

LADA

inquadramento clinico e terapia insulinica

Ernesto Maddaloni



THE DARK SIDE
OF DIABETES



Il dr. Ernesto Maddaloni dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- Abbott
- Astra-Zeneca
- Eli-Lilly
- MSD
- MTD
- NovoNordisk
- PikDare

Type 1 diabetes?



Symptoms of
Diabetes
in Children
Type-1

Diabetes mellitus type 1 symptoms in children usually develop quickly and may include

- Reduction in weight
- Increase urine frequency / bedwetting (in children more than four years)
- Feeling excess hunger and thirst
- Bad breath / Fruity- smell
- Feeling tired or lack of energy

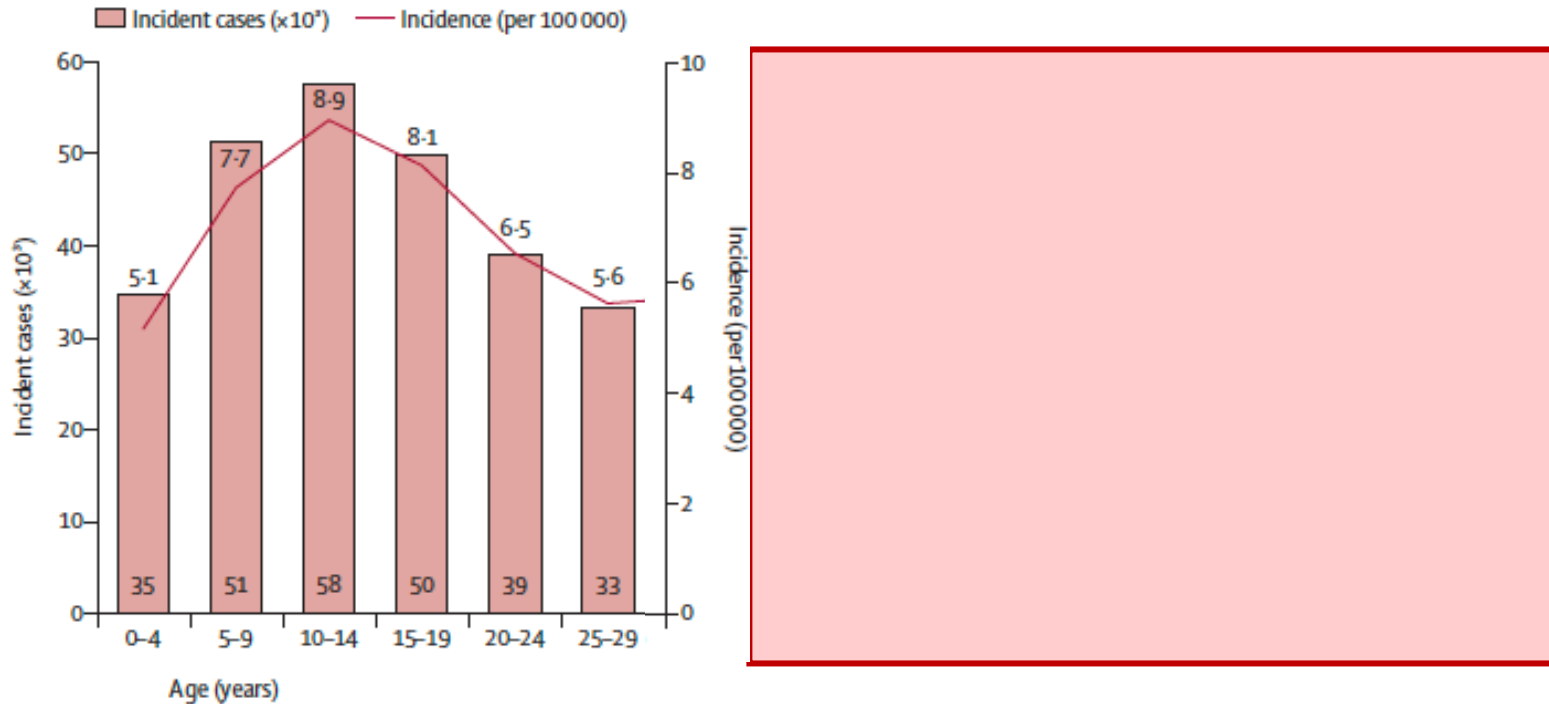
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Type 1 diabetes epidemiology



- Peak incidence: 10-14 years of age
- Greater number of total new cases among adults

- New cases of autoimmune diabetes in adults have been underreported

- Prolonged phase of onset
- Subtleties in distinguishing different diabetes types among adults

Latent autoimmune diabetes in adults (LADA)

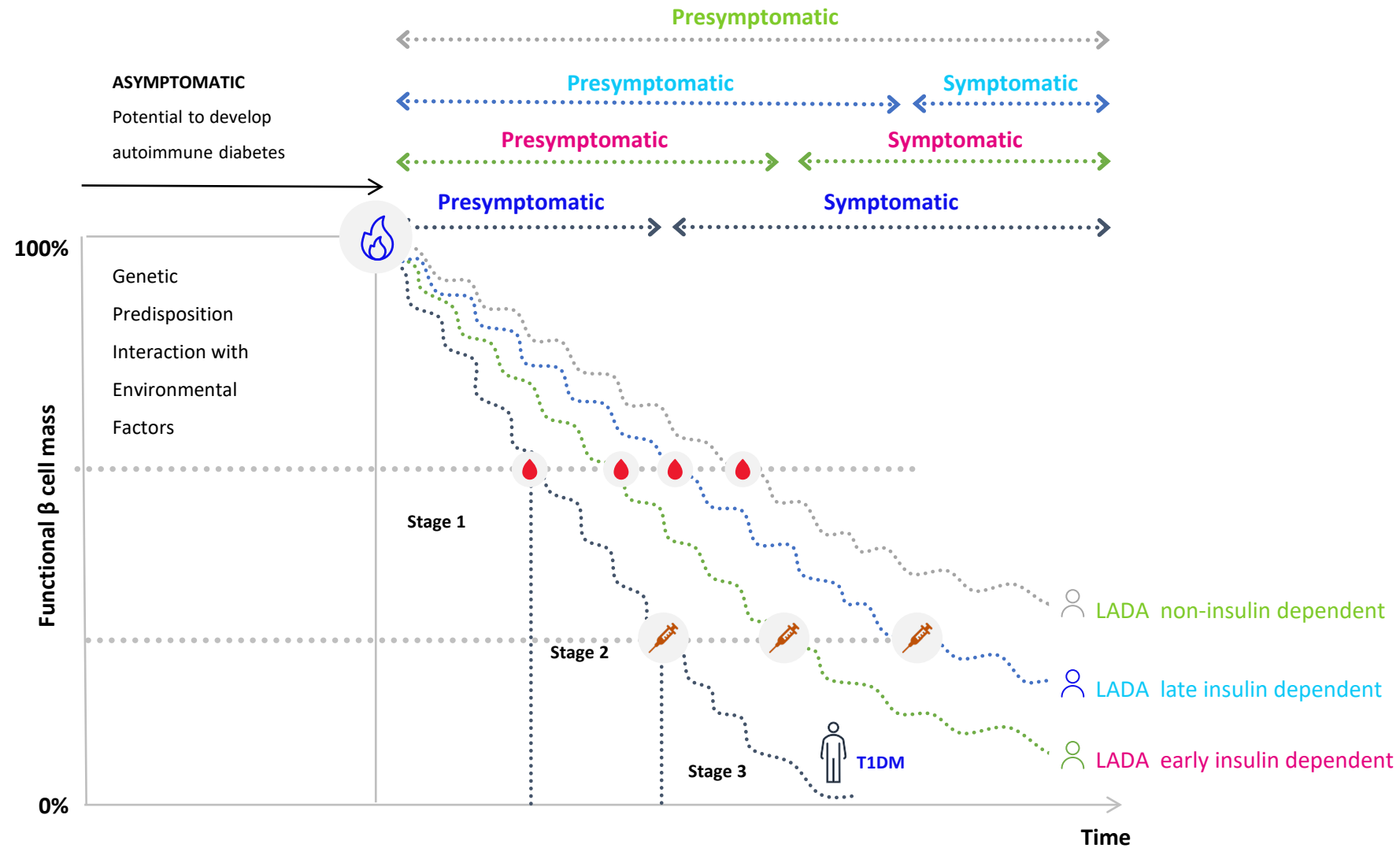
LADA is the most common form of adult-onset **autoimmune diabetes**

