Congresso Regionale SID-AMD Abruzzo/Molise

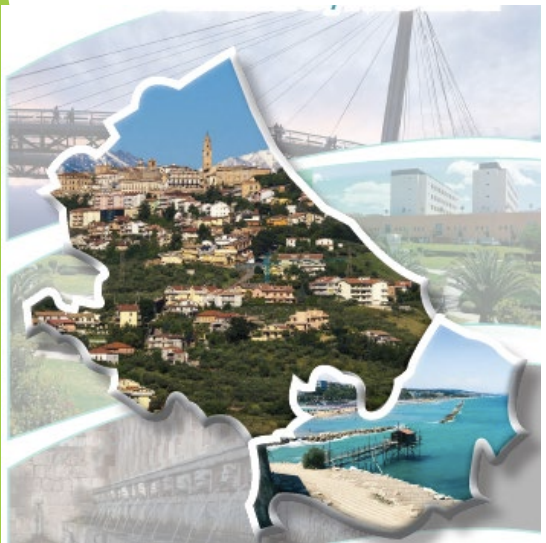
CITTA' SANT'ANGELO (PE)
16 NOVEMBRE 2024

GESTIONE DELL'IPERGLICEMIA

FIORE PELLICCIONE
fiore.pelliccione@gmail.com

ASL TERAMO

U.O.C. MALATTIE ENDOCRINE E DIABETOLOGIA
U.O.S. Diabetologia
Ospedale "S. Liberatore " - Atri - TE



Financial Disclosure

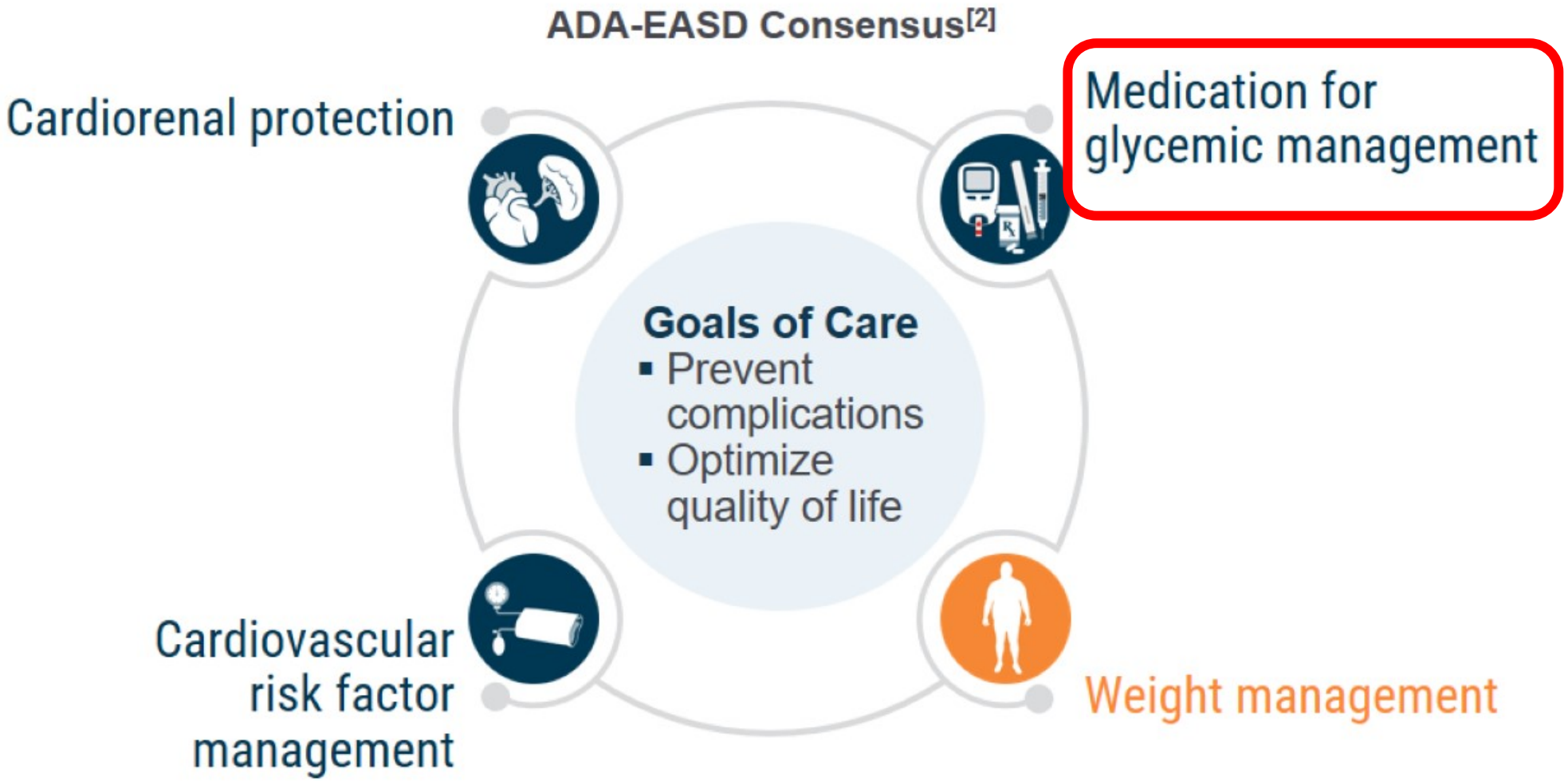
Dichiaro di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:
- Abbot
- Lilly
- Novonordisk

