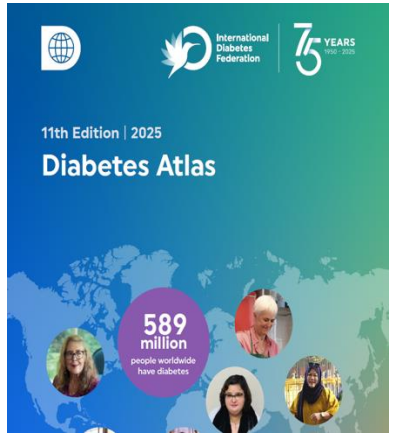
LA PRESA IN CARICO DEL PAZIENTE CON SINDROME CARDIO-NEFRO-METABOLICA

Il valore della prevenzione nel diabete

Graziano Di Cianni
UOC Diabetologia e Malattie del Metabolismo
Azienda USL Toscana Nord Ovest



DIABETES PREVALENCE

World			
2050	852.5 Million	^	45% increase
2024	588.7 Million		
Africa (AFR)			
2050	59.5 Million	^	142% increase
2024	24.6 Million		
Europe (EUR)			
2050	72.4 Million	^	10% increase
2024	65.6 Million		
Middle-East and North Africa (MENA)			
2050	162.6 Million	^	92% increase
2024	84.7 Million		
North America and Caribbean (NAC)			
2050	68.1 Million	^	21% increase
2024	56.2 Million		
South and Central America (SACA)			
2050	51.5 Million	^	45% increase
2024	35.4 Million		
South-East Asia (SEA)			
2050	184.5 Million	^	73% increase
2024	106.9 Million		
Western Pacific (WP)			
2050	253.8 Million	^	18% increase
2024	215.4 Million		

Diabetes is a major health issue that has reached alarming levels. The 11th edition confirms that diabetes is one of the fastest-growing global health emergencies of the 21st century.

Tinotenda Dzikiti, Zimbabwe - Living with type 1 diabetes

Type 2 diabetes is the most common type of diabetes, accounting **for over 90% of all diabetes worldwide.**

Number of adults (20–79 years) with diabetes living in urban and rural areas in 2024 and 2050.

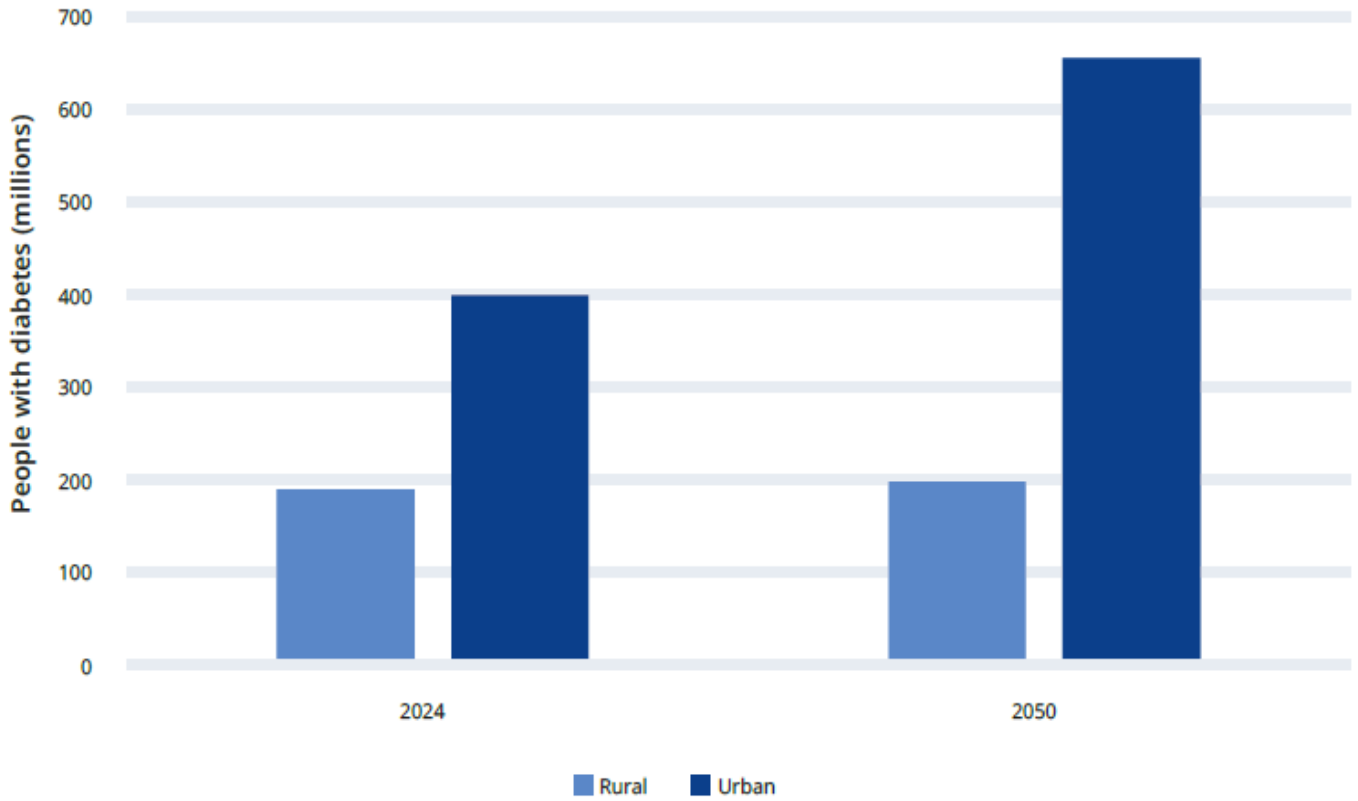
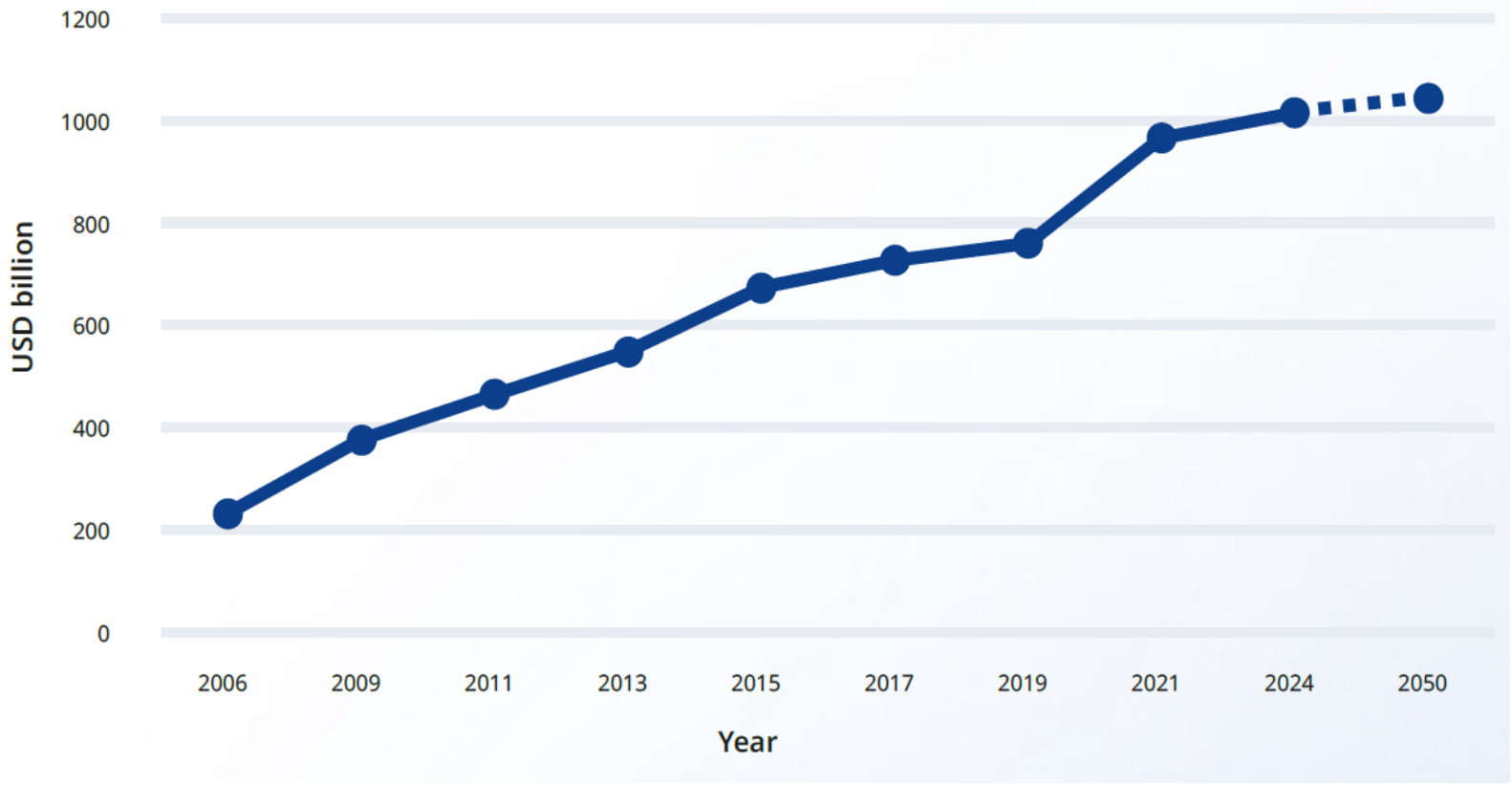


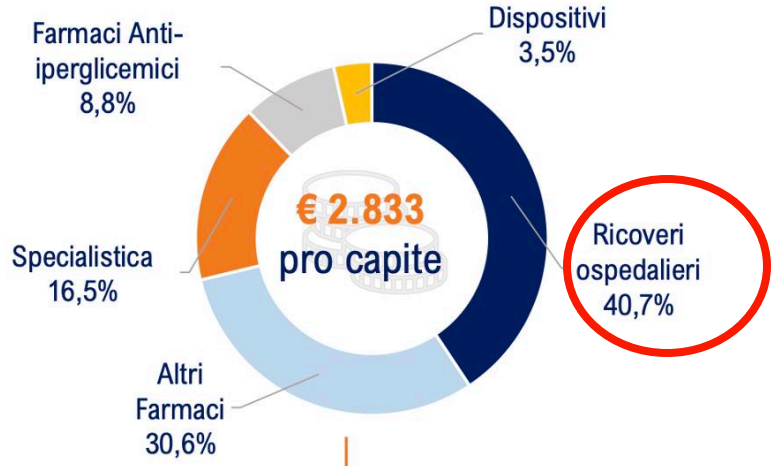
Figure 3.7 Total diabetes-related health expenditure for adults (20–79 years) with diabetes from 2006 to 2050.