- recognized by the ADA and the WHO
- **later onset** vs T1D
- **slower progression** toward an absolute insulin requirement vs T1D.

The diagnosis of LADA is based on the following criteria (IDS 2005)

- Age at diagnosis >30 years
- Presence of at least one circulating antibody (GADA, IA2)
- Insulin independence for the first 6 months after the diagnosis

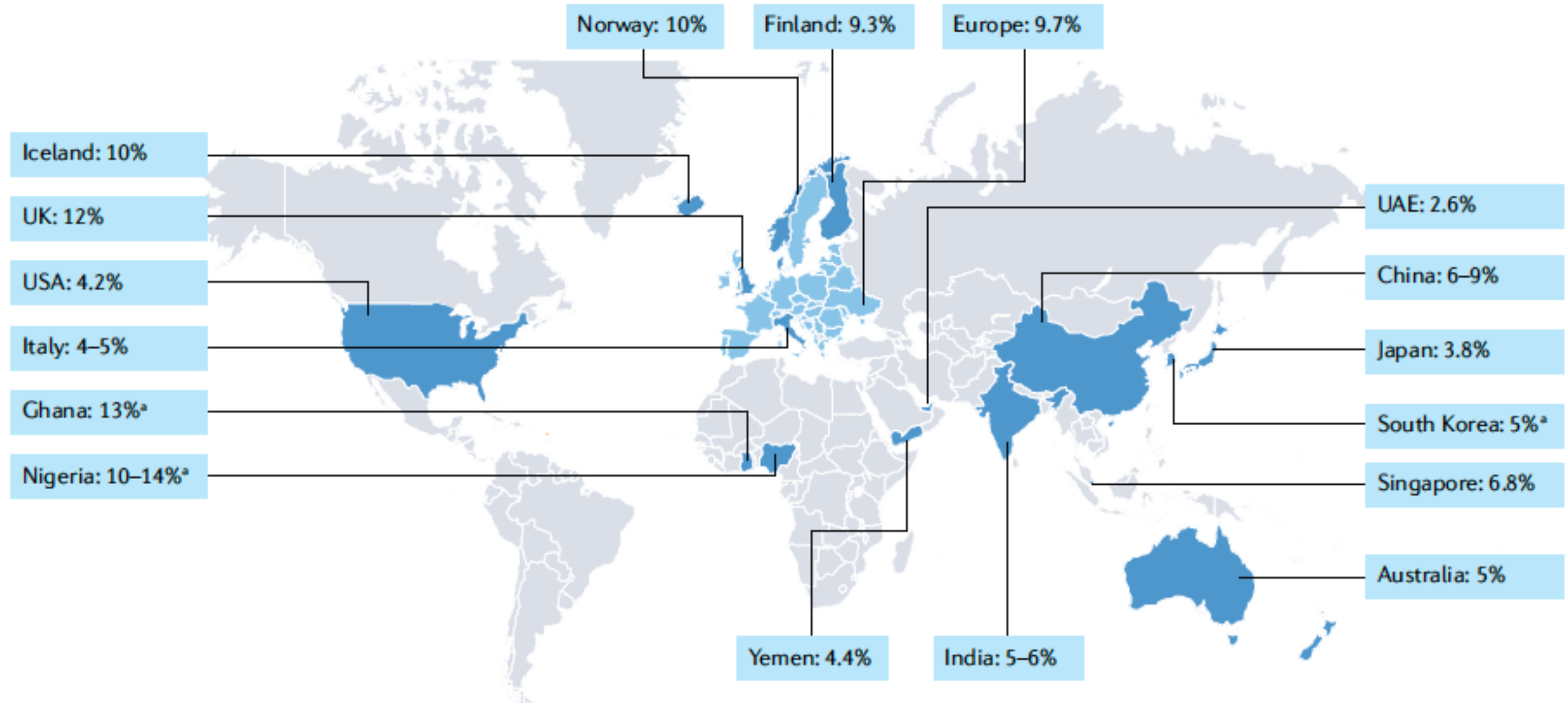
Natural history of autoimmune diabetes



Clinical features by type of diabetes

	Type 1 Diabetes	LADA
Age at diagnosis	Childhood-young adults	Adults
Onset	Acute onset	Slow
Beta-cell function	↓↓↓	↓
Insulin-dependence	At the onset	> 6 months (even years)
Insulin-resistance	↔	↑ ↔
Body Mass Index	Normal-underweight	Normal-overweight
Metabolic syndrome	↔	↑ ↔

Frequency of pancreatic autoantibodies in adults with a clinical diagnosis of type **2** diabetes



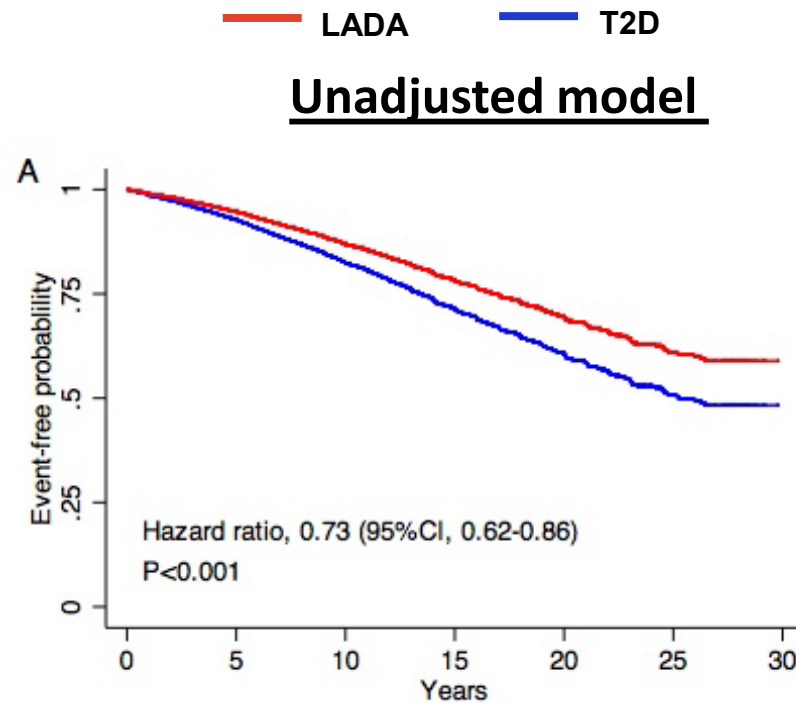


Do differences in the pathophysiology and metabolic features translates in different clinical outcomes?