Dichiaro altresì il mio impegno ad astenermi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

In fede

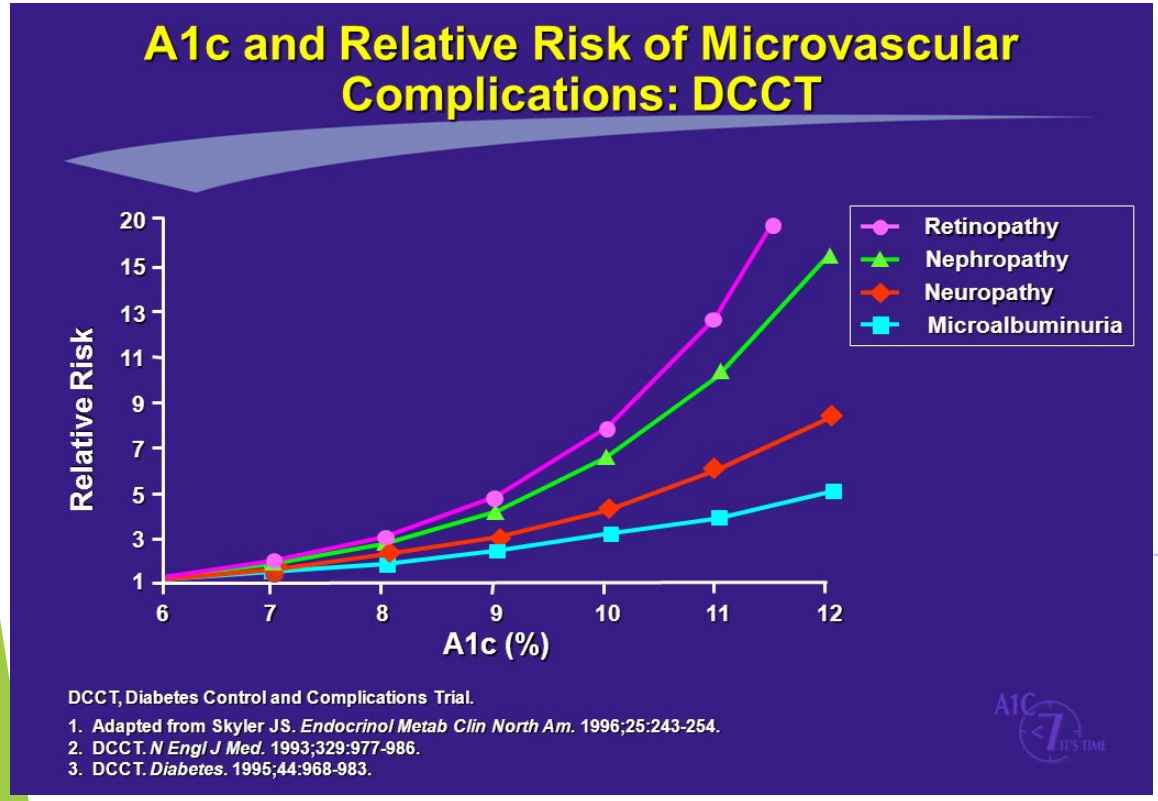
Fiore Pelliccione

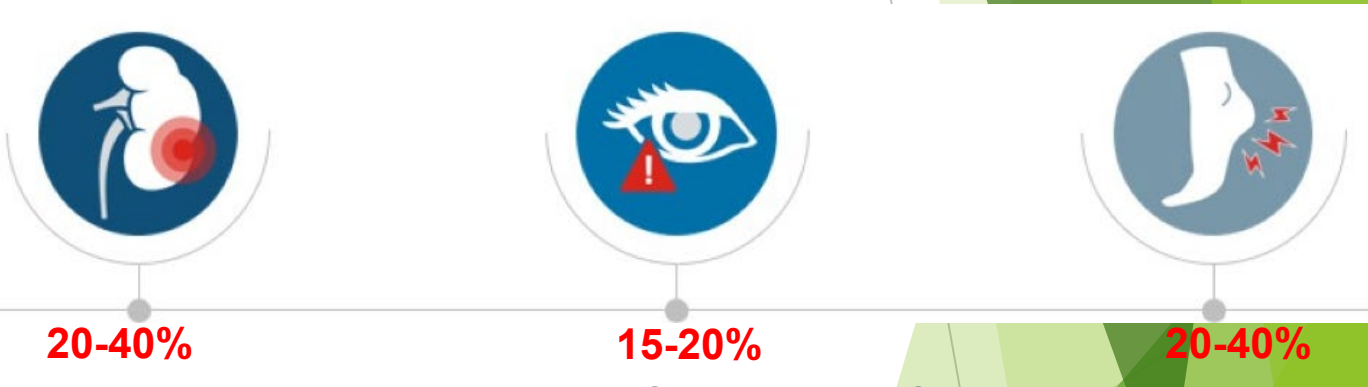
Holistic Approach to T2D Management Including Weight Loss
2022 ADA-EASD Consensus



1. Sattar N, et al. Lancet Reg Health Southeast Asia. 2023;9:100111; 2. Davies MJ, et al. Diabetes Care. 2022;45:2753-2786.

IPERGLICEMIA CRONICA E COMPLICANZE m-VASCOLARI





Standards of Care in Diabetes—2024

Nerve, retinal and kidney cells do not require insulin for intracellular glucose entry

Elevated ambient glucose levels exposure (even in the presence of insulin deficiency absolute or relative) → intracellular metabolic dysfunction → microvascular complications.

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A BREVE TERMINE SU COMPLICANZE m-VASCOLARI

DCCT

Intensive (mean A1C ≃ 7%) versus standard (mean A1C ≃ 9%) glycemic control in T1D is associated with 50–76% reductions in rates of development and progression of microvascular complications.

Nathan DM et alN Engl J Med 1993;329:977–986

UKPDS

Intensive (mean A1C 7%) versus standard (mean A1C ≃ 7.9%) glycemic control in T2D is associated with 25% reductions in rates of development and progression of microvascular complications.

UKPDS 33. Lancet 1998;352:837

Meta-analysis of 4 trials (ACCORD, ADVANCE, UKPDS, and VADT) involving 27,049 participants allocated to more vs less intensive glucose control treatment* [1,2]

Zoungas S, et al. Lancet Diabetes Endocrinol. 2017;5:431-437.

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA : EFFETTI A LUNGO TERMINE SU COMPLICANZE m-VASCOLARI

DCCT POST TRIAL MONITORING PHASE (EDIC)

Persistence of microvascular benefits of intensive versus standard glycemic control in T1D (retinopathy -43%; neuropathy -22%).

