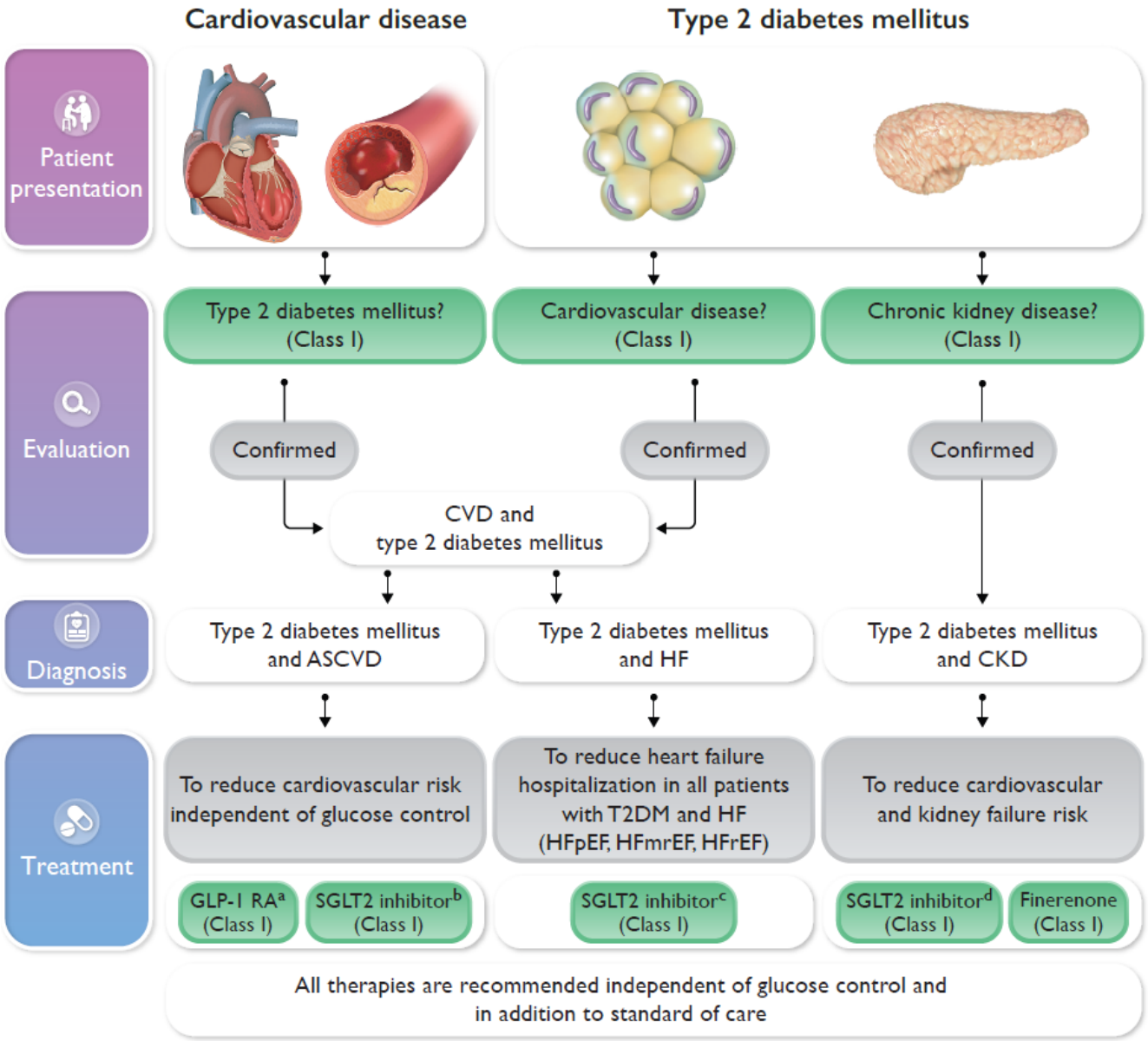
Management of Patients with T۲DM and Cardiovascular Disease Based on ESC ۲۰۲۳ Guideline[1]



This guideline represents the cooperation of European Society of Cardiology (ESC) and its partner, the European Society for the Study of Diabetes (EASD), for management of patients with diabetes and cardiovascular disease[1].