Major adverse cardiovascular events

Clinical outcomes

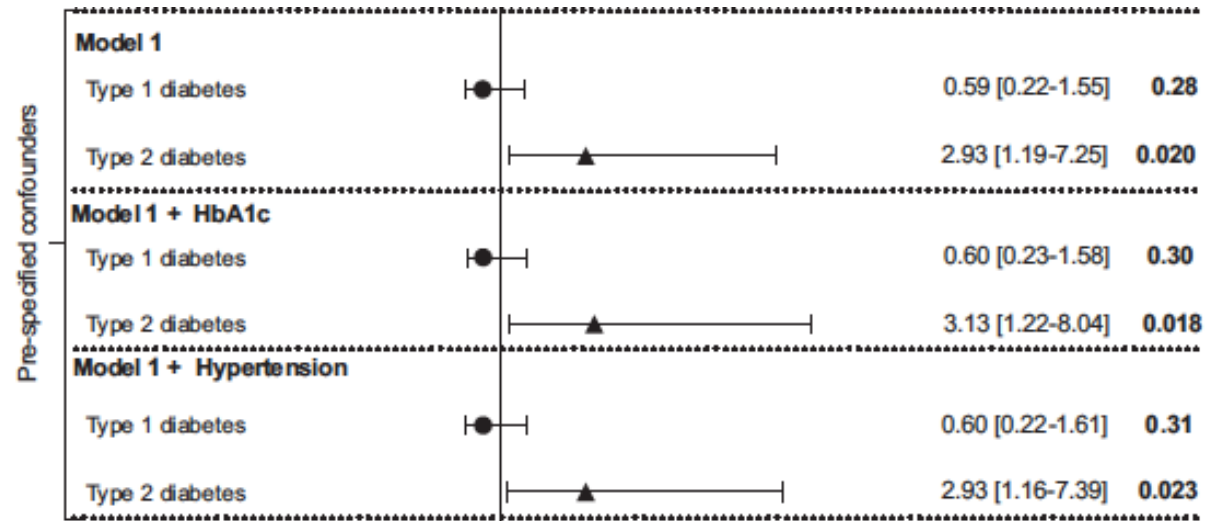
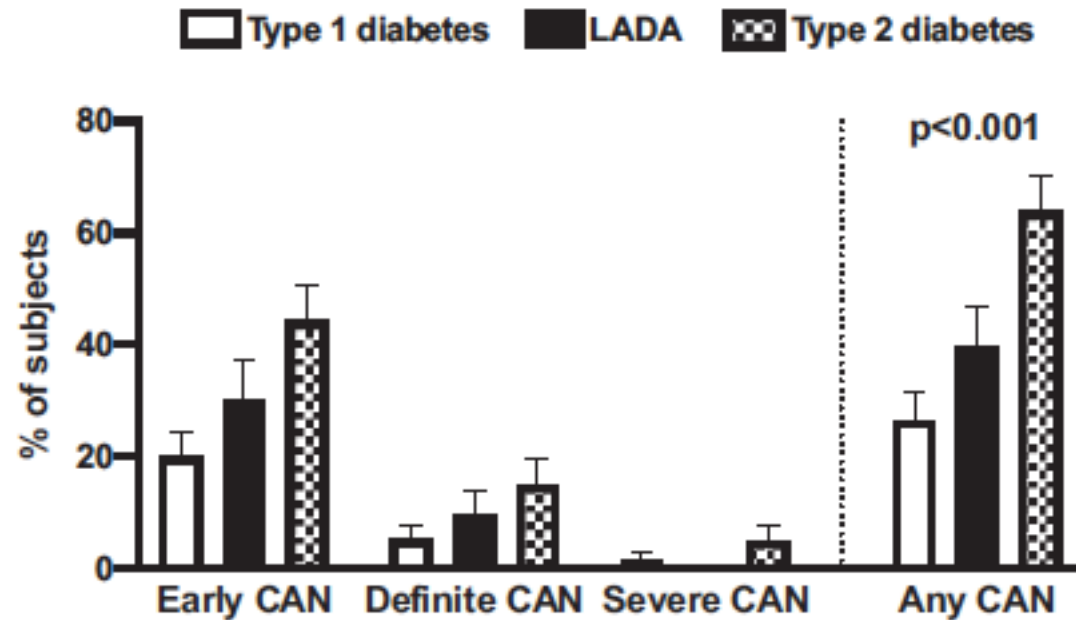
Cox-proportional hazard regression survival curves for MACE



Among subjects with a clinical diagnosis of T2D, those with LADA have a lower risk of cardiovascular events