Il burden socio-economico del diabete

The European House Ambrosetti healthcare

Distribuzione dei costi diretti medi annui pro capite del paziente diabetico (%), 2019



Voce di costo	Valore
Ricoveri ospedalieri	**€ 1.152**
Prestazioni specialistiche	€ 467
Farmaci anti-iperglicemici	€ 249
Altri farmaci	€ 867
Dispositivi	€ 98

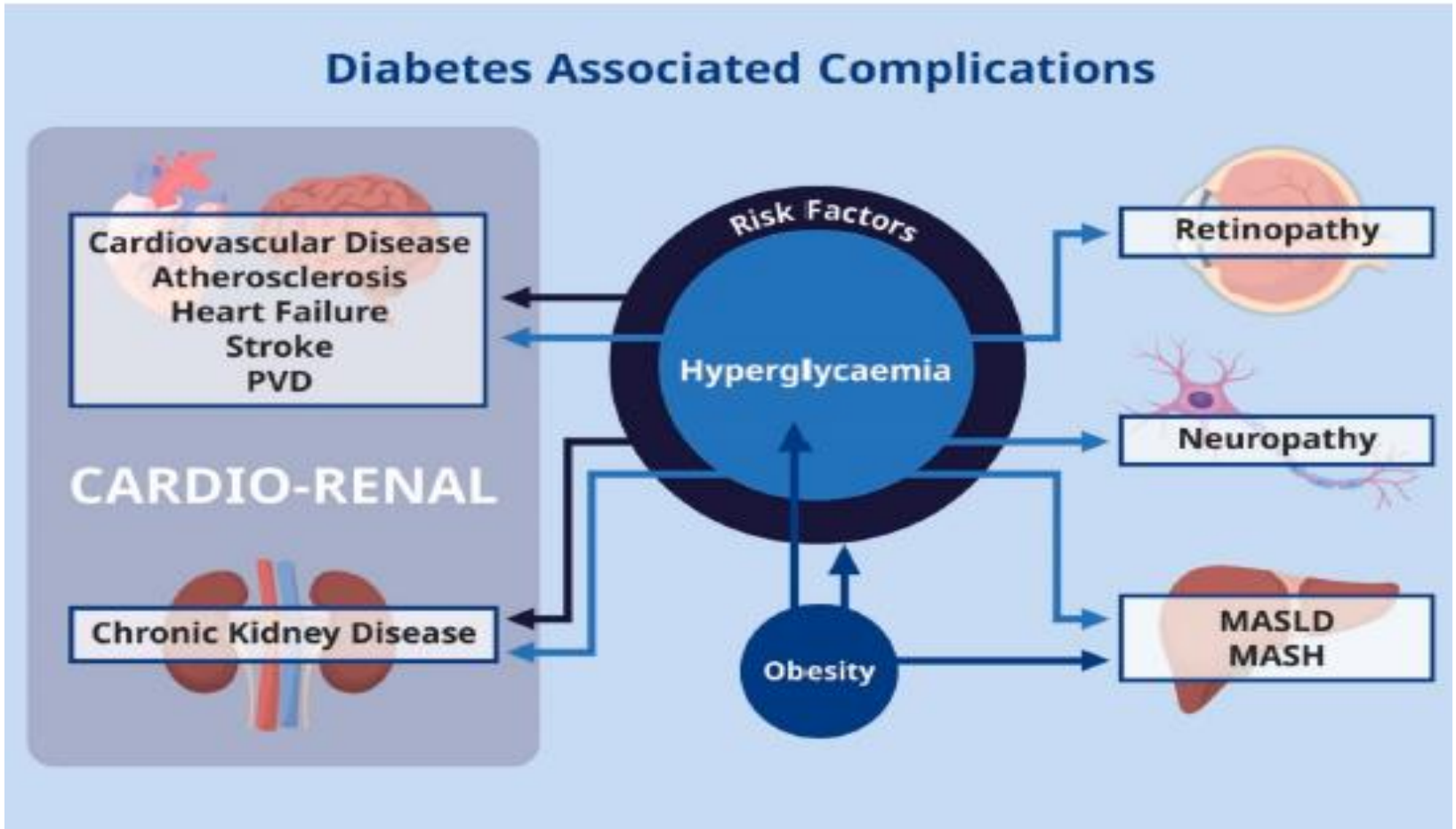
Distribuzione dei costi dei malati di DM in Italia (euro e % su totale), 2019

Voci di costo
Assenza dal lavoro
Perdita di produttività
Prepensionamento

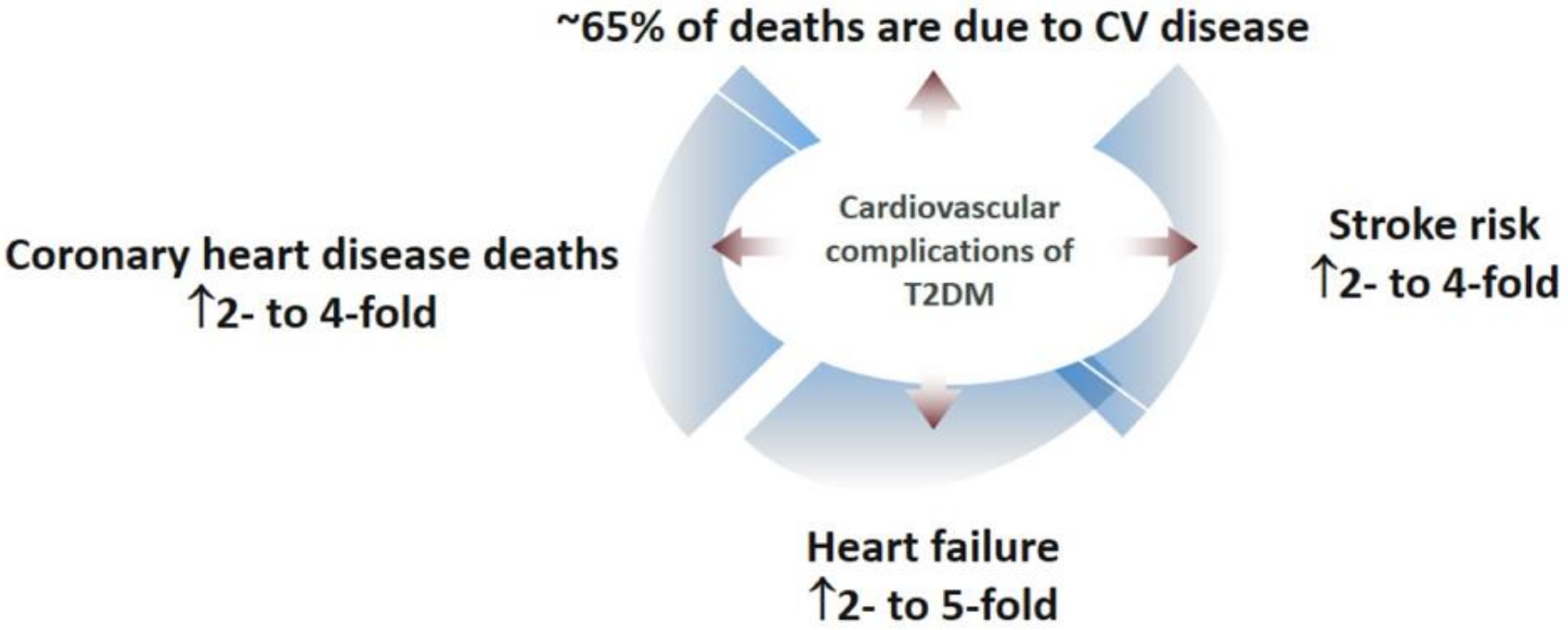
Voci di costo
Gestione malattia (10%)
Gestione complicanze e comorbidità (90%)

(*) Marcellusi, A., Viti, R., Mecozzi, A., & Mennini, F. S. (2016), "The direct and indirect cost of diabetes in Italy: a prevalence probabilistic approach". *The European Journal of Health Economics*, *17*, 139-147.

Fonte: The European House – Ambrosetti su dati Osservatorio ARNO Diabete 2019, 2024


Diabetes Associated Complications
Cardiovascular Disease
Atherosclerosis
Heart Failure
Stroke
PVD
CARDIO-RENAL
Chronic Kidney Disease
Risk Factors
Hyperglycaemia
Obesity
Retinopathy
Neuropathy
MASLD
MASH

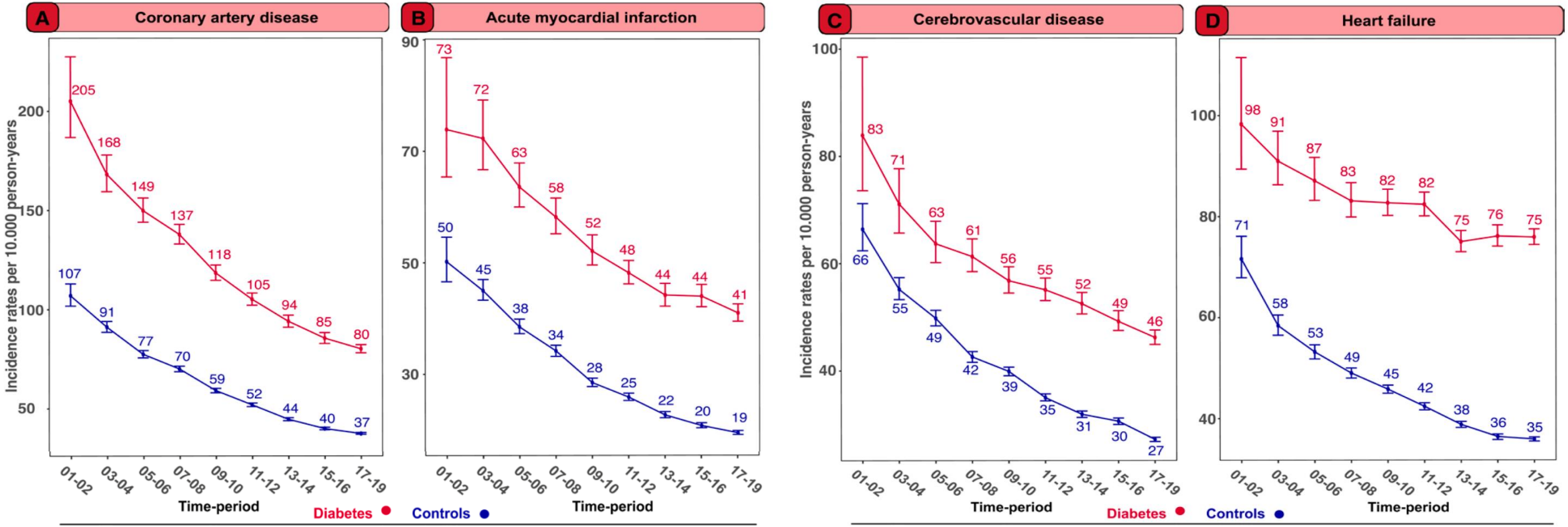
Cardiovascular Disease and diabetes



1. Klimek P et al. PLoS Comput Biol 2015;11:e1004125; 2. Pantalone KM et al. BMJ Open Diabetes Res Care 2015;3:e000093.

Twenty Years of Cardiovascular Complications and Risk Factors in Patients With Type 2 Diabetes: A Nationwide Swedish Cohort Study

In all, 679 072 individuals with T2D and 2 643 800 of their control subjects were included in the study.