۱- European Heart Journal (۲۰۲۳) ۰۰, ۱–۹۸

Management of CVD in Type ٢ Diabetes[1]



[a]GLP-١ RAs with proven CV benefit: liraglutide, semaglutide s.c., dulaglutide, efpeglenatide.
[b]SGLT٢ inhibitors with proven CV benefit: empagliflozin, canagliflozin, dapagliflozin, sotagliflozin.
[c]Empagliflozin, dapagliflozin, sotagliflozin in HFrEF; empagliflozin, dapagliflozin in HFpEF and HFmrEF.
[d]Canagliflozin, empagliflozin, dapagliflozin.

١- European Heart Journal (٢٠٢٣) ٠٠, ١–٩٨

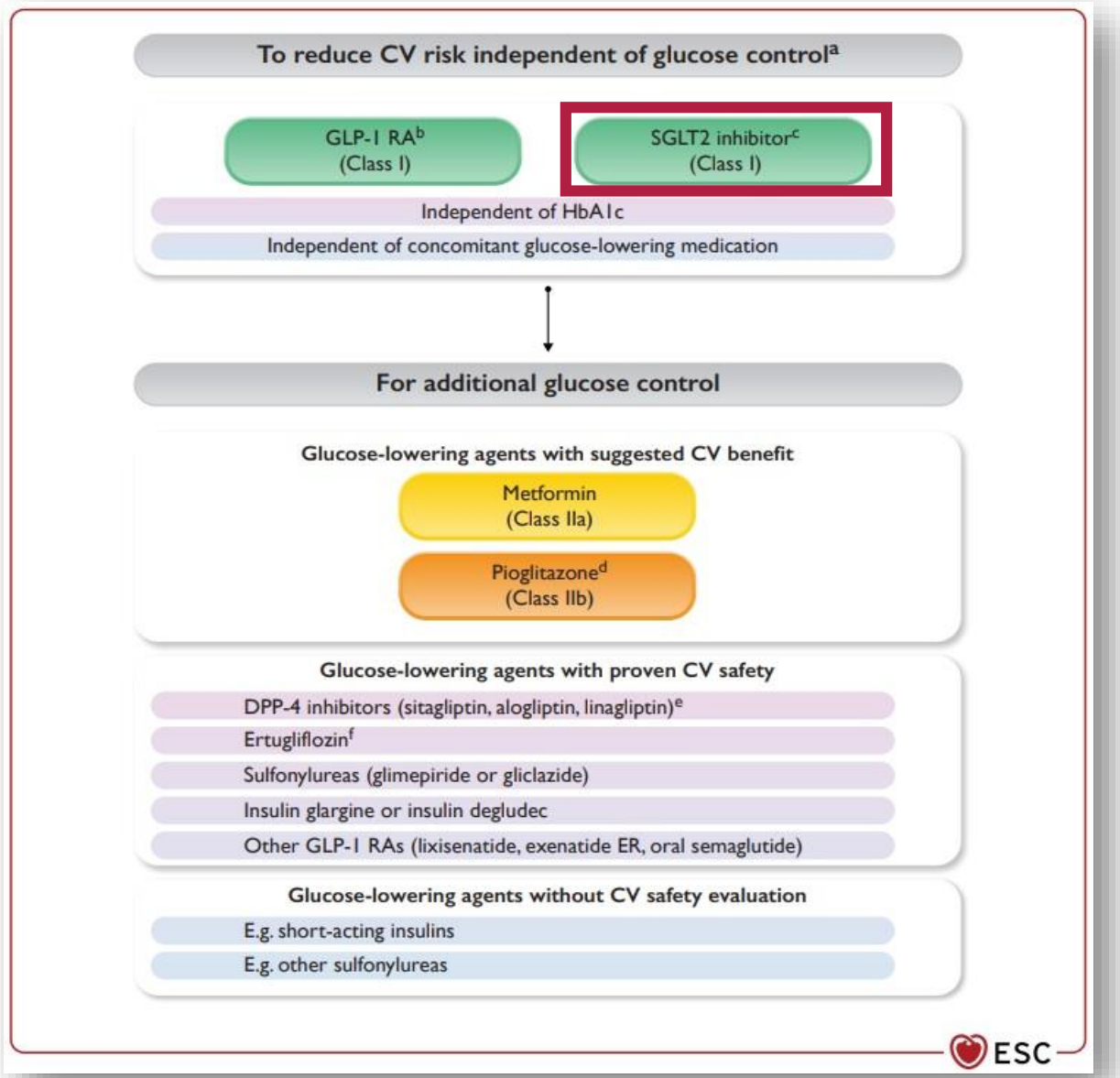
Cardiovascular Risk Categories in Patients with Diabetes[1]