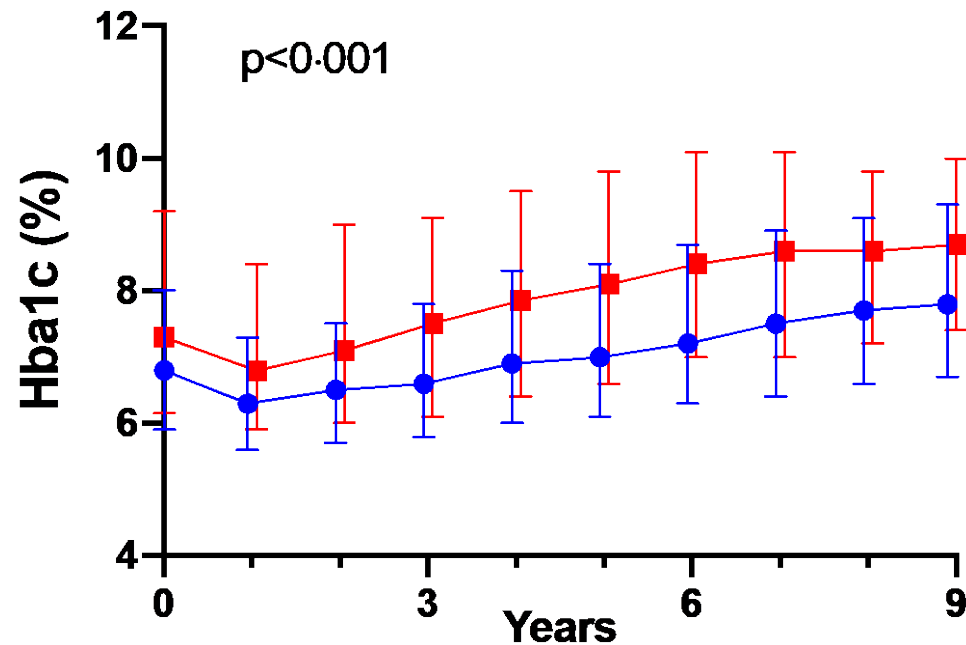
Cardiac autonomic neuropathy

Clinical outcomes

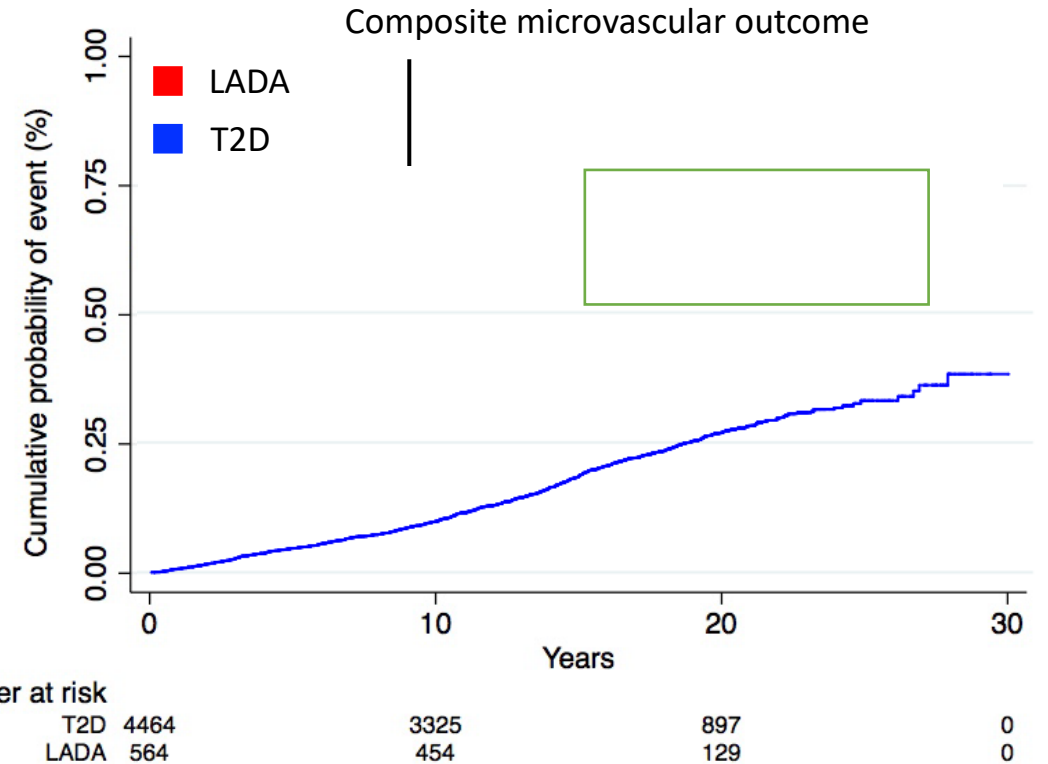


Microvascular complications

Among UKPDS participants, those with LADA show ~1% higher HbA1c compared to T2D



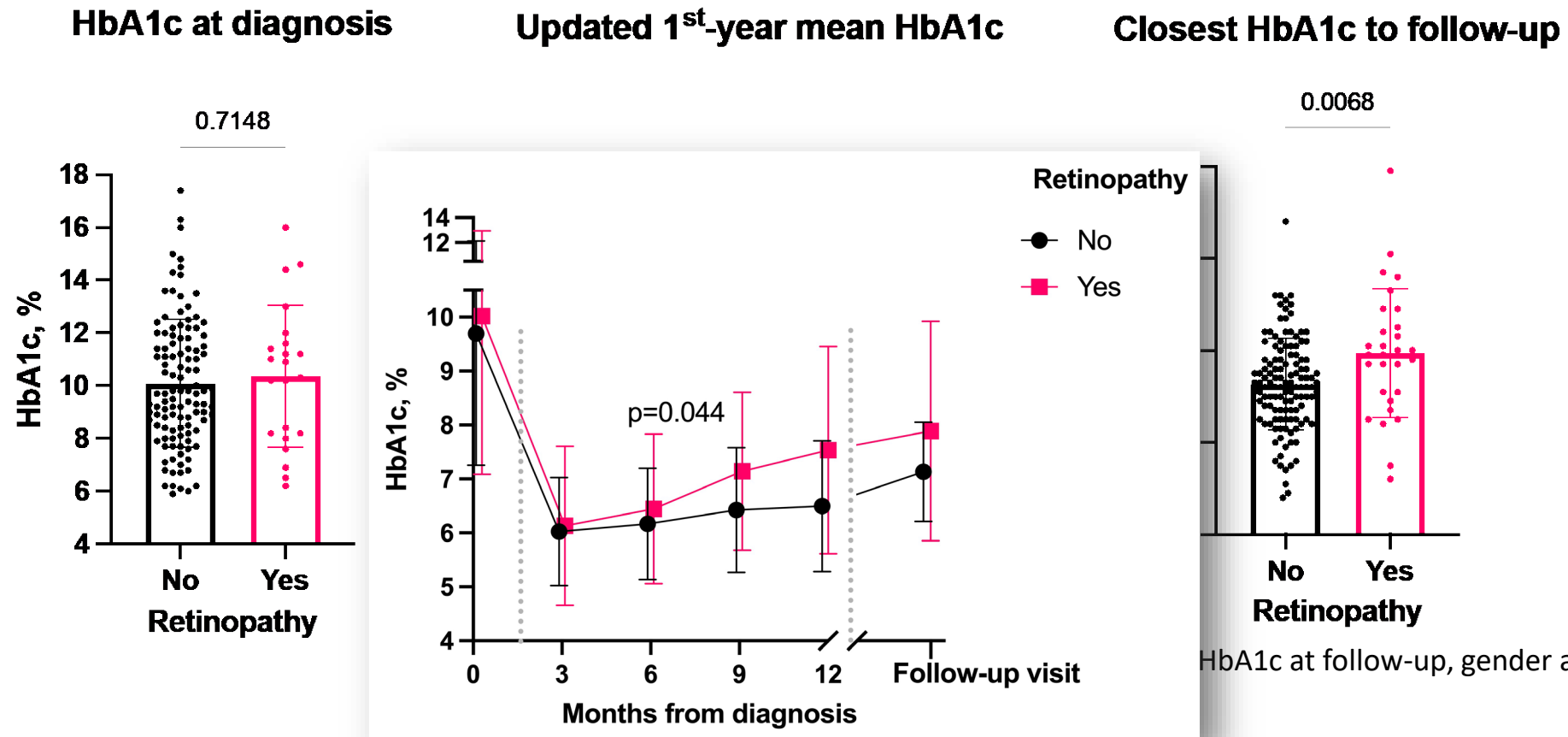
Updated 9-year means
T2D: 7.1 (6.3-8.2); LADA: 8.1 (6.8-9.3)



HR adjusted for updated 9-year mean
HbA1c: 0.99 [0.80-1.23]

Early legacy effect in T1D

Attaining lower HbA1c during the first year of the disease, is associated with lower rates of retinopathy at a follow-up of up to 30 years





Do differences in the pathophysiology and metabolic features translates in different clinical outcomes?

How can we improve metabolic control in LADA

- May we take advantage from the newest therapeutic strategies for T1D and T2D also in LADA

How can we improve metabolic control in LADA?