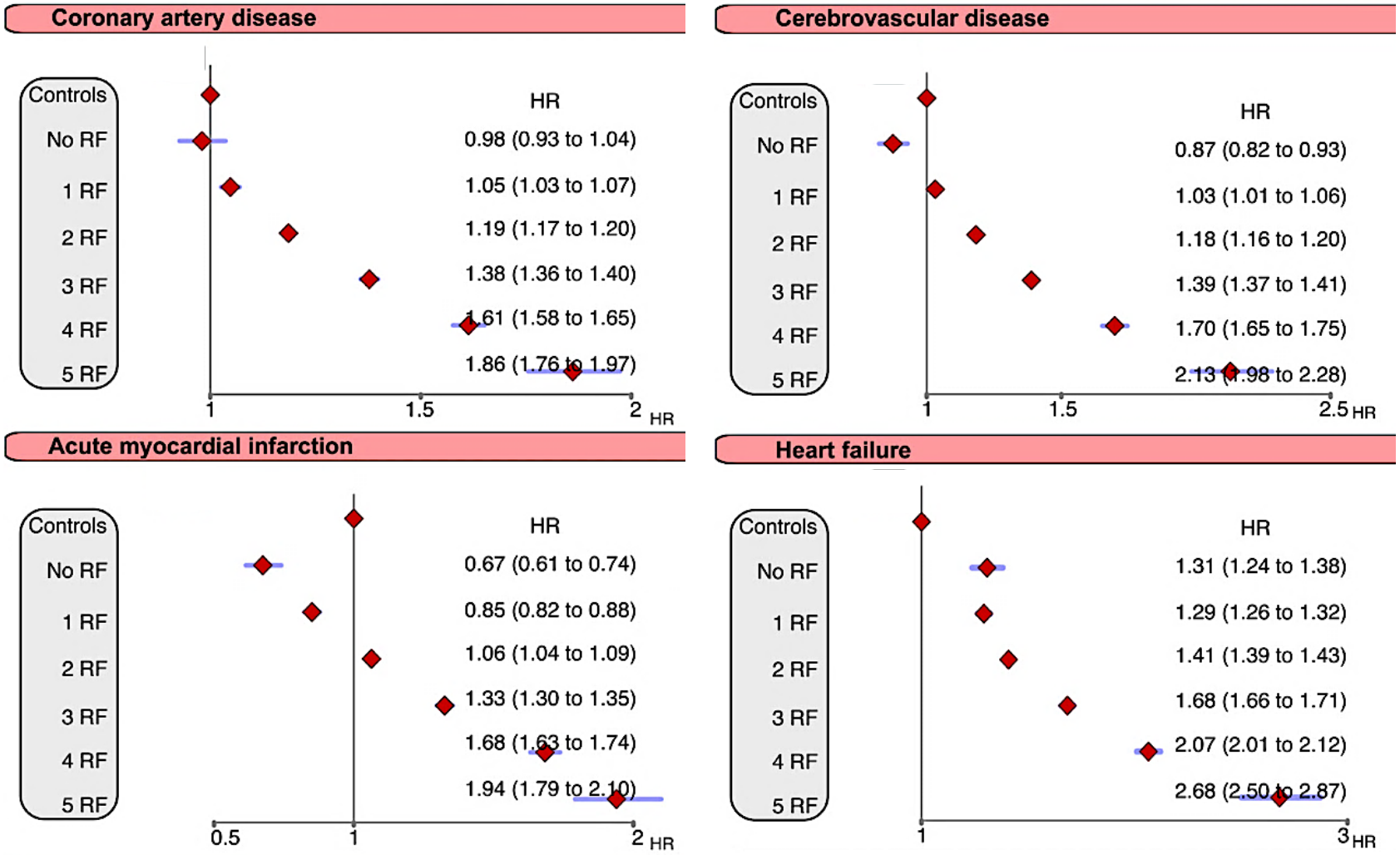


Sattar N, et al. Circulation. 2023;147:1872-1886.

Twenty Years of Cardiovascular Complications and Risk Factors in Patients With Type 2 Diabetes: A Nationwide Swedish Cohort Study

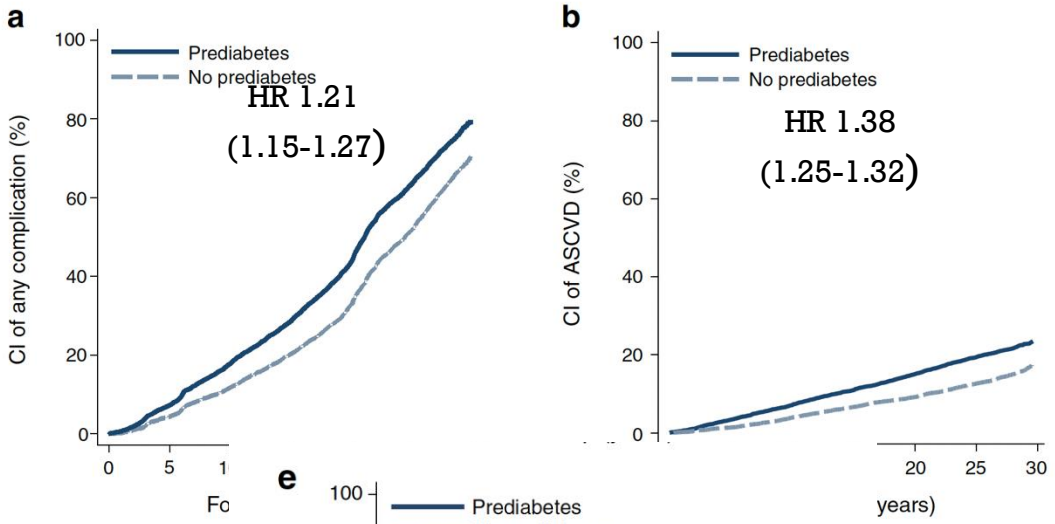
Risk factors included:

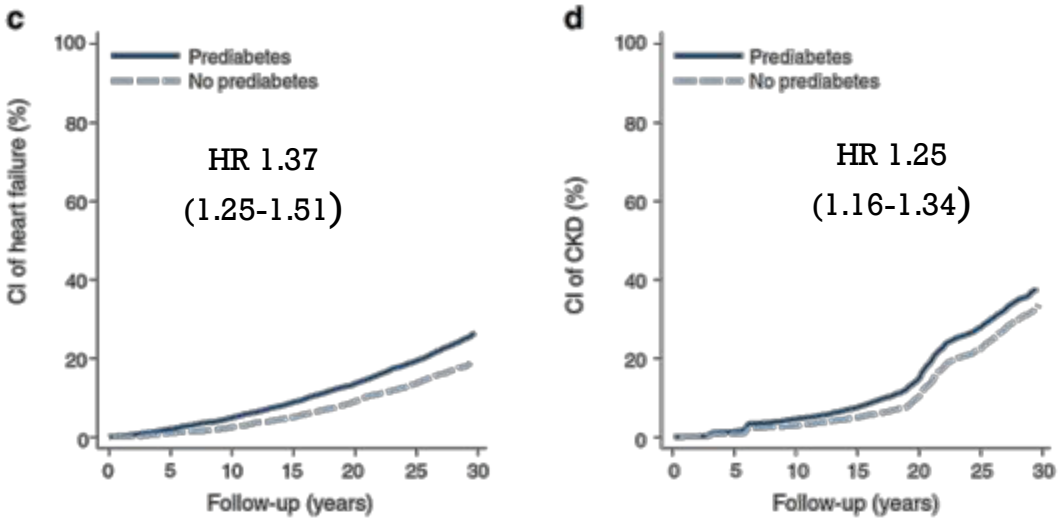
- HbA1c,
- BP (SBP and DBP),
- LDL-C,
- current smoking,
- albuminuria.

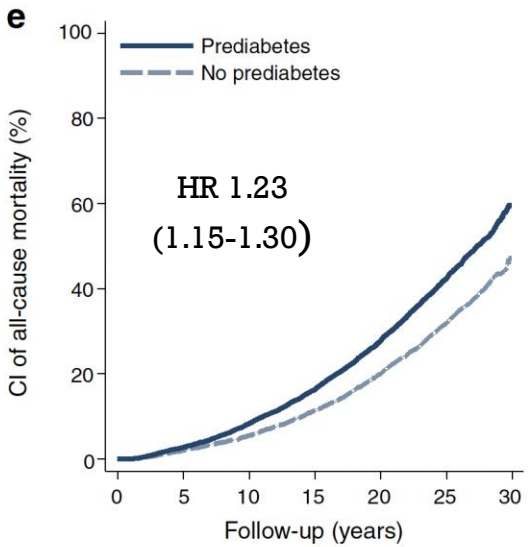


Sattar N, et al. Circulation. 2023;147:1872-1886.

Prediabetes is associated with elevated risk of clinical outcomes even without progression to diabetes



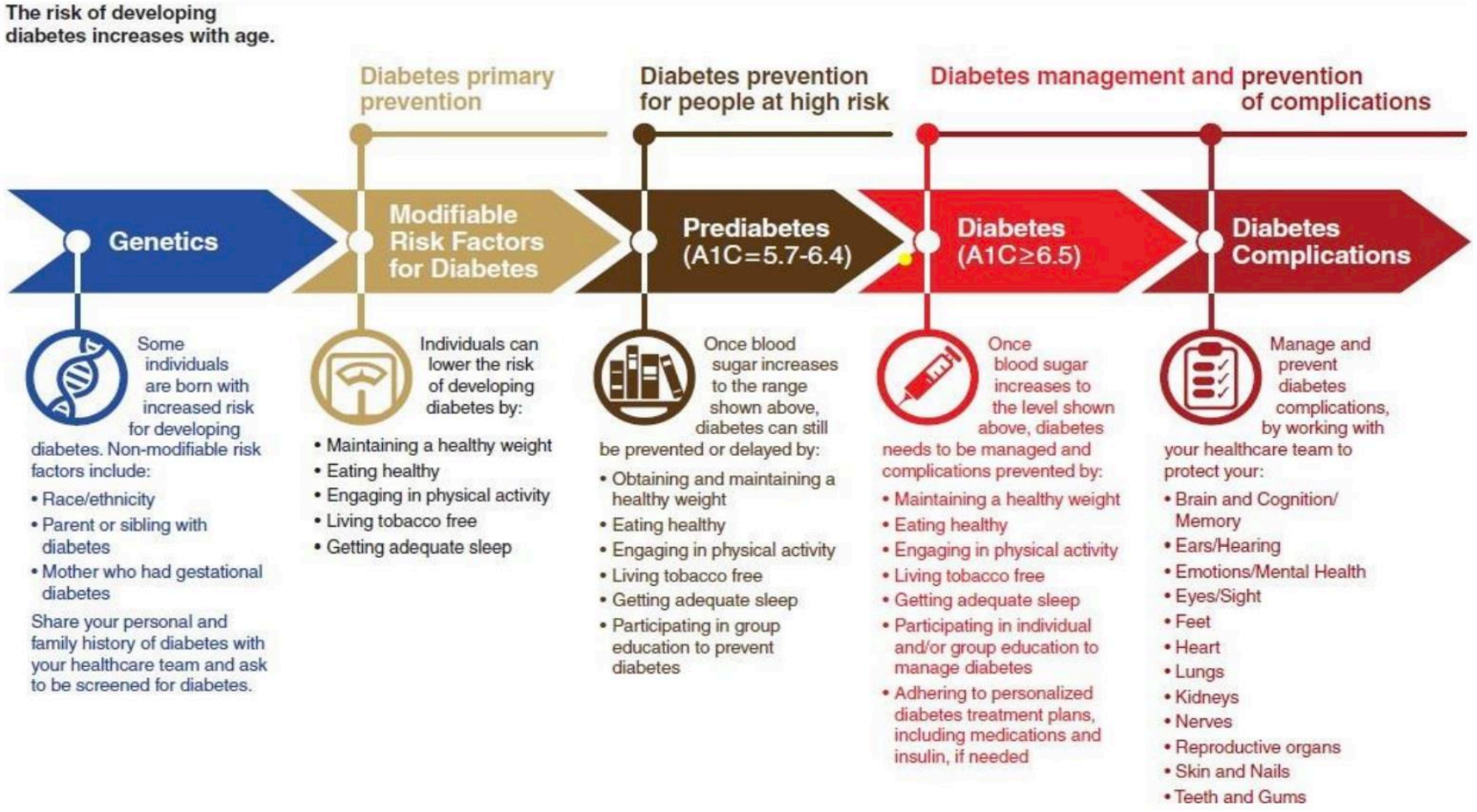




- In 10,310 participants from the Atherosclerosis Risk in Communities (ARIC) Study without diabetes at baseline (1990–1992), the associations of prediabetes with about 30 year incidence of complications has been evaluated.
- Prediabetes contributes to the risk of clinical outcomes even without progression to diabetes.