Very high CV risk	Patients with T2DM with: • Clinically established ASCVD or • Severe TOD or • 10-year CVD risk ≥20% using SCORE2-Diabetes
High CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 10 to <20% using SCORE2-Diabetes
Moderate CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 5 to <10% using SCORE2-Diabetes
Low CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk <5% using SCORE2-Diabetes

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; SCORE2-Diabetes, type 2 diabetes-specific 10-year CVD risk score; T2DM, type 2 diabetes mellitus; TOD, target-organ damage; UACR, urinary albumin-to-creatinine ratio.
Severe TOD defined as eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria; or eGFR 45–59 mL/min/1.73 m^2 and microalbuminuria (UACR 30–300 mg/g; stage A2); or proteinuria (UACR >300 mg/g; stage A3); or presence of microvascular disease in at least three different sites [e.g. microalbuminuria (stage A2) plus retinopathy plus neuropathy].[43–45]

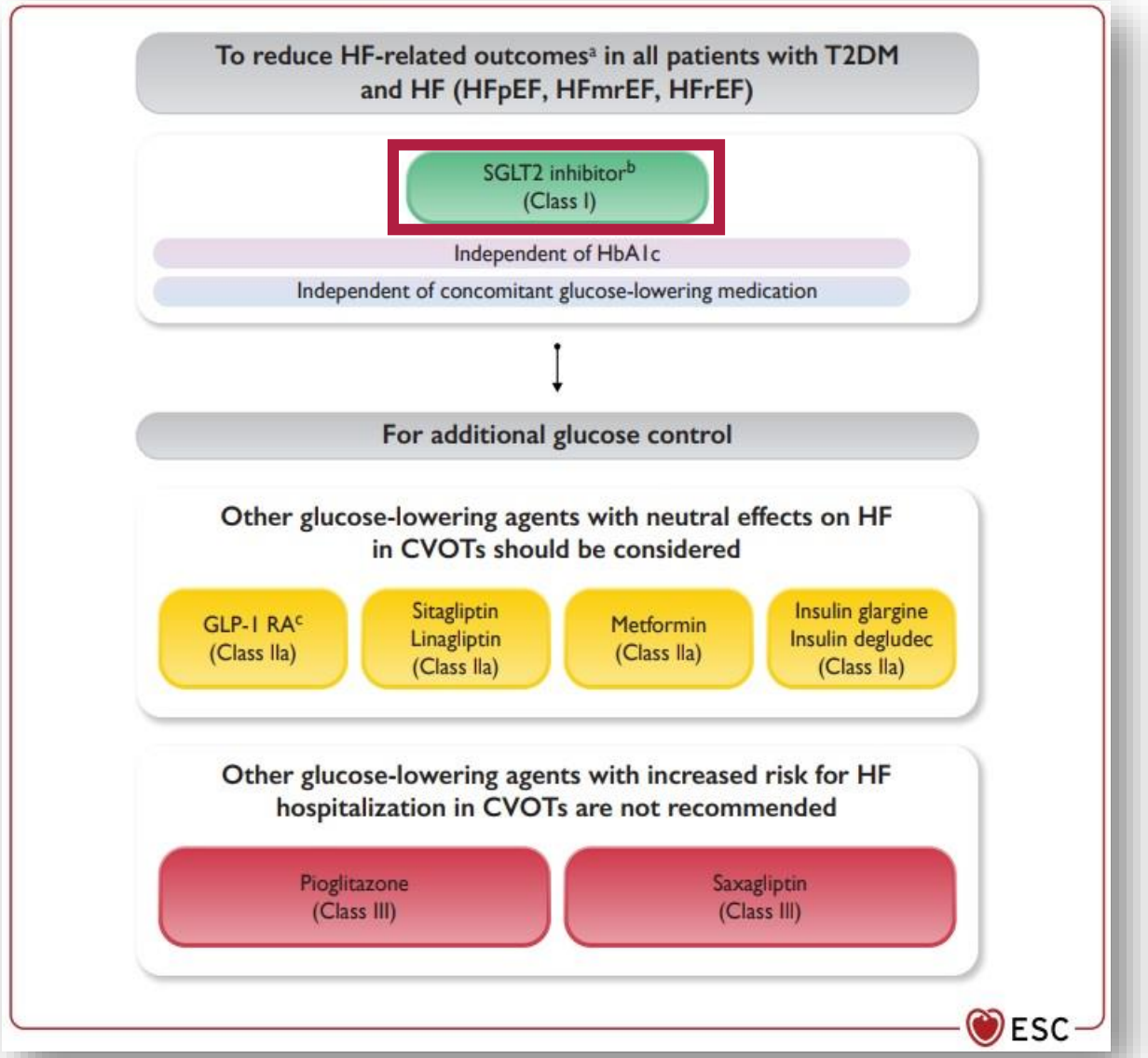
١- European Heart Journal (٢٠٢٣) ٠٠, ١–٩٨