Murray P, Curr Atheroscler Rep 2010; Lachin et al., Diabetes 2015;64:631–642

UKPDS POST TRIAL MONITORING PHASE

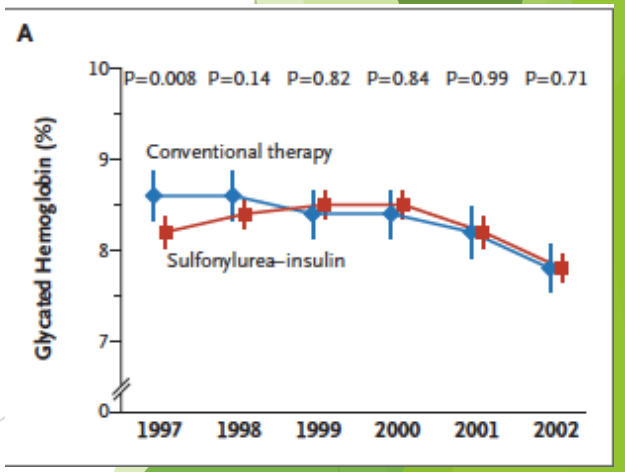
Persistence of microvascular benefits of intensive versus standard glycemic control in T2D (-24%).

Holman RR et al; N Engl J Med2008

Table 1—Clinical characteristics of the former DCCT INT and CONV participants at DCCT baseline, DCCT closeout, and EDIC years 15–18

	DCCT baseline (1983–1989) (*n* = 1,441)		End of DCCT (1993) (*n* = 1,423)		EDIC years 15–18 (2007–2012) (*n* = 1,214)	
	INT	CONV	INT	CONV	INT	CONV
Laboratory values						
HbA_{1c} (%)#	9.1 (1.6)	9.1 (1.6)	7.2 (0.9)	9.1 (1.3)‡	8.0 (1.1)	8.0 (1.0)
mmol/mol	76 (17.5)	76 (17.5)	55 (9.8)	76 (14.2)	64 (12.0)	64 (10.9)