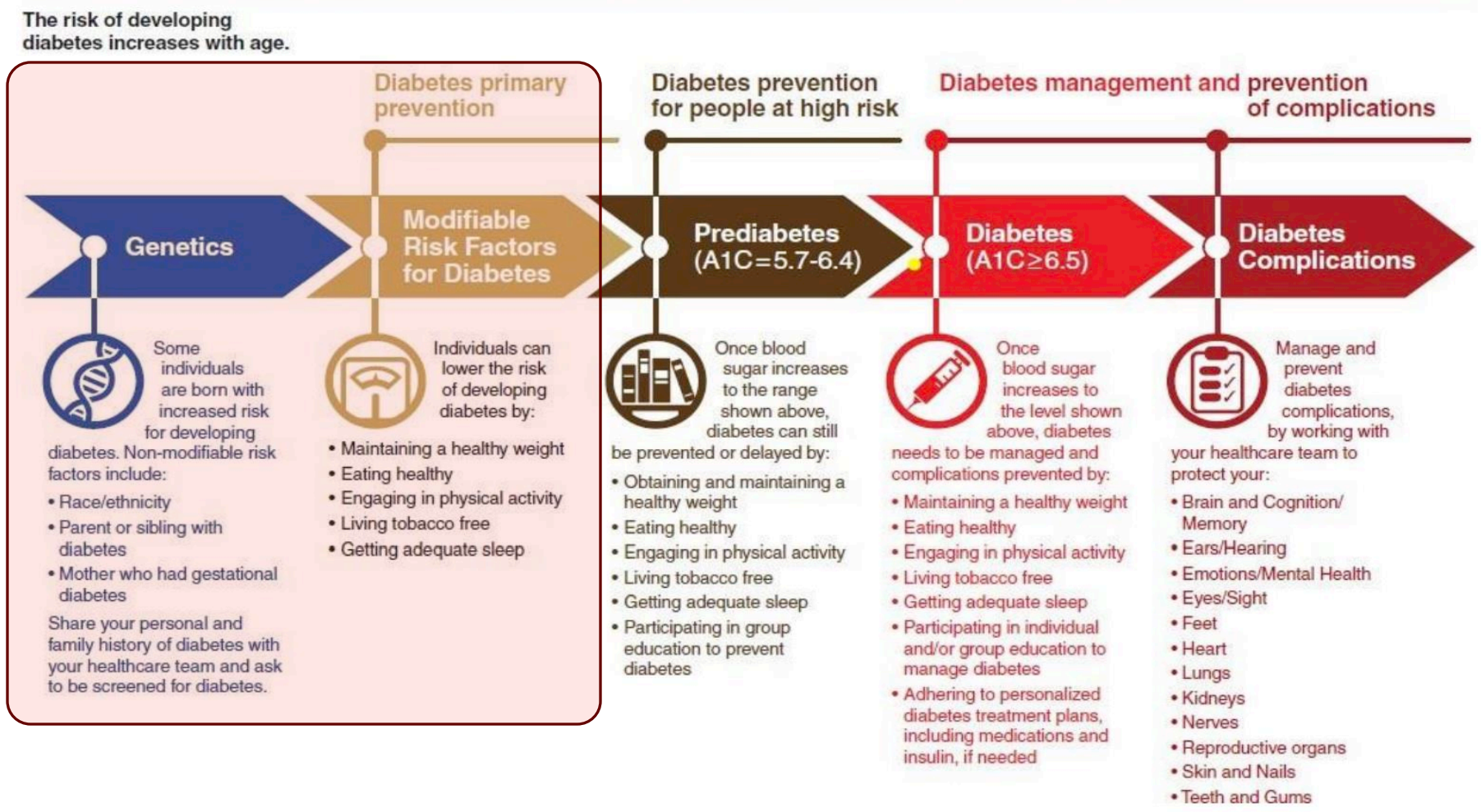
Rooney MR et al. Diabetologia 2024. Published online 12 novembre 2024

Lifetime management of risk factors in prevention of (type 2) diabetes and its complications



ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline – Type 2 Diabetes. Accessed at: https://www.ecuhealth.org

Lifetime management of risk factors in prevention of (type 2) diabetes and its complications



ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline – Type 2 Diabetes. Accessed at: https://www.ecuhealth.org

HEALTHY LIFESTYLE:
Adoption of a healthy lifestyle is critical for prevention and delay of T2D and is the first line in the treatment of T2D.

Healthy lifestyle prevention strategies include:

5. Get adequate sleep

2. Adopt healthy eating

4. Live tobacco free

3. Be more physically active

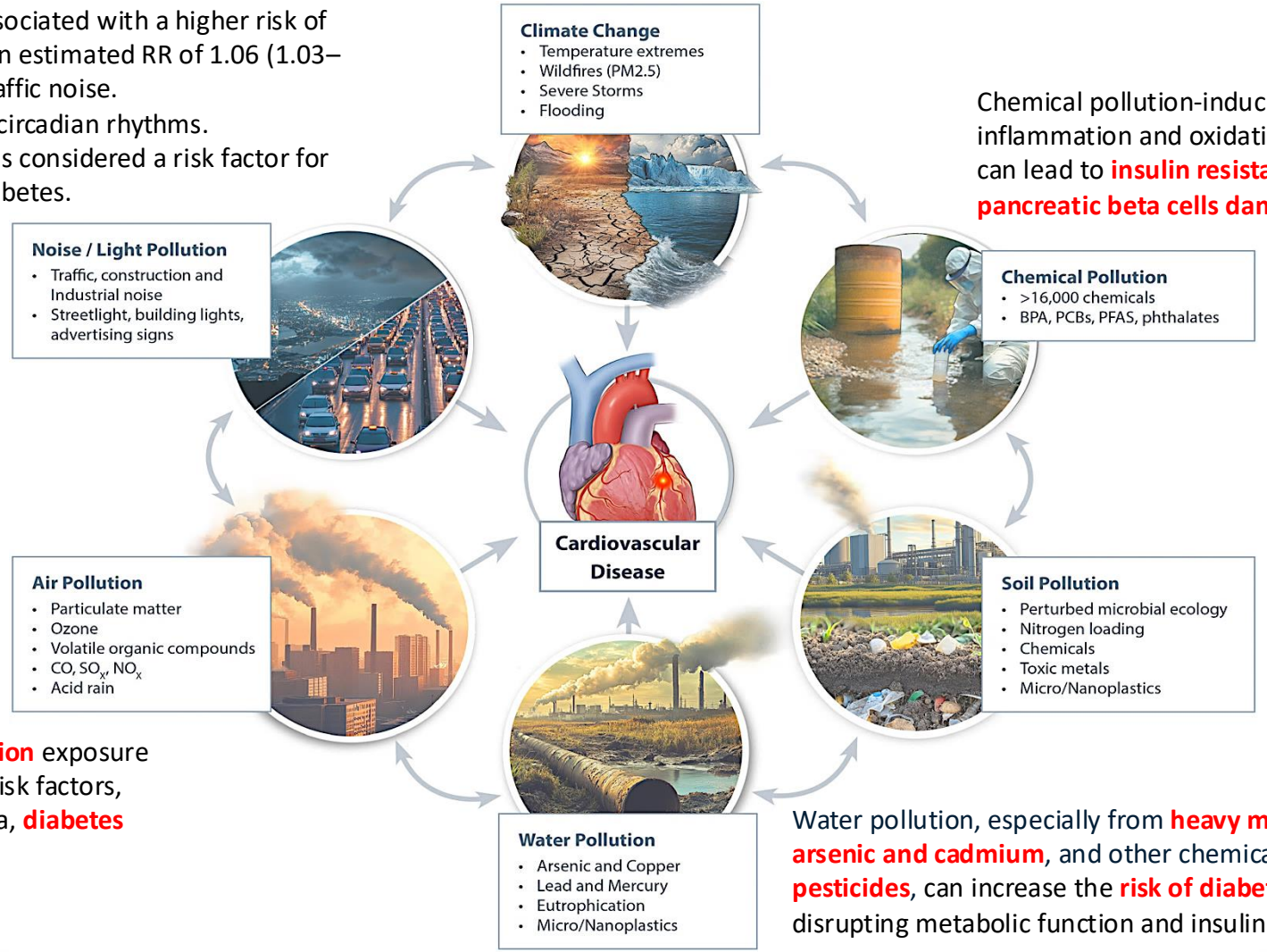
1. Maintain a healthy weight

6. Receive recommended vaccines

ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline – Type 2 Diabetes. Accessed at: https://www.ecuhealth.org

A comprehensive review/expert statement on environmental risk factors of cardiovascular disease (and diabetes)

Road traffic noise is associated with a higher risk of **type 2 diabetes**, with an estimated RR of 1.06 (1.03–1.09) per 10 dB road traffic noise.
Nocturnal noise alters circadian rhythms.
Artificial light at night is considered a risk factor for the development of diabetes.