Glucose-lowering Treatment for Patients with T٢DM and ASCVD to Reduce Cardiovascular Risk[1]



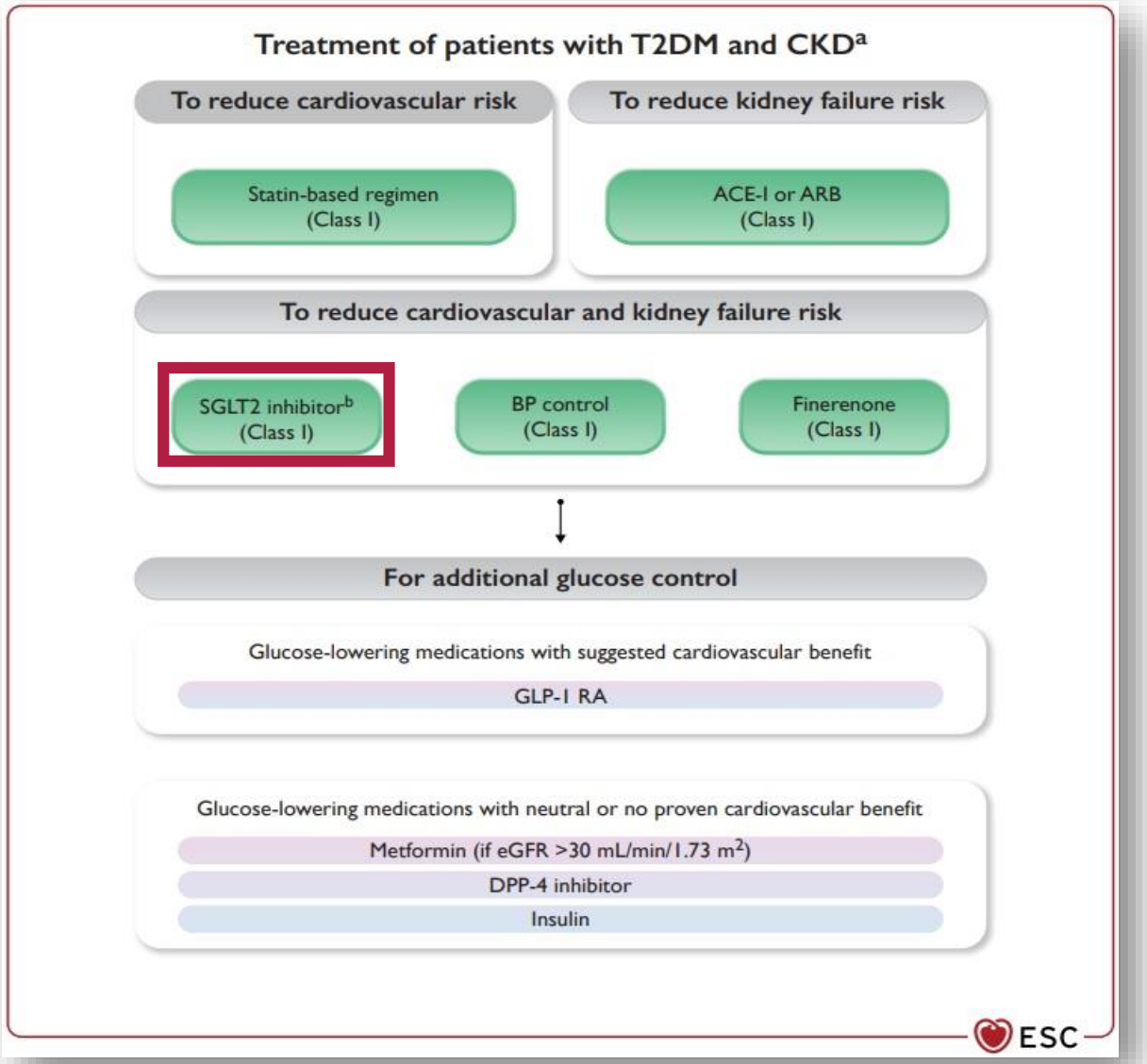
١- European Heart Journal (٢٠٢٣) ٠٠, ١–٩٨