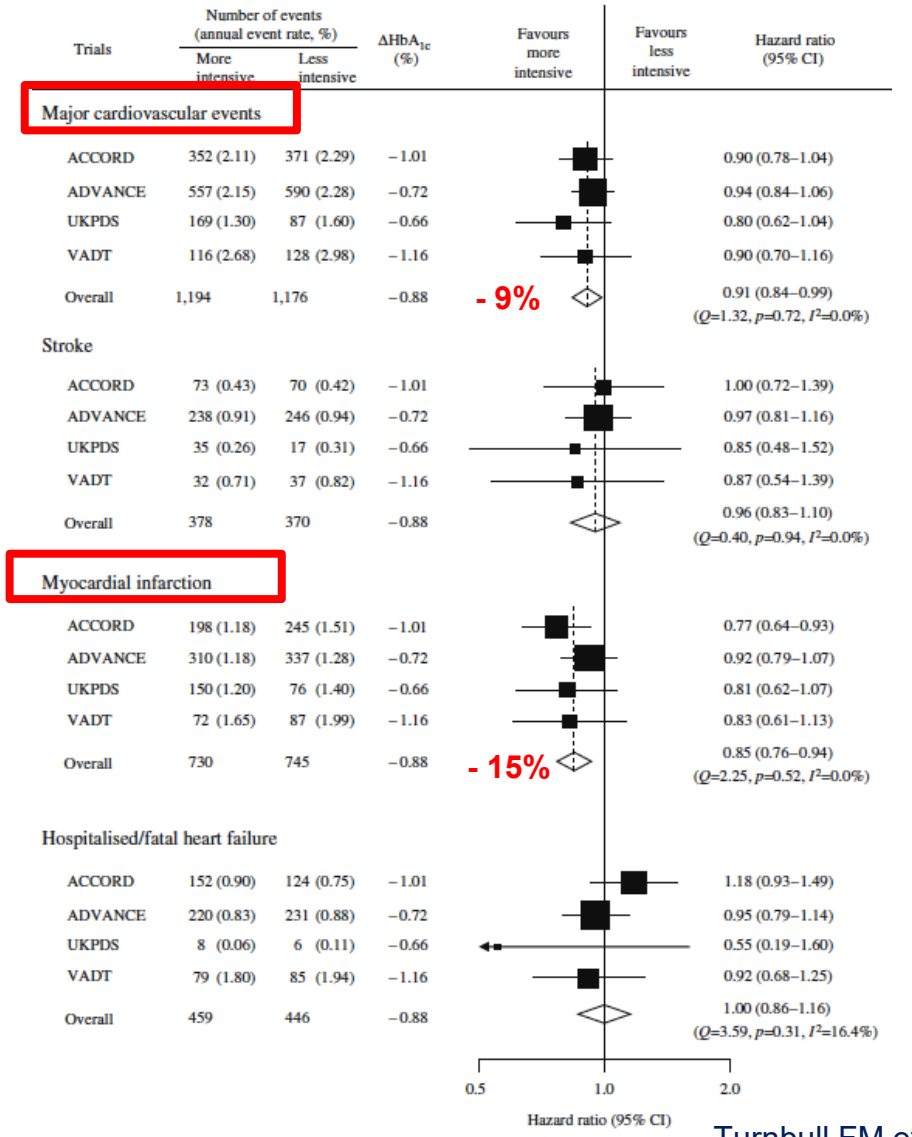
LEGACY

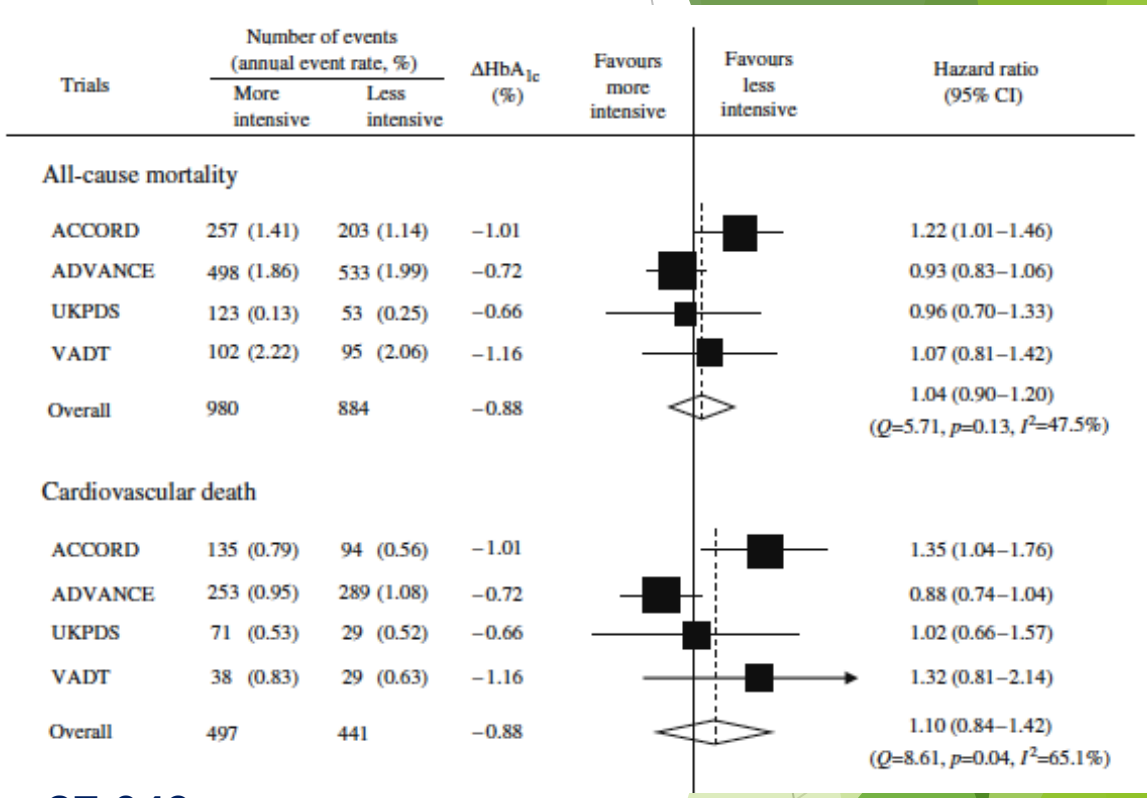


Globalmente il 70% delle morti nei pazienti diabetici è legato ad un evento cardiovascolare;