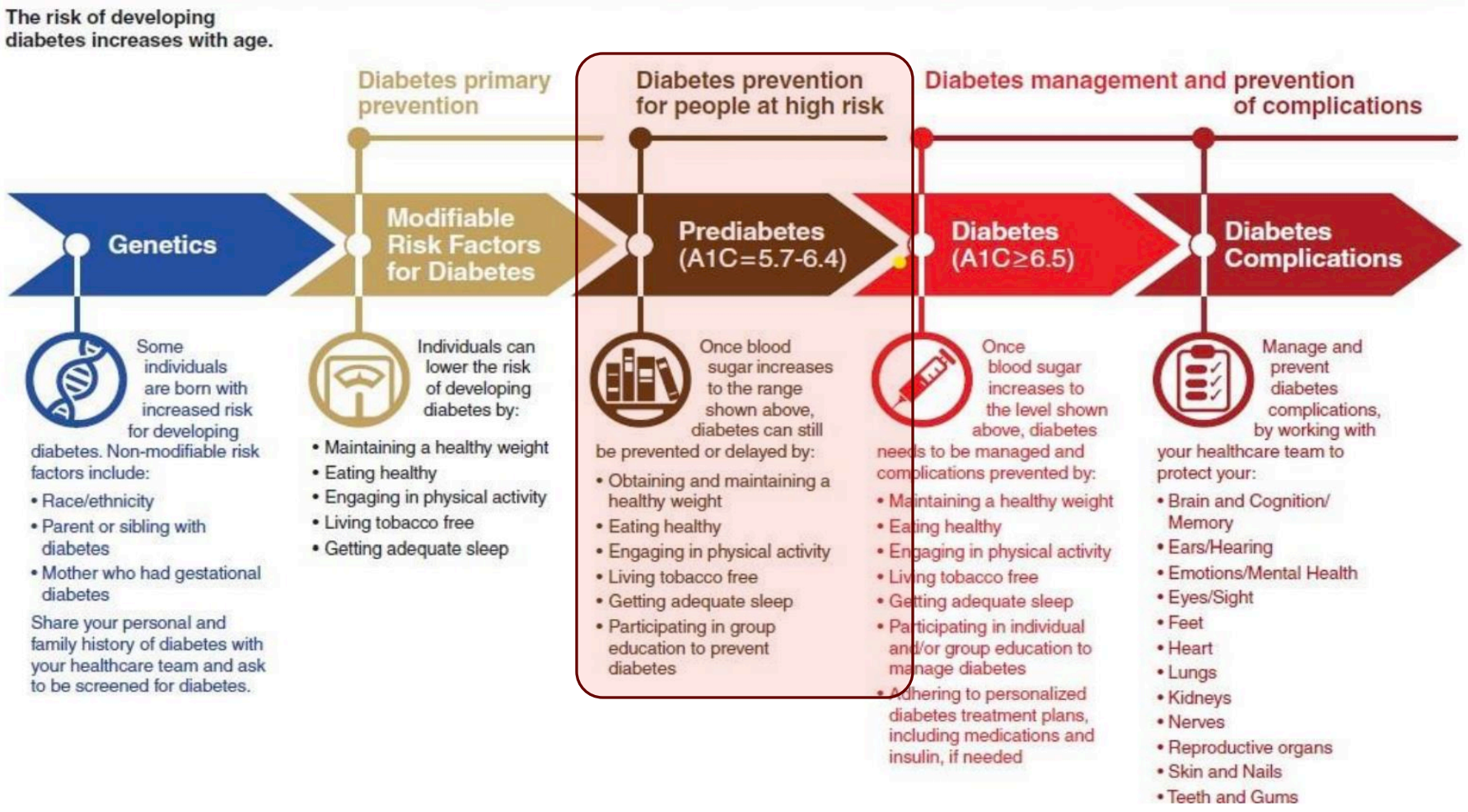
Chemical pollution-induced inflammation and oxidative stress can lead to **insulin resistance and pancreatic beta cells damage**.

There is robust evidence that **air pollution** exposure contributes to the development of CV risk factors, including hypertension, hyperlipidaemia, **diabetes mellitus**, and obesity.

Water pollution, especially from **heavy metals like arsenic and cadmium**, and other chemicals such as **pesticides**, can increase the **risk of diabetes** by disrupting metabolic function and insulin action.

Munzel T et al. Cardiovascular Research 2025; 121: 1653–1678

Lifetime management of risk factors in prevention of (type 2) diabetes and its complications



ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline – Type 2 Diabetes. Accessed at: https://www.ecuhealth.org

SCREENING:

Screening is an effective way to detect T2D at its earliest stages when lifestyle and medication options might be the most effective in preventing further progression or complications.

Screening through

- an informal assessment of risk factors or
- with risk test

is recommended to guide on whether performing a diagnostic test for prediabetes and previously undiagnosed T2D.

Finnish Diabetes Association

Type 2 diabetes risk assessment form

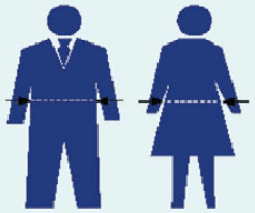
Circle the right alternative and add up your points.

1. Age
0 p. Under 45 years
2 p. 45–54 years
3 p. 55–64 years
4 p. Over 64 years

2. Body mass index
(See reverse of form)
0 p. Lower than 25 kg/m²
1 p. 25–30 kg/m²
3 p. Higher than 30 kg/m²

3. Waist circumference measured below the ribs (usually at the level of the navel)

	MEN	WOMEN
0 p.	Less than 94 cm	Less than 80 cm
3 p.	94–102 cm	80–88 cm
4 p.	More than 102 cm	More than 88 cm



4. Do you usually have daily at least 30 min of physical activity at work and/or during leisure time (including normal daily activity)?
0 p. Yes
2 p. No

5. How often do you eat vegetables, fruit, or berries?
0 p. Every day
1 p. Not every day

6. Have you ever taken antihypertensive medication regularly?
0 p. No
2 p. Yes

7. Have you ever been found to have high blood glucose (e.g. in a health examination, during an illness, during pregnancy)?
0 p. No
5 p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?
0 p. No
3 p. Yes: grandparent, aunt, uncle, or first cousin (but no own parent, brother, sister or child)
5 p. Yes: parent, brother, sister, or own child

Total risk score
The risk of developing type 2 diabetes within 10 years is

Lower than 7	Low: estimated one in 100 will develop disease
7–11	Slightly elevated: estimated one in 25 will develop disease
12–14	Moderate: estimated one in 6 will develop disease
15–20	High: estimated one in three will develop disease
Higher than 20	Very high: estimated one in 2 two will develop disease

Please turn over

American Diabetes Association.
Connected for Life.

Are you at risk for type 2 diabetes?

Diabetes Risk Test

WRITE YOUR SCORE IN THE BOX.

1. How old are you?
Less than 40 years (0 points)
40–49 years (1 point)
50–59 years (2 points)
60 years or older (3 points)

2. Are you a man or a woman?
Man (1 point) Woman (0 points)

3. If you are a woman, have you ever been diagnosed with gestational diabetes?
Yes (1 point) No (0 points)

4. Do you have a mother, father, sister or brother with diabetes?
Yes (1 point) No (0 points)

5. Have you ever been diagnosed with high blood pressure?
Yes (1 point) No (0 points)

6. Are you physically active?
Yes (0 points) No (1 point)

7. What is your weight category?
See chart at right.

Height	Weight (lbs.)		
4′ 10″	119–142	143–190	191+
4′ 11″	124–147	148–197	198+
5′ 0″	128–152	153–203	204+
5′ 1″	132–157	158–210	211+
5′ 2″	136–163	164–217	218+
5′ 3″	141–168	169–224	225+
5′ 4″	145–173	174–231	232+
5′ 5″	150–179	180–239	240+
5′ 6″	155–185	186–246	247+
5′ 7″	159–190	191–254	255+
5′ 8″	164–196	197–261	262+
5′ 9″	169–202	203–269	270+
5′ 10″	174–208	209–277	278+
5′ 11″	179–214	215–285	286+
6′ 0″	184–220	221–293	294+
6′ 1″	189–226	227–301	302+
6′ 2″	194–232	233–310	311+
6′ 3″	200–239	240–318	319+
6′ 4″	205–245	246–327	328+
	1 point	2 points	3 points

If you weigh less than the amount in the left column: **0 points**

ADD UP YOUR SCORE

Adapted from Bang et al., Ann Intern Med 151:775–783, 2009 • Original algorithm was validated without gestational diabetes as part of the model

If you scored 5 or higher:

You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes, a condition in which blood glucose levels are higher than normal but not yet high enough to be diagnosed as diabetes. Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanic/Latino individuals, Native Americans, Asian Americans, and Native Hawaiians and Pacific Islanders.

Higher body weight increases diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weight than the rest of the general public (about 15 pounds lower).

Lower your risk:

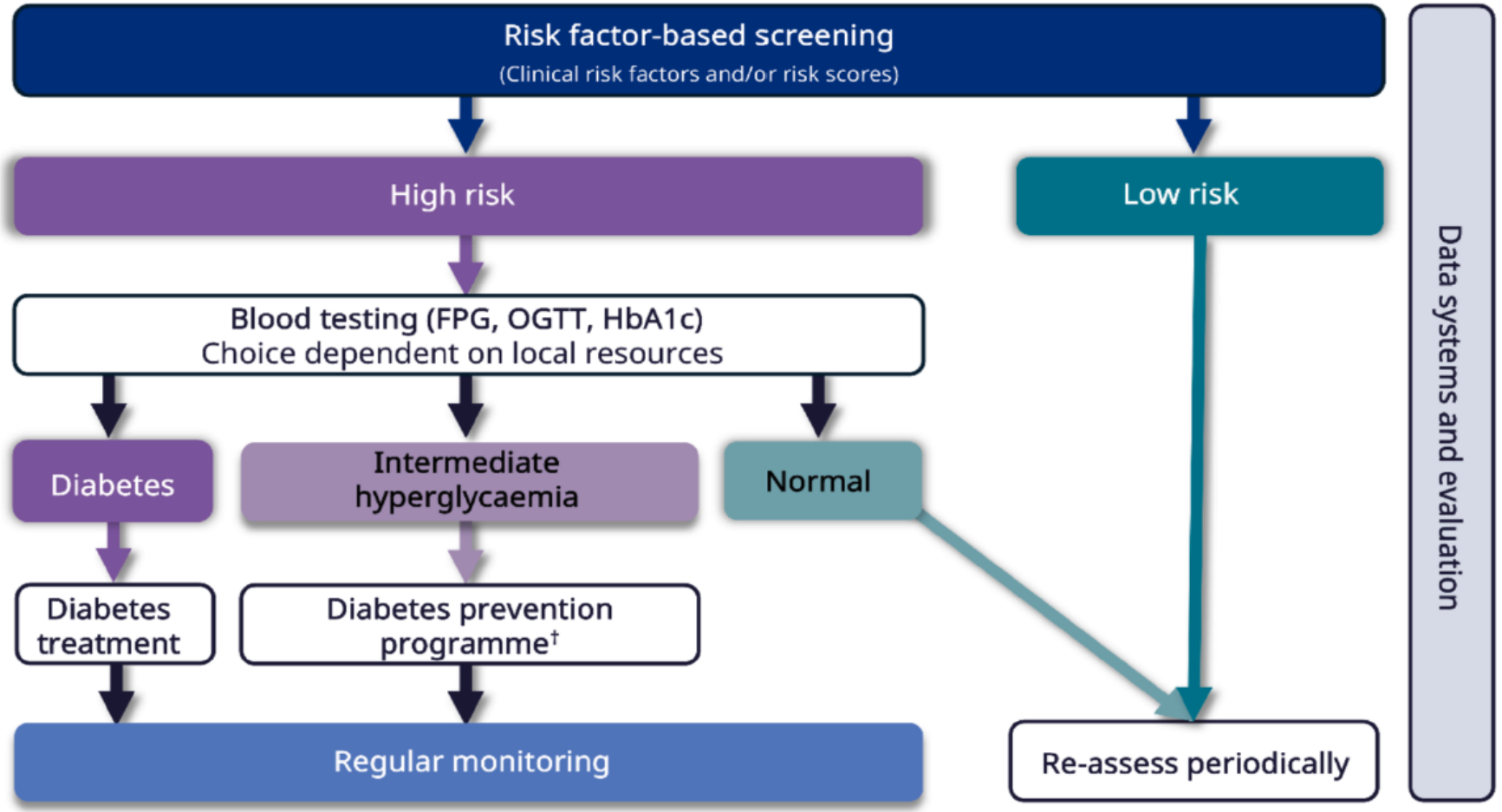
The good news is you can manage your risk for type 2 diabetes. Small steps make a big difference in helping you live a longer, healthier life.