Recommendations for the Treatment of Patients with T٢DM to Reduce Heart Failure Risk[1]



١- European Heart Journal (٢٠٢٣) ٠٠, ١–٩٨

Recommendations for the Treatment of Patients with T٢DM to Reduce CKD Risk[1]

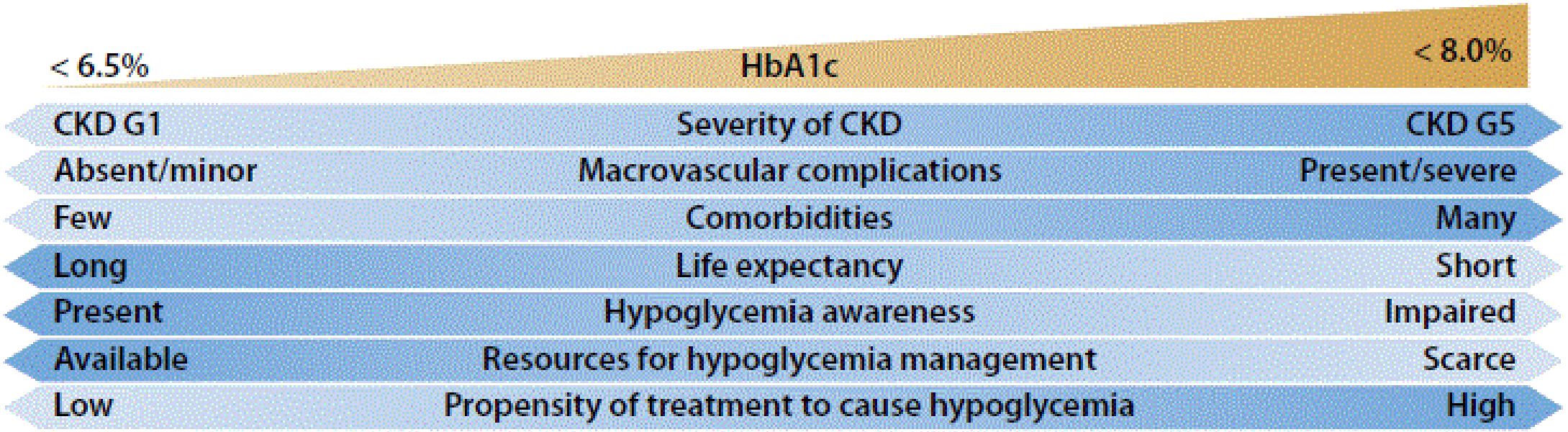


١- European Heart Journal (٢٠٢٣) ٠٠, ١–٩٨

KDIGO 2020 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE

Kidney Int. ۲۰۲۰; ۹۸(۴S): S۱–S۱۱۵

Glycemic target in patients with Diabetes and Chronic Kidney Disease: an individualized HbA١c target ranging from <٦,٥% to <٨,٠% [١]