The LADA-AHCLS study

Observational multicenter retrospective study



Objective

To evaluate whether the use of a HCLS system in people with LADA is associated with glycemic benefits as observed in T1D



- P** People with LADA matched 1:2 with T1D for age, sex and BMI
- E** AHCLS
- C** Multiple Daily Insulin Injection
- O** Time in range (Primary) – TAR, TBR, GMI, CV (secondary)
- C** onfounders: disease duration, age, sex and BMI

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The LADA-AHCLS study

Baseline characteristics

LADA

Type 1 Diabetes

MDI therapy

AHCLS

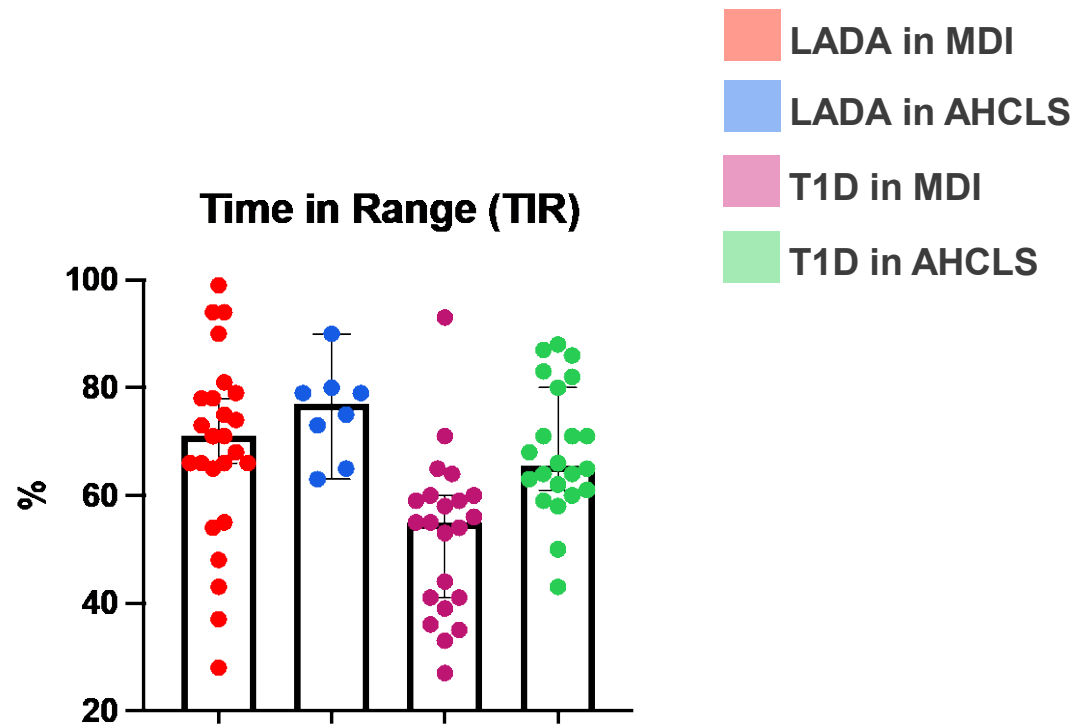
MDI therapy

AHCLS

Users, n	36	17	33	33
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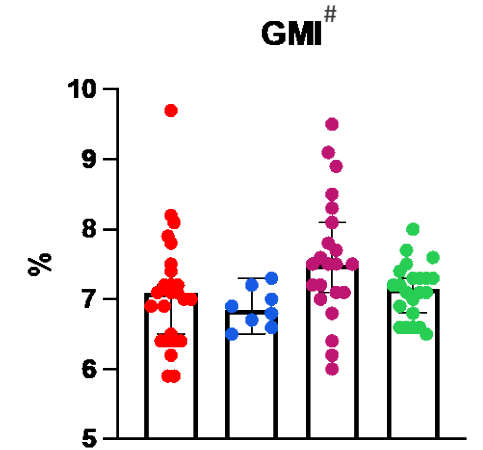
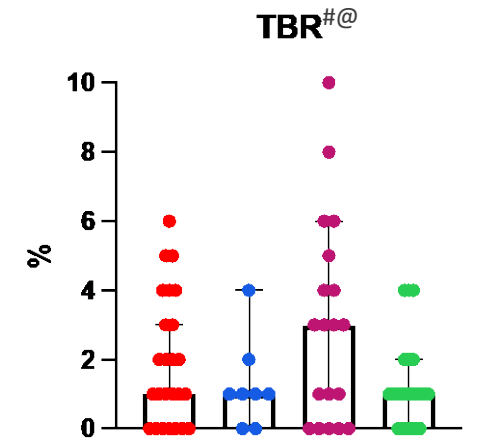
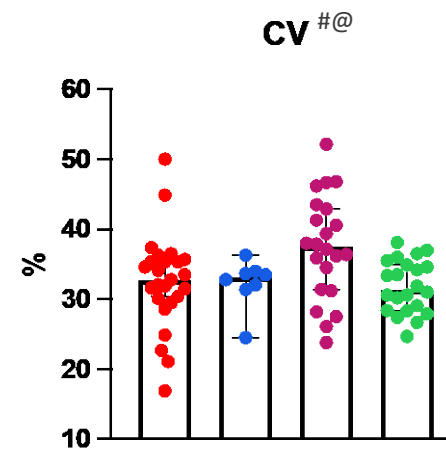
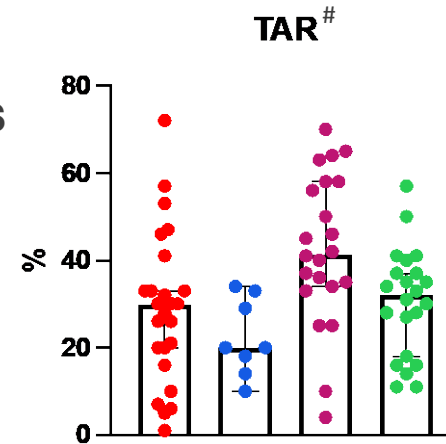
The LADA-AHCLS study