Le malattie CV hanno un impatto molto maggiore sulla mortalità vs complicanze microvascolari

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A BREVE TERMINE SU COMPLICANZE M-VASCOLARI





- **27.049 pz;**
- **Durata media follow-up: 4 aa;**
- **Età media: 62 aa;**
- **Durata diabete: 9 aa;**
- **HbA1c media: ≃ 8%;**
- **Rischio ipoglicemia più che raddoppiato!!**

Turnbull FM et al.; Diabetologia 2009;52:2288–2298

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A LUNGO TERMINE SU COMPLICANZE M-VASCOLARI (I)

Prattichizzo et al., Metab Clin Exp 2020

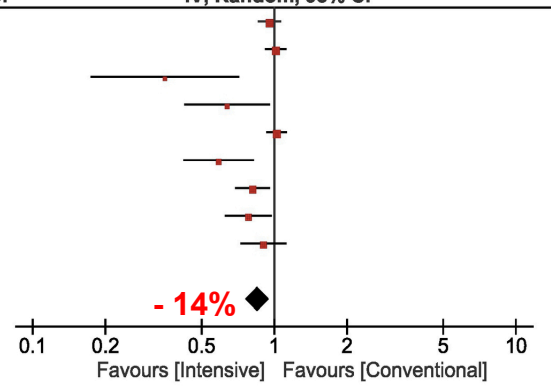
METANALISI DEGLI STUDI DI FOLLOW-UP OSSERVAZIONALE POST-SPERIMETALE

- 40346 pz (66% M; 1441 T1D)
- Durata media DM: 8 aa;
- Età media: 63.2 aa;

A) All studies

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Random, 95% CI
ACCORD ON 2016	-0.0465	0.0516	5128	5123	16.2%	0.95 [0.86, 1.06]
ADVANCE ON 2014	0.0133	0.0479	5571	5569	16.5%	1.01 [0.92, 1.11]
DCCT EDIC 2005	-1.0436	0.3574	593	589	2.2%	0.35 [0.17, 0.71]
DCCT EDIC 2016	-0.4509	0.2047	630	607	5.5%	0.64 [0.43, 0.95]
ORIGINALE 2016	0.0227	0.0458	6264	6273	16.6%	1.02 [0.94, 1.12]
UKPDS* Metformin group 2008	-0.5301	0.1668	279	309	7.2%	0.59 [0.42, 0.82]
UKPDS* Sulphonylurea/Insulin group 2008	-0.2068	0.0804	2118	880	13.6%	0.81 [0.69, 0.95]
VADT 10-years 2015	-0.2474	0.1102	703	688	11.0%	0.78 [0.63, 0.97]
VADT 15-years 2019	-0.1045	0.1074	703	688	11.2%	0.90 [0.73, 1.11]
Total (95% CI)			**21989**	**20726**	**100.0%**	**0.86 [0.77, 0.96]**

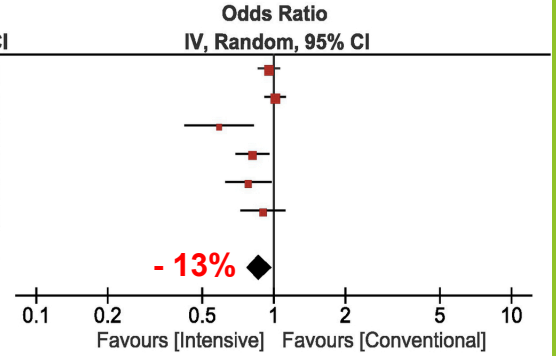
Heterogeneity: Tau² = 0.02; Chi² = 31.23, df = 8 (P = 0.0001); I² = 74%
Test for overall effect: Z = 2.71 (P = 0.007)