If you are at high risk, your first step is to visit your doctor to see if additional testing is needed.

Visit diabetes.org or call 1-800-DIABETES (800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk

ECU Health Clinical Evidence Review. Accessed at: https://www.ecuhealth.org - ADA Standards of Care in Diabetes—2025. Diabetes Care 2025;48(Suppl. 1):S50–S58

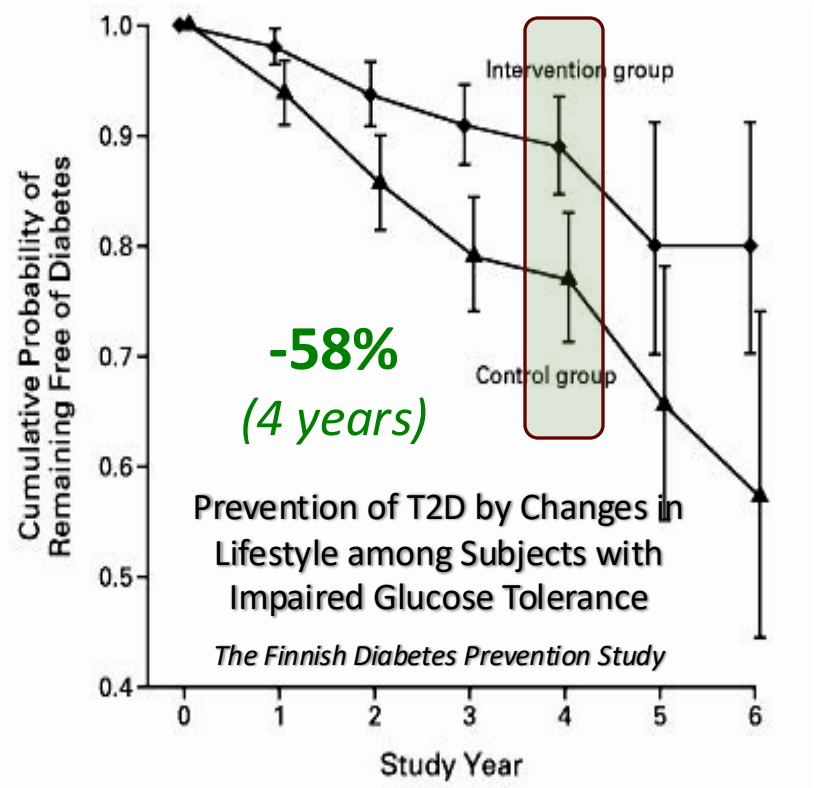
Overview of high-risk type 2 diabetes screening and prevention programmes



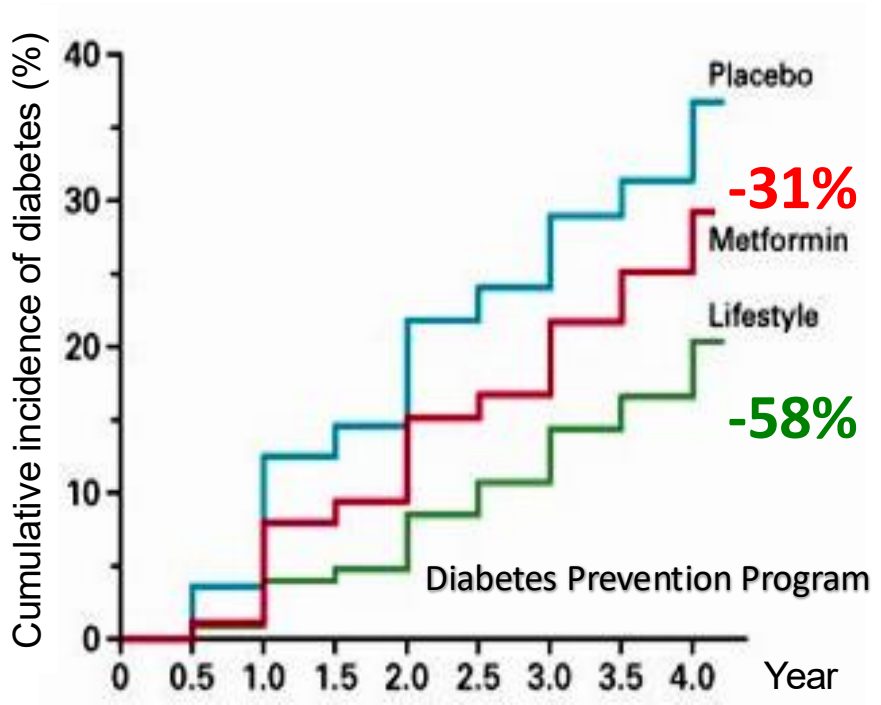
Colagiuri S et al. Diabetes Research and Clinical Practice 2025; 222: 112145

Effects on diabetes incidence of changes in lifestyles in high-risk subjects

DPS



DPP



Refer to an intensive lifestyle behavior change program to achieve and maintain a weight reduction of at least 7% through

- healthy reduced-calorie
- diet and
- ≥150 min/week of moderate-intensity physical activity

Tuomilehto J et al., N Engl J Med 344: 1343-1350, 2001
DPP Research Group. N Engl J Med 346: 393-403, 2002

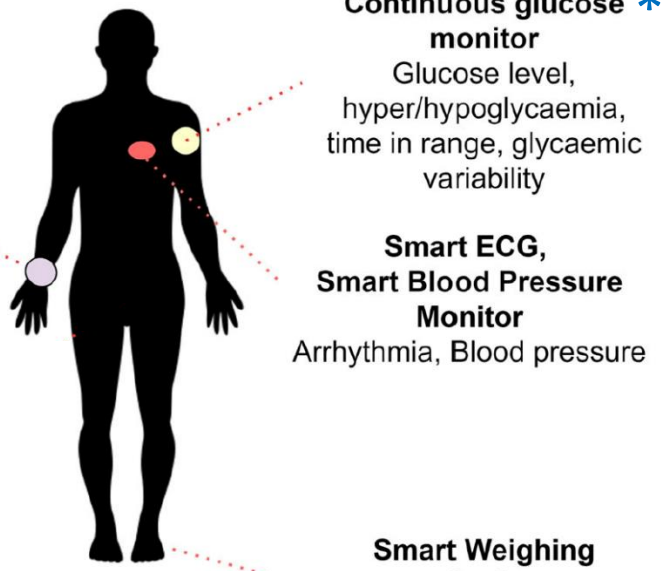
Use of technology in prediabetes and precision prevention

Integrating technologies as part of a multicomponent strategy in diabetes prevention

Certified technology-assisted programs may effectively deliver prevention lifestyle interventions

Wearable

Wearable and technologies for weight control, activity tracking, and glucose monitoring among people with prediabetes



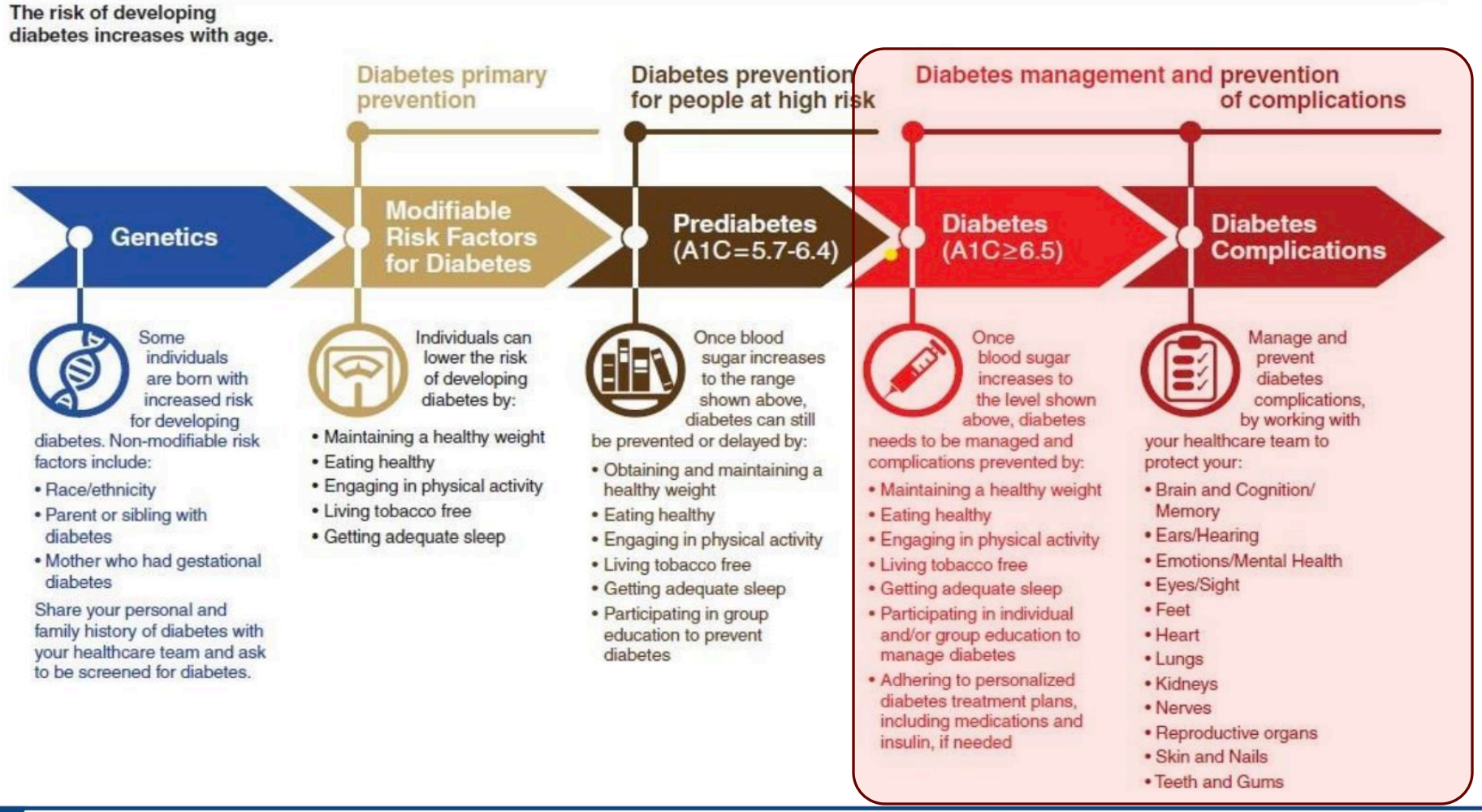
* As a motivational tool to promote lifestyle change.

Different Modes in Lifestyle Intervention for the Prevention of Type 2 Diabetes and the Reversion to Normoglycemia in Adults With Prediabetes

Modes	Incidence of T2DM	Regression to normo-glycemia
Lyfestyle interventions	-46% P<0.001	+45% P=0.006
Mixed interventions	-37% P<0.001	+87% P=0.001
Digital health interventions	-12% P=0.06	NS

He J, et al. J Diabetes Investig. 2025 Jul;16(7):1217-1231.
Wang Y, et al. J Med Internet Res. 2025 Jan 29;27:e63975.