Main results



*Effect of HCLS: $P < 0.001$

§interaction between AHCLS and diabetes type: $P = 0.23$



[#] Effect of HCLS: $P < 0.05$

[@] interaction between AHCLS and diabetes type: $P < 0.05$

The LADA-780G study

LADA

Type 1 Diabetes

MDI therapy

AHCLS

MDI therapy

AHCLS

Users, n

36

17

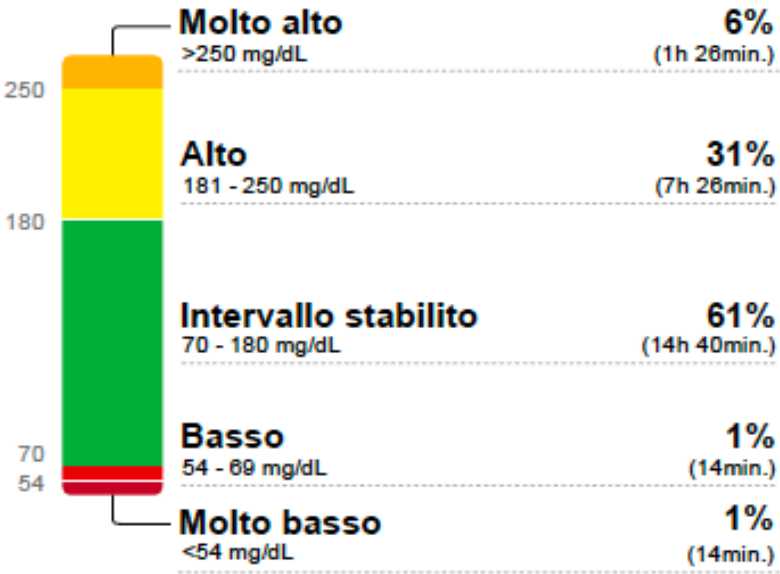
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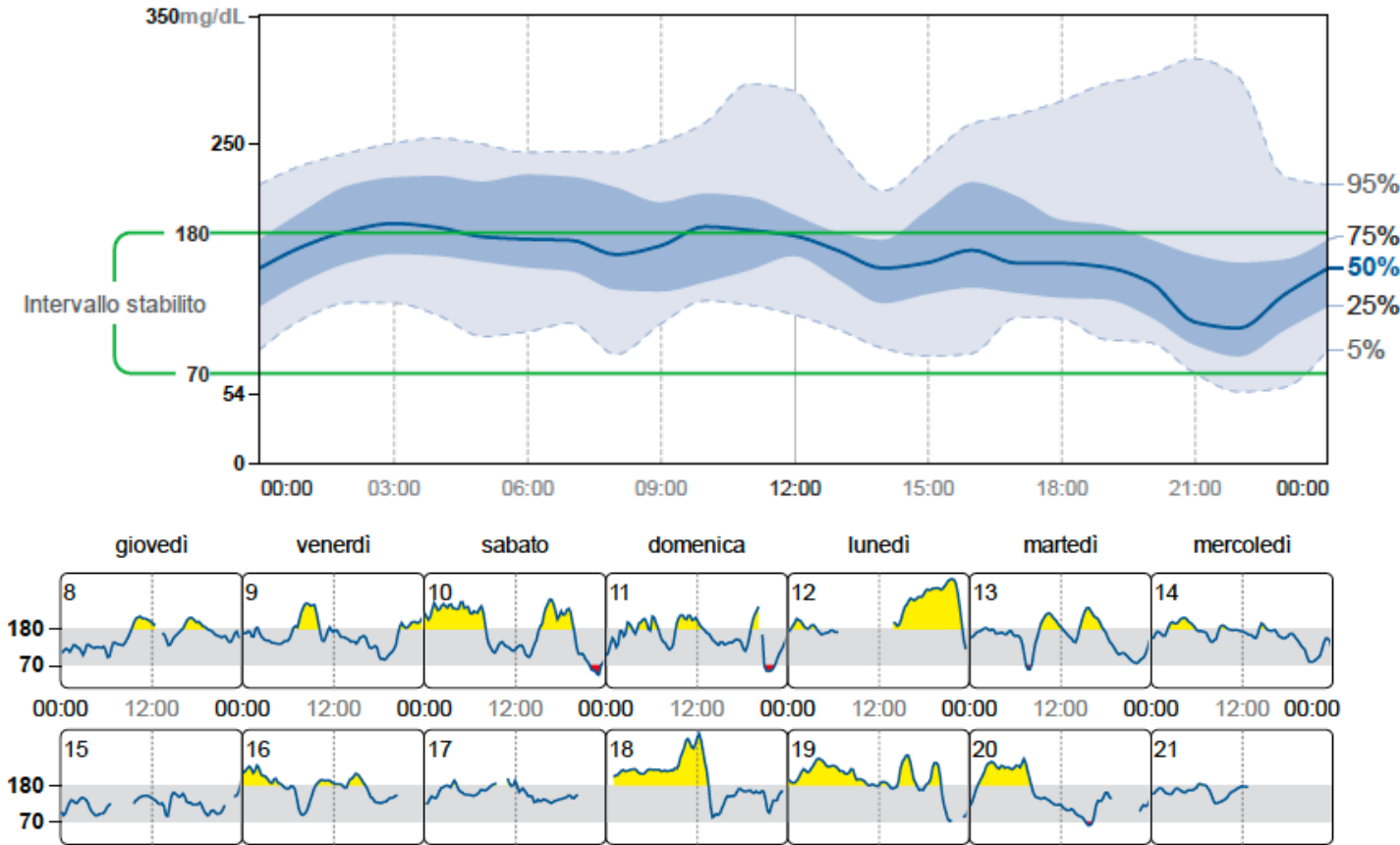
Time in Ranges, %



Bianca, 48 years old, affected by LADA on MDI

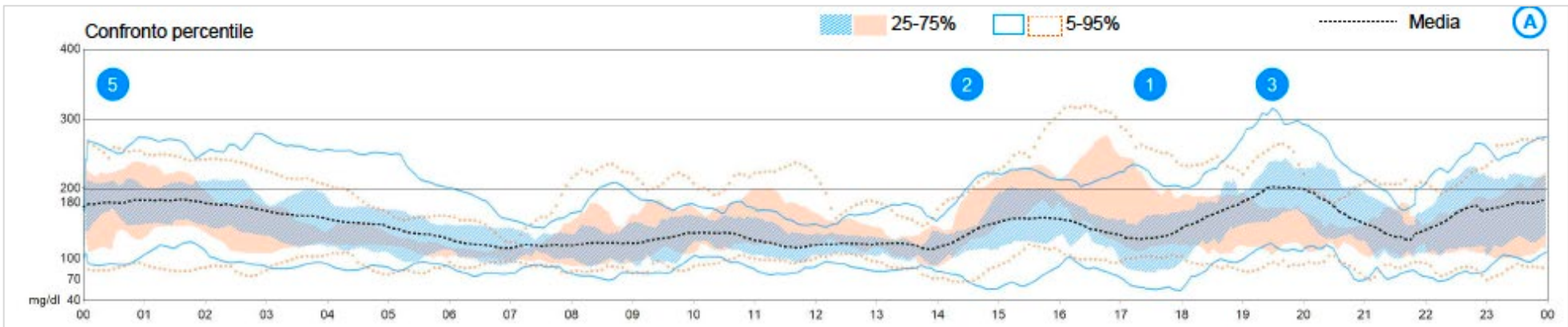
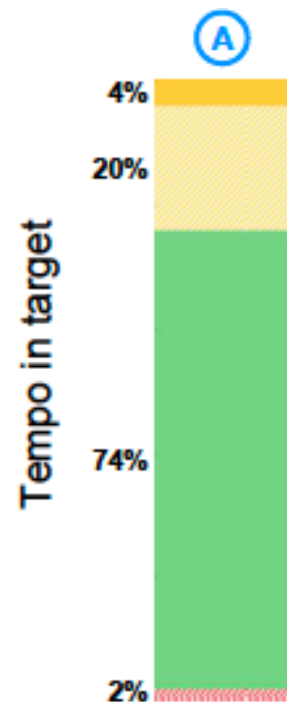


Mean glucose	170 mg/dL
GMI	7.4% or 57 mmol/mol
Glucose variability (CV)	30.1%



The name depicted herein is fictional.