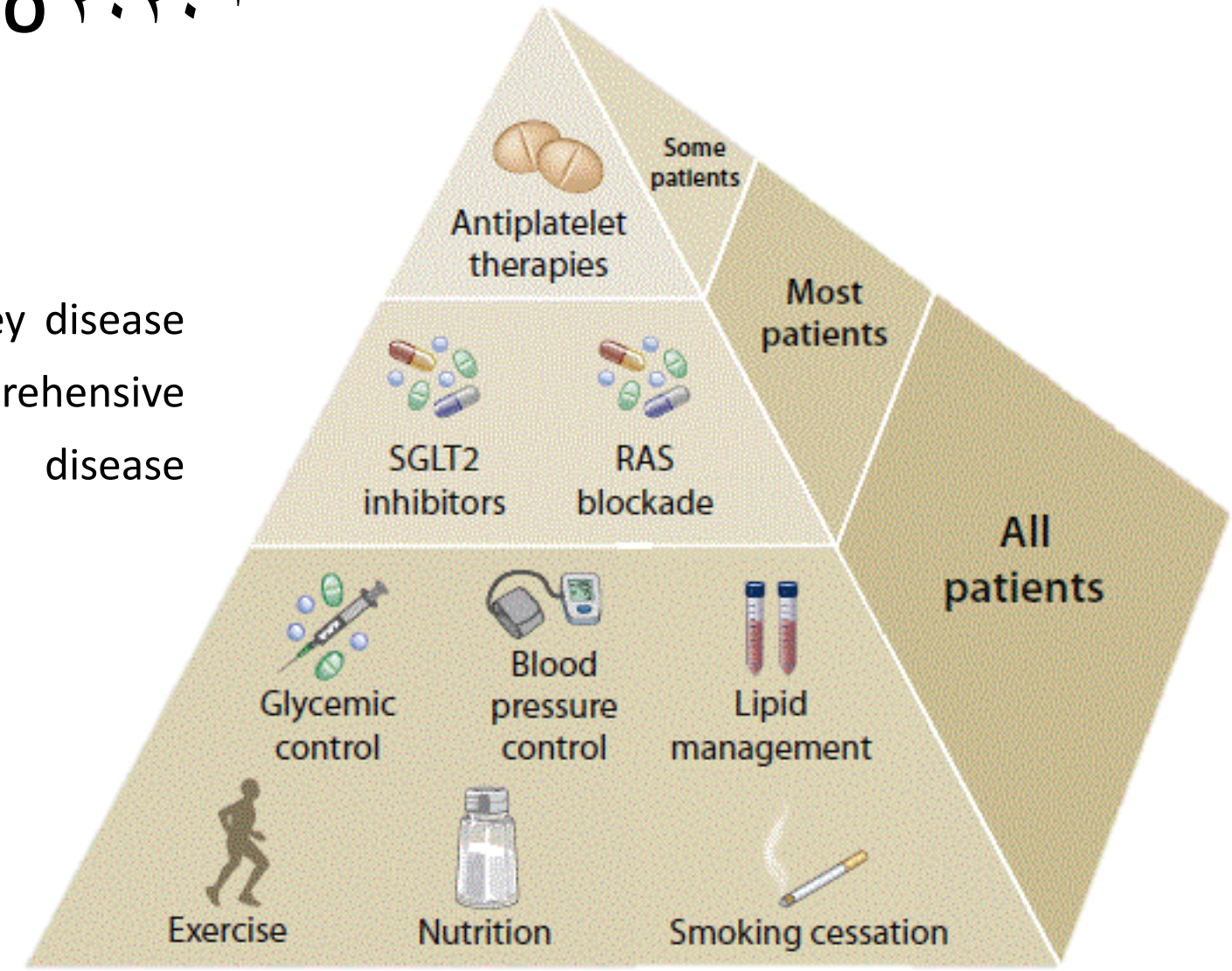


CKD, chronic kidney disease; G١, estimated glomerular filtration rate (eGFR) $٩٠ ml/min per ١,٧٣ m٢; G٥, eGFR <١٥ ml/min per ١,٧٣ m٢; HbA١c, glycated hemoglobin.