A) Only patients with T2DM

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Random, 95% CI
ACCORD ON 2016	-0.0465	0.0516	5128	5123	22.3%	0.95 [0.86, 1.06]
ADVANCE ON 2014	0.0133	0.0479	5571	5569	22.8%	1.01 [0.92, 1.11]
UKPDS* Metformin group 2008	-0.5301	0.1668	279	309	8.6%	0.59 [0.42, 0.82]
UKPDS* Sulphonylurea/Insulin group 2008	-0.2068	0.0804	2118	880	18.0%	0.81 [0.69, 0.95]
VADT 10-years 2015	-0.2474	0.1102	703	688	14.0%	0.78 [0.63, 0.97]
VADT 15-years 2019	-0.1045	0.1074	703	688	14.3%	0.90 [0.73, 1.11]
Total (95% CI)			**14502**	**13257**	**100.0%**	**0.87 [0.77, 0.98]**

Heterogeneity: Tau² = 0.01; Chi² = 16.34, df = 5 (P = 0.006); I² = 69%
Test for overall effect: Z = 2.35 (P = 0.02)

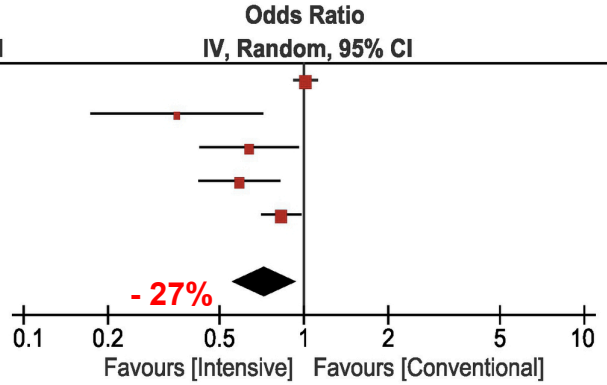


TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A LUNGO TERMINE SU COMPLICANZE M-VASCOLARI (II)

A) Only trials enrolling patients with diabetes duration < 10 years

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Random, 95% CI
ADVANCE ON 2014	0.0133	0.0479	5571	5569	28.0%	1.01 [0.92, 1.11]
DCCT EDIC 2005	-1.0436	0.3574	593	589	9.1%	0.35 [0.17, 0.71]
DCCT EDIC 2016	-0.4509	0.2047	630	607	16.9%	0.64 [0.43, 0.95]
UKPDS* Metformin group 2008	-0.5301	0.1668	279	309	19.7%	0.59 [0.42, 0.82]
UKPDS* Sulphonylurea/Insulin group 2008	-0.1868	0.0801	2118	889	26.2%	0.83 [0.71, 0.97]
Total (95% CI)			**9191**	**7963**	**100.0%**	**0.73 [0.56, 0.94]**

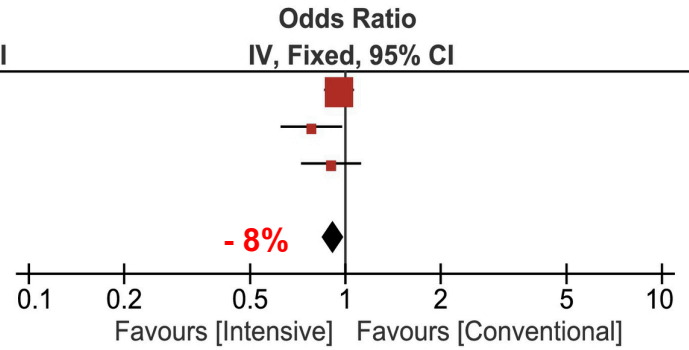
Heterogeneity: Tau² = 0.06; Chi² = 23.29, df = 4 (P = 0.0001); I² = 83%
Test for overall effect: Z = 2.47 (P = 0.01)