Glycemic values of Bianca after AHCLS start



Statistiche

A

SmartGuard (settimana)	92% (6g 10h)
Modalità manuale (settimana)	1% (02h)
Uso sensore (settimana)	91% (6g 09h)
Media glucosio sensore ± DS	148 ± 53 mg/dl
GMI***	6,9%
Coefficiente di variazione (%)	36,0%

LADASAXADAPA Study

A proof-of-concept randomized clinical study

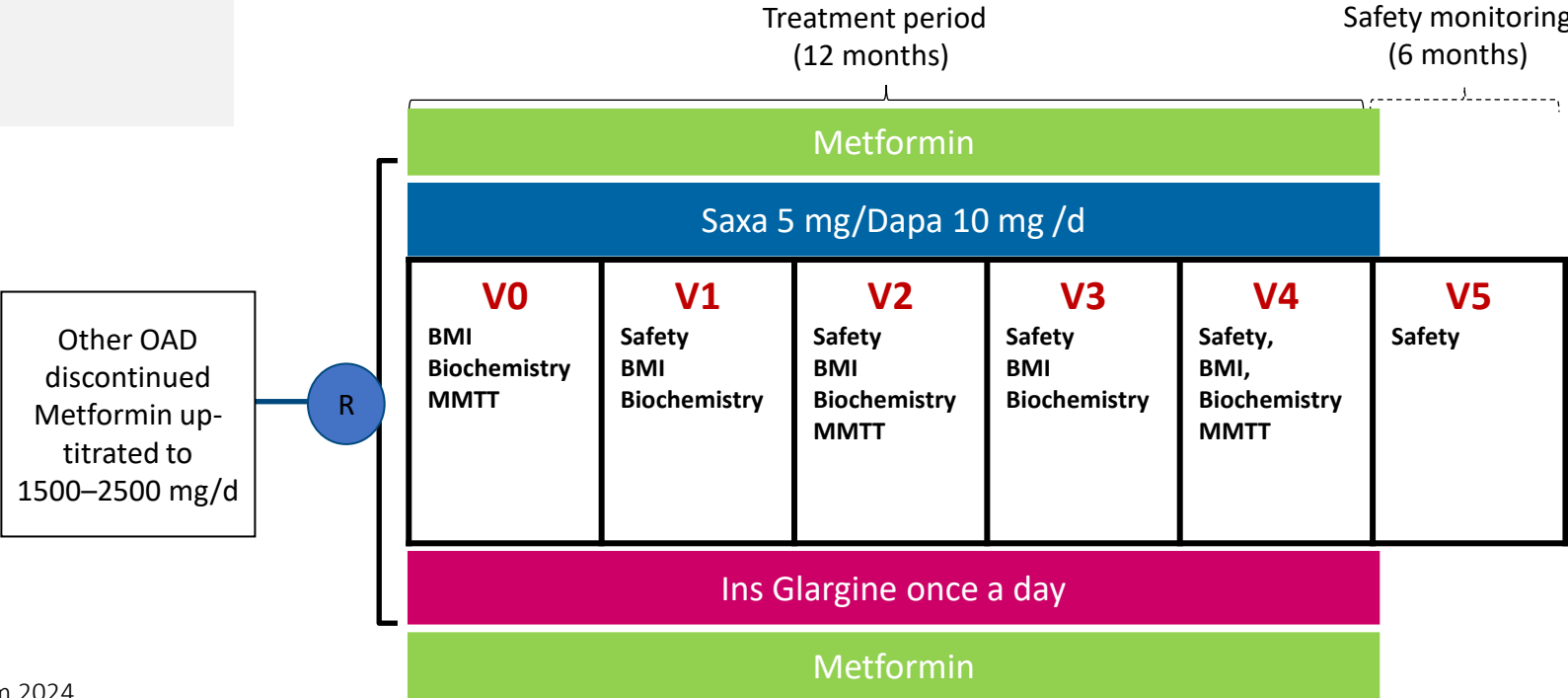


Objective

To evaluate the feasibility of using Saxagliptin/Dapagliflozin instead of basal insulin in people with LADA and detectable fasting C-peptide (>0.2 nmol/L)



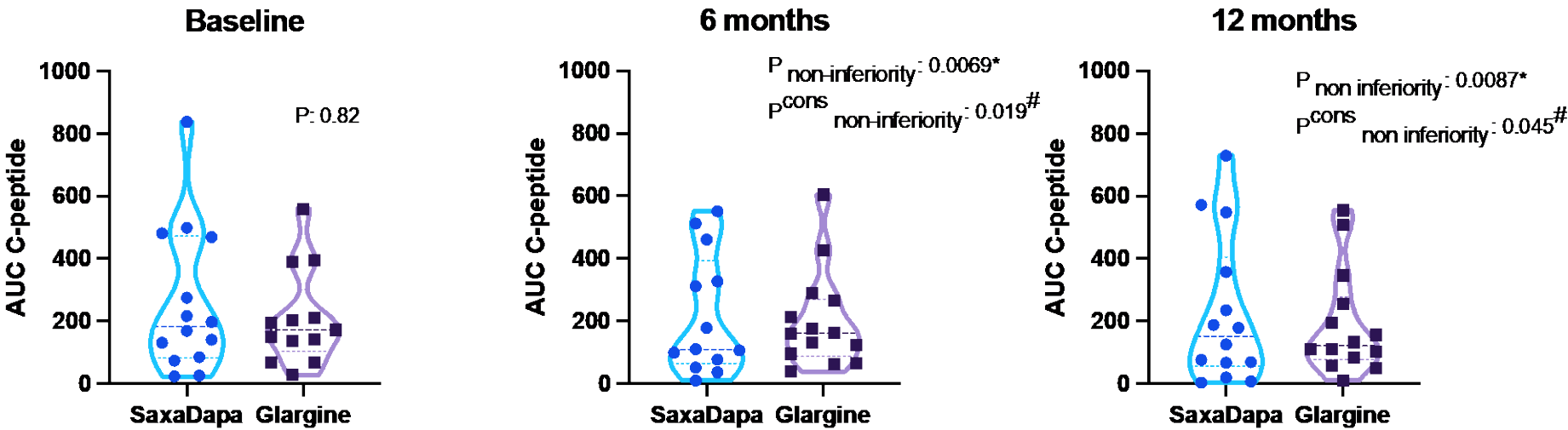
- P** LADA with fasting C-peptide >0.6 ng/ml
- I** Saxagliptin/Dapagliflozin
- C** Insulin Glargine
- O** C-peptide area under the curve following MMTT