١. Kidney Int. ٢٠٢٠; ٩٨(٤S): S١–S١١٥

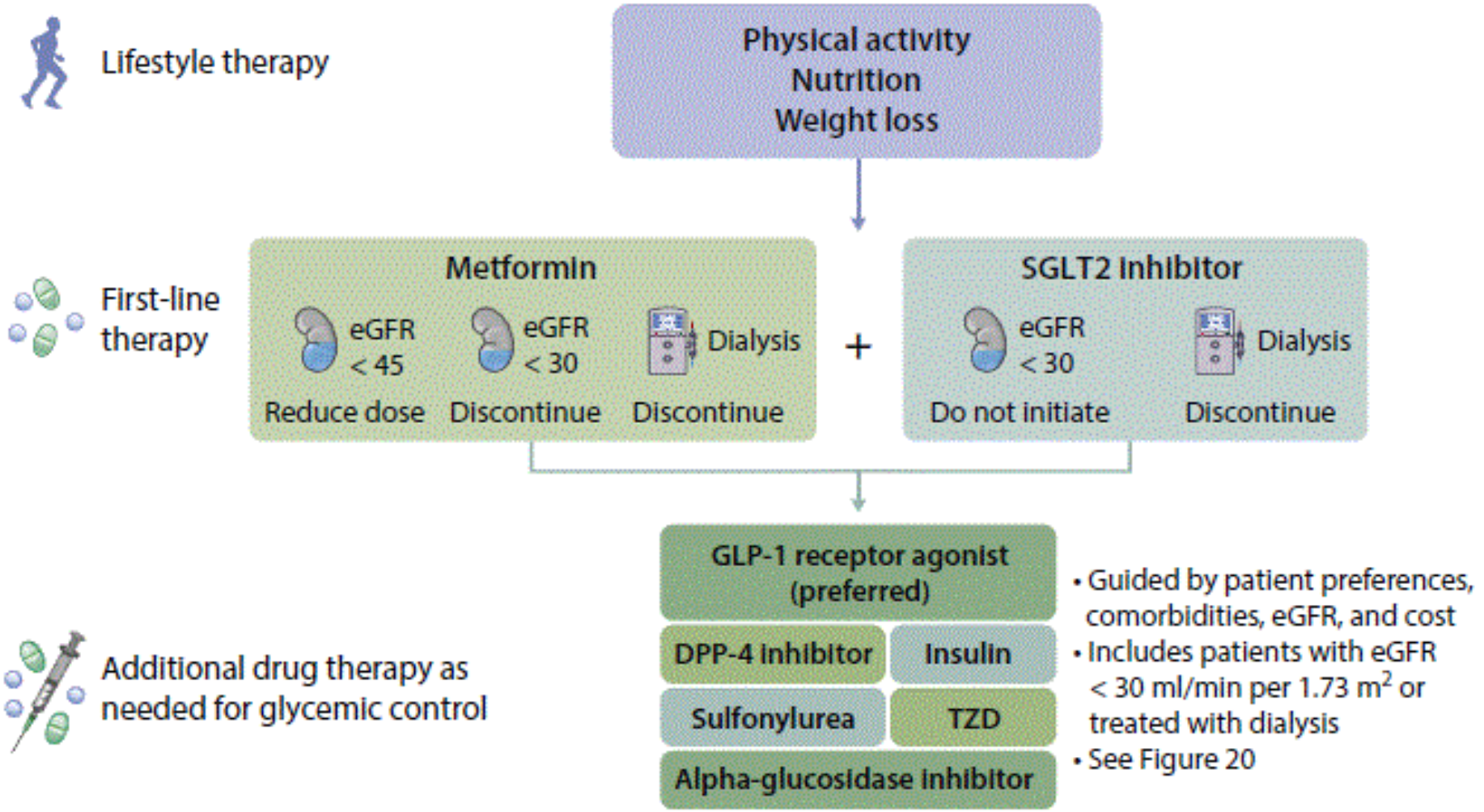
Comprehensive strategy – KDIGO ۲۰۲۰ [۱]

Patients with diabetes and chronic kidney disease (CKD) should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease



Kidney–heart risk factor management

۱. Kidney Int. ۲۰۲۰; ۹۸(۴S): S۱–S۱۱۵



١. Kidney Int. ٢٠٢٠; ٩٨(٤S): S١–S١١٥

Conclusion

The last, not the least…

In the era of growing number of diabetes medications and new data, we should consider the below factors to select the proper component for each individual patient:

Effectiveness	Safety profiles	Side effects
Extra-glycemic effects	Cardiovascular effects	Our experience in handling
Availability	Patient preference	Cost


Thank you