Lifetime management of risk factors in prevention of (type 2) diabetes and its complications



ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline – Type 2 Diabetes. Accessed at: https://www.ecuhealth.org

Cardiovascular and Kidney Outcomes and Mortality With Injectable and Oral GLP-1RAs in Individuals With Type 2 Diabetes: A Systematic Review and Meta-analysis of Randomized Trials

Do long-acting glucagon-like peptide 1 receptor agonists including subcutaneous and oral formulations, improve cardiovascular and kidney outcomes and mortality in type 2 diabetes?

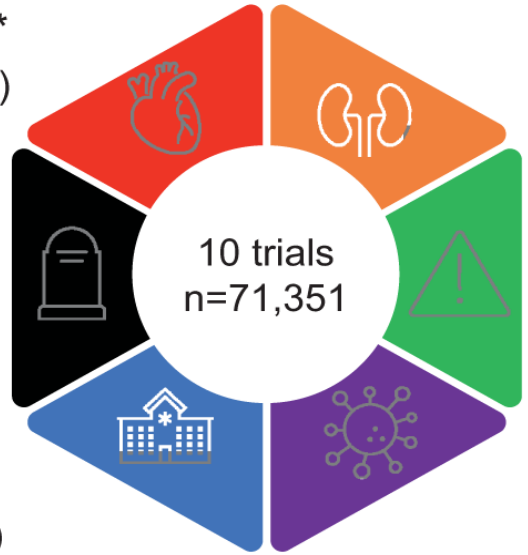
Systematic review & meta-analysis of randomized placebo-controlled trials including new data from SOUL & FLOW

Major adverse cardiovascular events*

↓ 14% (HR 0.86; 95% CI 0.81, 0.90)

Composite kidney outcome*

↓ 17% (HR 0.83; 95% CI 0.75, 0.92)



All-cause mortality*

↓ 12% (HR 0.88; 95% CI 0.82, 0.93)

Safety outcomes

↔ severe hypoglycemia, retinopathy, pancreatitis

Hospitalization for heart failure*

↓ 14% (HR 0.86; 95% CI 0.79, 0.93)

Safety outcomes (cancers)

↔ total cancer, pancreatic cancer, any thyroid cancer

*No significant heterogeneity by drug route (subcutaneous vs. oral)

PROSPERO registration number: CRD42024607253

Lee MMY, et al; SOUL Trial Investigators. Diabetes Care. 2025 Mar 29:dc250241.

Cardiovascular and Kidney Outcomes and Mortality With SGLT2 inhibitors in Individuals With Type 2 Diabetes: A Systematic Review and Meta-analysis of Randomized Trials

Do SGLT2 inhibitors improve cardiovascular and kidney outcomes and mortality in type 2 diabetes?

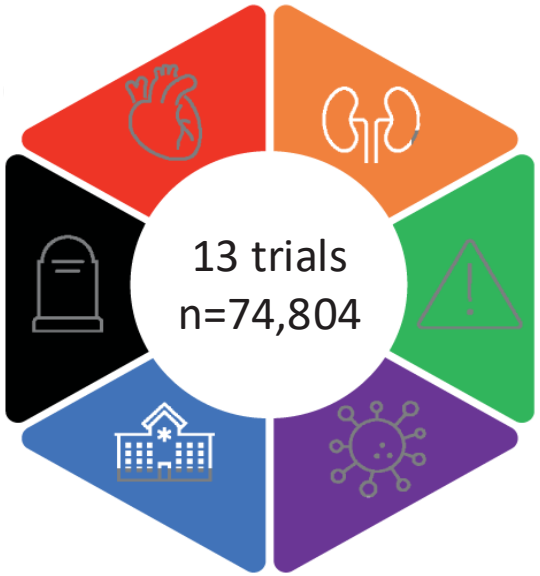
Systematic review and meta-analysis of randomized placebo-controlled trials

Cardiovascular death
↓ 14% (HR 0.86; 95% CI 0.80, 0.94)

Non-fatal myocardial infarction
↓ 10% (HR 0.90; 95% CI 0.82, 0.98)

All-cause mortality
↓ 12% (HR 0.88; 95% CI 0.84, 0.93)

Hospitalization for heart failure
↓ 34% (HR 0.66; 95% CI 0.60, 0.73)



Composite kidney outcome*
↓ 38% (HR 0.62; 95% CI 0.56, 0.68)

Acute kidney injury
↓ 21% (HR 0.79; 95% CI 0.72, 0.88)

Safety outcomes
↔ severe hypoglycemia,
↑ amputations (?), ↑ euglycemic DK, genital infection

Safety outcomes (cancers)
promise as potential anticancer agents

Shi Q et al. BMJ 2023 Apr 6; 381: e074068

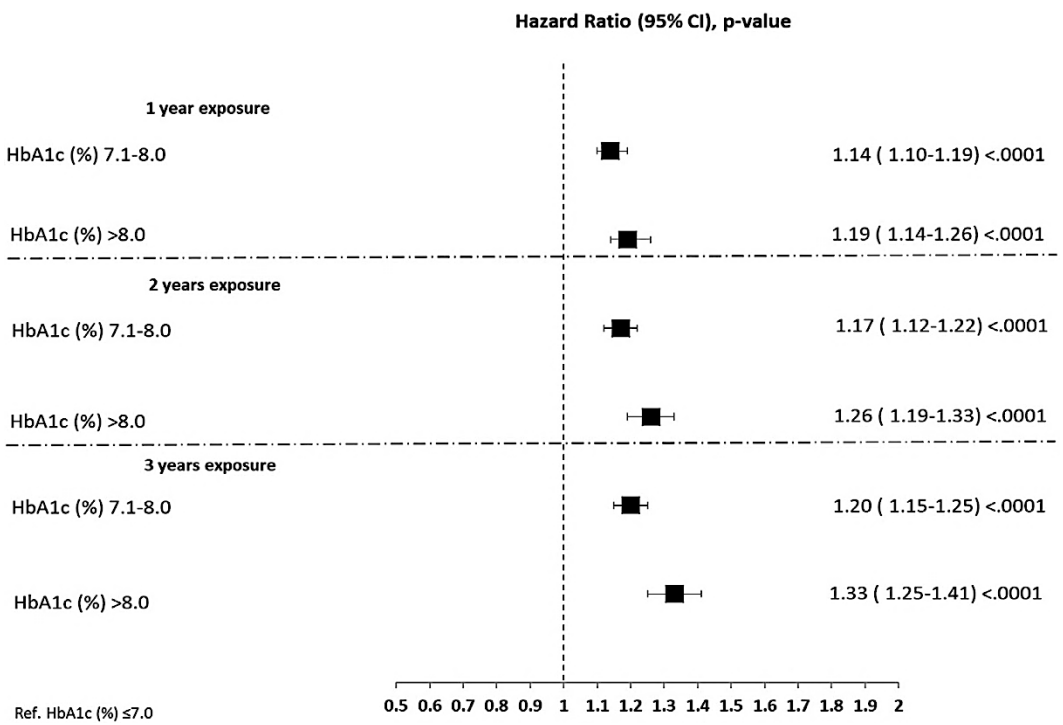
PROSPERO registration number: CRD42022351618

The Nuffield Department of Population Health Renal Studies Group and the SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium. Lancet 2022; 400: 1788-1801

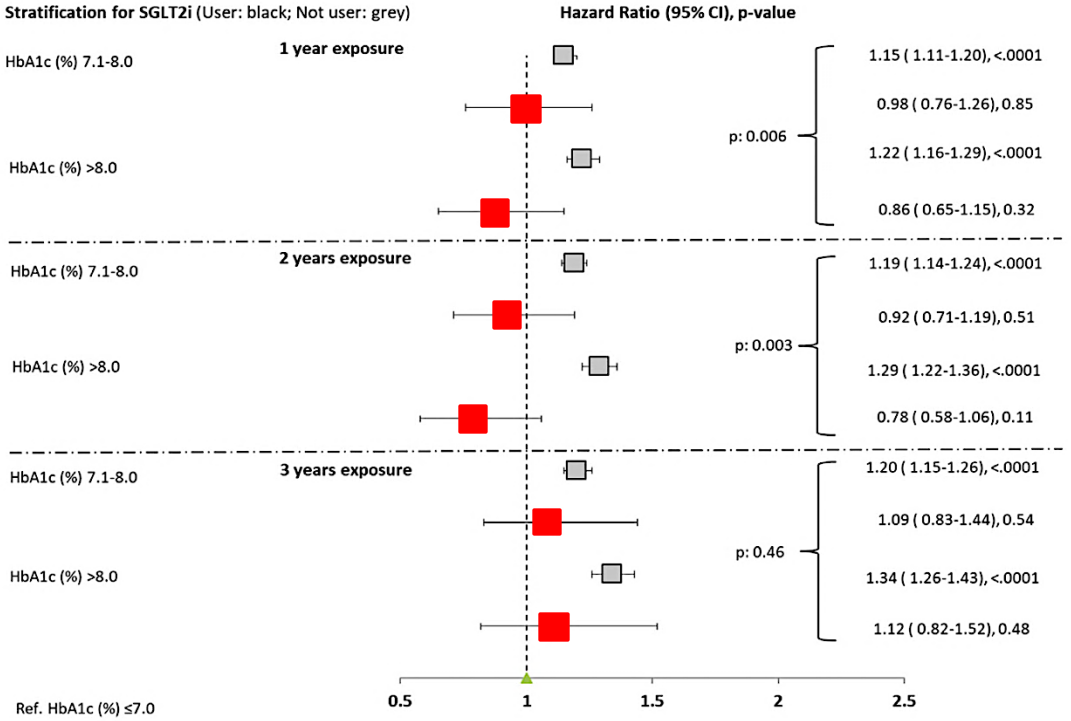
The legacy effect of hyperglycemia and early use of SGLT-2 inhibitors: a cohort study with newly-diagnosed people with type 2 diabetes

AMD Annals; 251,339 subjects with newly-diagnosed T2D and without CVD at baseline

Poor, early glycemic control and the subsequent risk of cardiovascular diseases (*HbA1c ≤ 7% is the reference*)