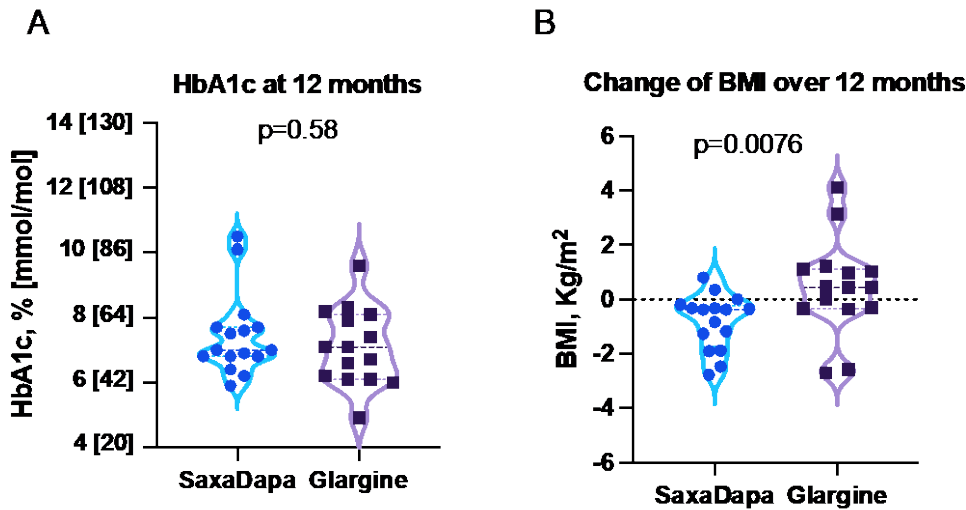
LADASAXADAPA Study

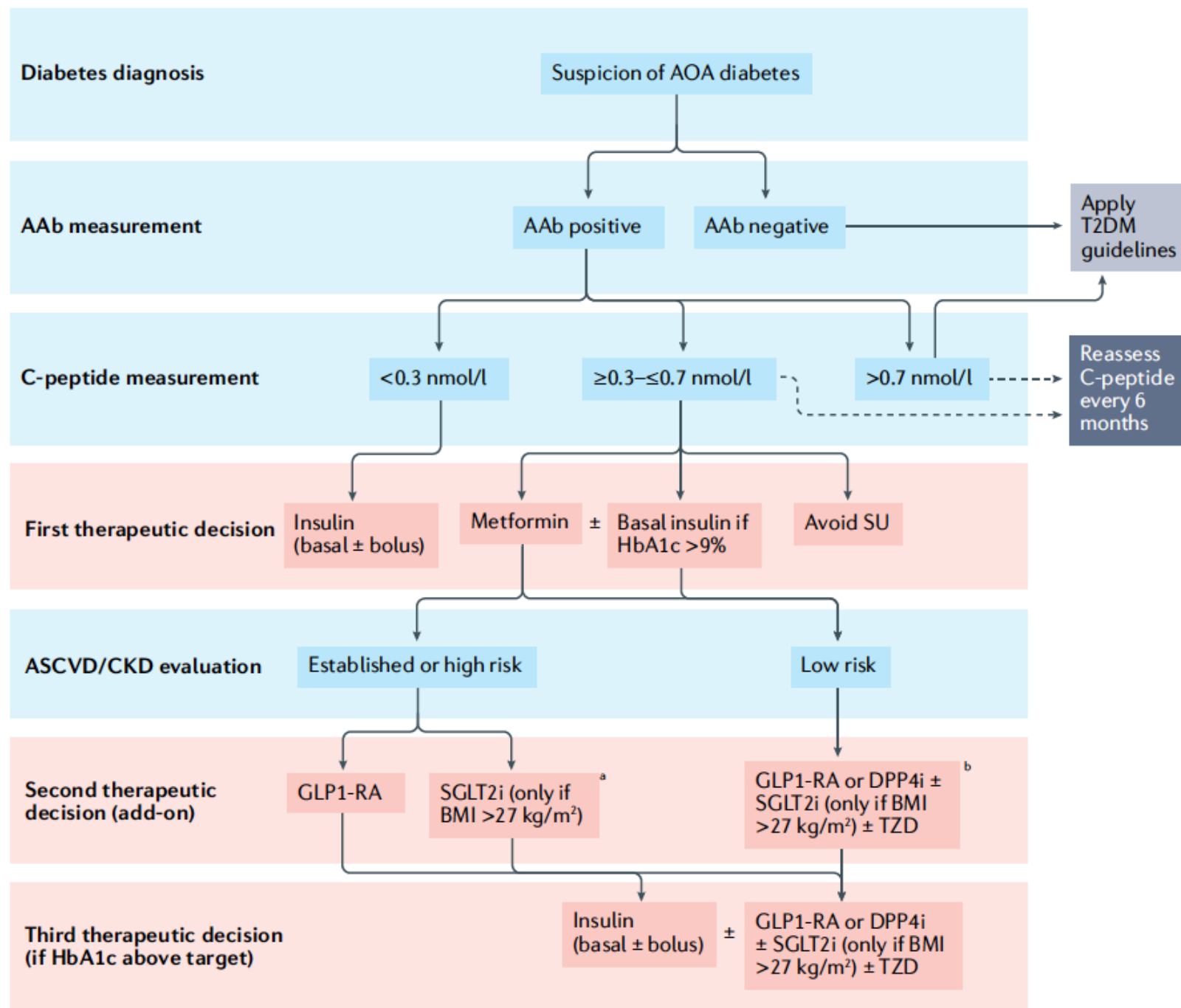
Main results

Primary Outcome:
C-peptide area under the curve following MMTT



Secondary Outcomes:
HbA1c and BMI





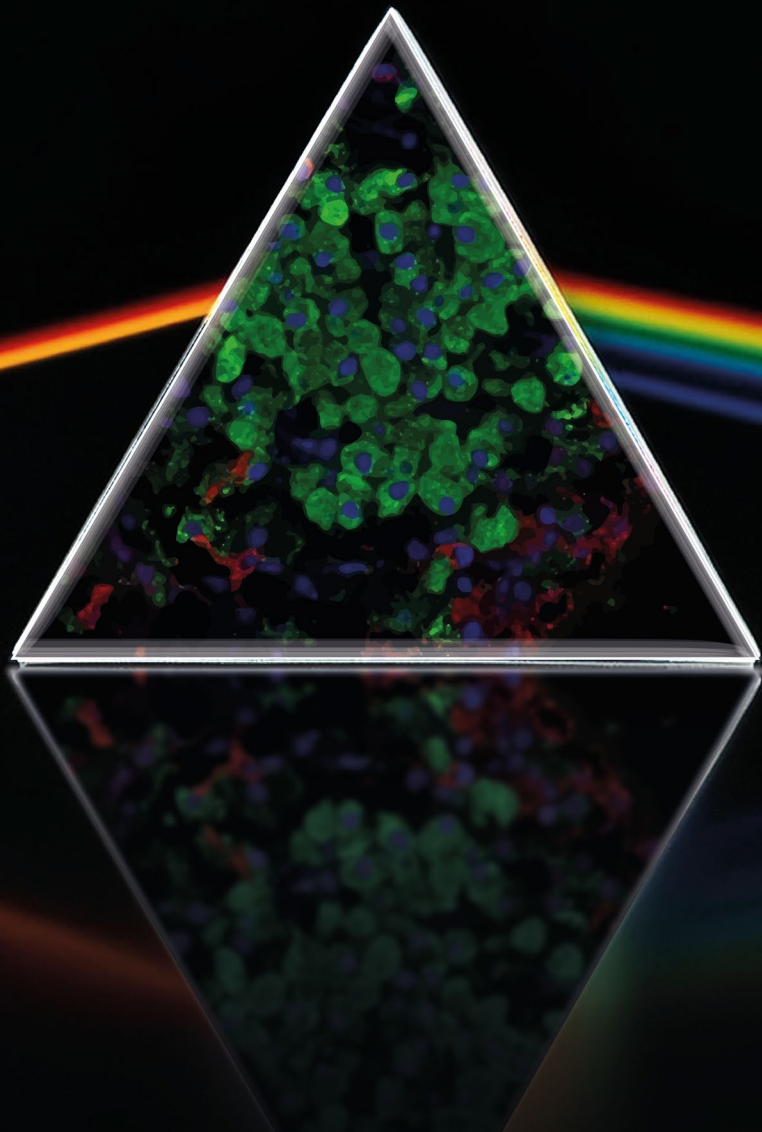
Summary

The landscape of autoimmune diabetes is rapidly changing

- Frequent onset during adulthood, LADA being the most prevalent form of adult-onset autoimmune diabetes
- More prevalent overweight/obesity compared to previous decades, an open field of research

LADA is a therapeutic challenge

- Worse glycemic control compared to T2D, with higher risk of complications
- Benefits from hybrid closed loop systems for insulin infusion
- Insulin use is associated with weight gain in LADA compared to SGLT2i



THE DARK SIDE OF DIABETES

MILANO

FABBRICA DEL VAPORE

20 SETTEMBRE 2024