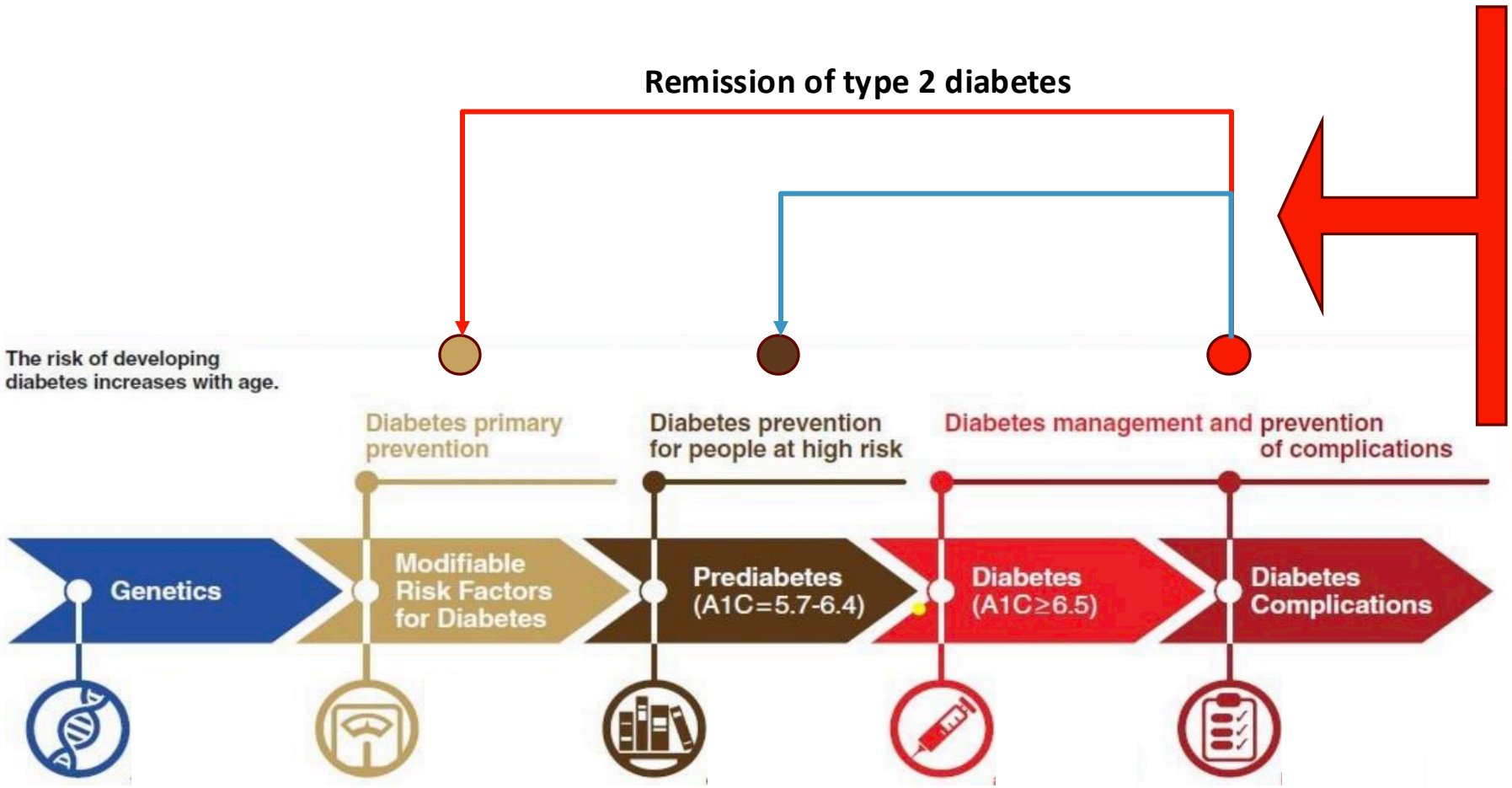


SGLT-2i, introduced in the first two years, attenuate the phenomenon of legacy effect (*HbA1c ≤ 7% is the reference*)



Ceriello A et al. Lancet Regional Heatth - Europe. 2023; 31: 100666

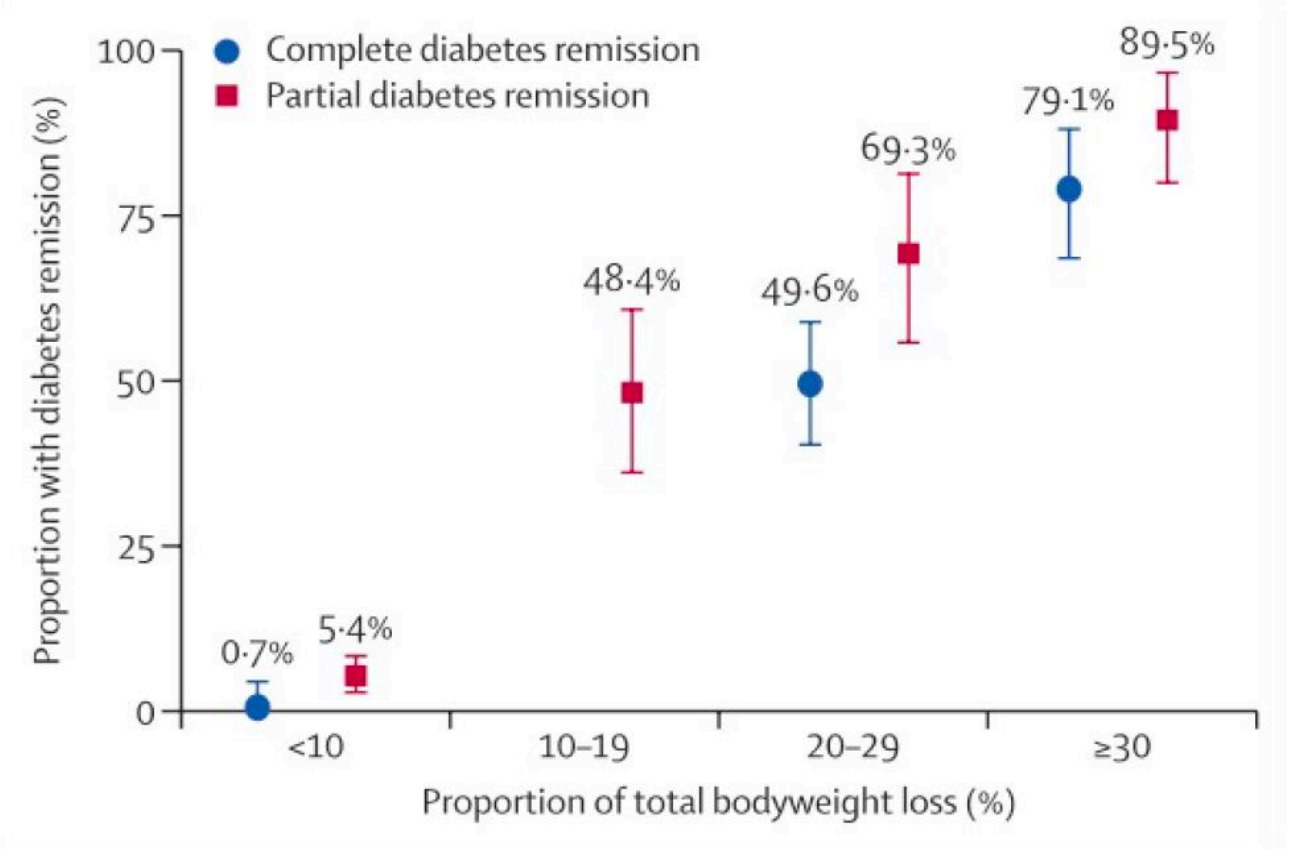
Lifetime management of risk factors in prevention of (type 2) diabetes and its complications



- Transient intensified insulin regimens
- Lifestyle interventions
- Metabolic surgery
- GLP1-RAs, GIP/GLP1-RAs

ECU Health Clinical Evidence Review: Adult, Non-Pregnant Care Guideline – Type 2 Diabetes. Accessed at: https://www.ecuhealth.org

Impact of bodyweight loss on type 2 diabetes remission: systematic review and meta-regression analysis of randomised controlled trials



Complete diabetes remission:

- HbA_{1c} <6·0%
- FPG <100 mg/dL
- Both

with no use of glucose-lowering drugs …

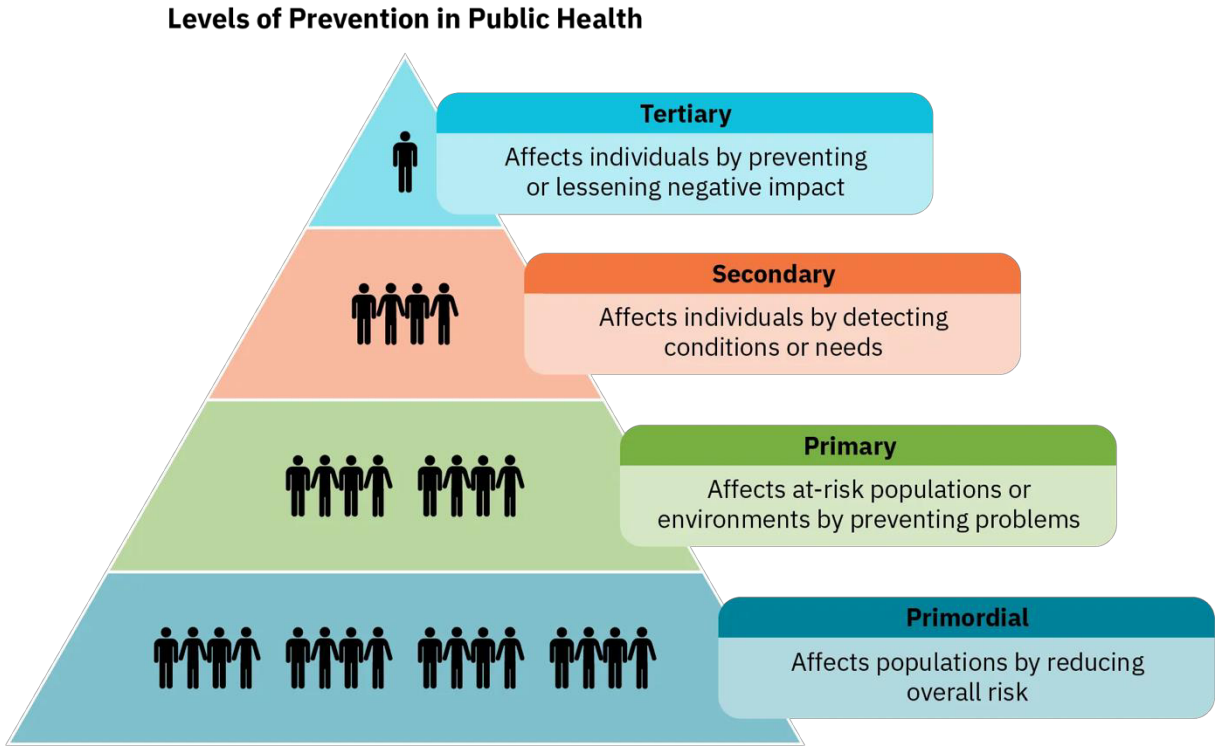
Partial diabetes remission:

- HbA_{1c} <6·5%
- FPG <126 mg/dL
- both,

with no use of glucose-lowering drugs …

… at least 1 year after a bodyweight loss intervention.

Kanbour S et al. Lancet Diabetes Endocrinol. 2025;13: 294-306.



The goals of the (Type 2) Diabetes Lifetime Care Pathway are:

- To prevent T2D to the greatest degree possible (primordial prevention)
- To delay onset of T2D for as long as possible (primary prevention and prevention in people at high risk)
- Provide a framework for T2D evidenced based care delivery in the most effective, efficient manner possible in order to prevent diabetes complications
- Engage with the opportunity to obtain T2D remission

Conclusioni e Prospettive Future

La gestione ottimale della sindrome CKM richiede un approccio olistico che integri prevenzione, screening e gestione attraverso team multidisciplinari.

1. **Approccio Integrato**
   Superare i silos specialistici per una cura collaborativa e interdisciplinare
2. **Intervento Precoce**
   Identificazione e trattamento tempestivi per prevenire la progressione della malattia
3. **Terapie Basate sull'Evidenza**
   Implementazione di farmacoterapie guidate dalle linee guida per ridurre eventi cardiovascolari e renali
4. **Equità nella Salute**
   Affrontare i determinanti sociali della salute per eliminare le disparità

Grazie per l'attenzione