B) Only trials enrolling patients with diabetes duration > 10 years

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Fixed, 95% CI
ACCORD ON 2016	-0.0465	0.0516	5128	5123	69.0%	0.95 [0.86, 1.06]
VADT 10-years 2015	-0.2474	0.1102	703	688	15.1%	0.78 [0.63, 0.97]
VADT 15-years 2019	-0.1045	0.1074	703	688	15.9%	0.90 [0.73, 1.11]
Total (95% CI)			**6534**	**6499**	**100.0%**	**0.92 [0.84, 1.00]**

Heterogeneity: Chi² = 2.76, df = 2 (P = 0.25); I² = 28%
Test for overall effect: Z = 2.01 (P = 0.04)



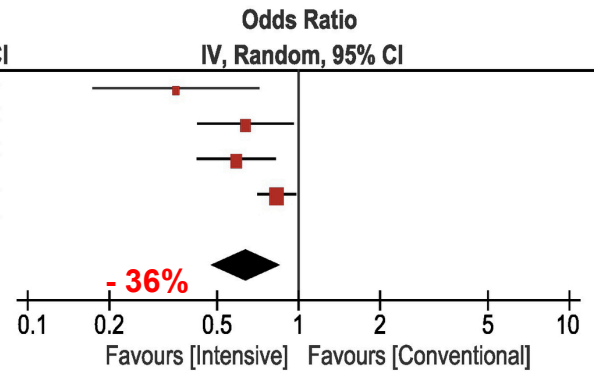
Prattichizzo et al., Metab Clin Exp 2020

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A LUNGO TERMINE SU COMPLICANZE M-VASCOLARI (III)

A) Only trials enrolling patients without cardiovascular diseases at baseline

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Random, 95% CI
DCCT EDIC 2005	-1.0436	0.3574	593	589	12.3%	0.35 [0.17, 0.71]
DCCT EDIC 2016	-0.4509	0.2047	630	607	23.3%	0.64 [0.43, 0.95]
UKPDS* Metformin group 2008	-0.5301	0.1668	279	309	27.3%	0.59 [0.42, 0.82]
UKPDS* Sulphonylurea/Insulin group 2008	-0.1868	0.0801	2118	889	37.0%	0.83 [0.71, 0.97]
Total (95% CI)			**3620**	**2394**	**100.0%**	**0.64 [0.48, 0.86]**

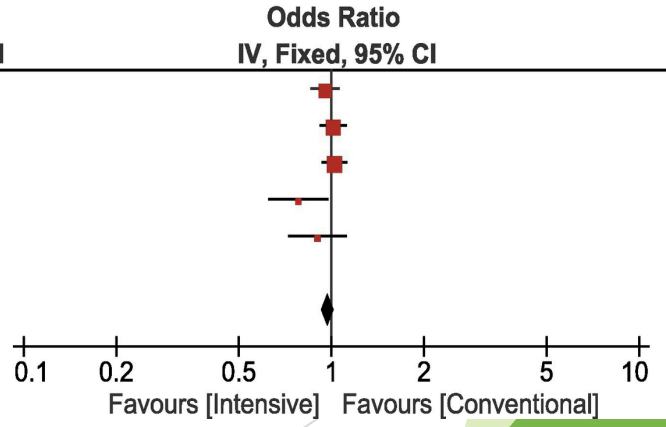
Heterogeneity: Tau² = 0.05; Chi² = 8.77, df = 3 (P = 0.03); I² = 66%
Test for overall effect: Z = 2.99 (P = 0.003)



B) Trials enrolling patients also with cardiovascular diseases at baseline

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Fixed, 95% CI
ACCORD ON 2016	-0.0465	0.0516	5128	5123	25.8%	0.95 [0.86, 1.06]
ADVANCE ON 2014	0.0133	0.0479	5571	5569	29.9%	1.01 [0.92, 1.11]
ORIGINALE 2016	0.0227	0.0458	6264	6273	32.7%	1.02 [0.94, 1.12]
VADT 10-years 2015	-0.2474	0.1102	703	688	5.7%	0.78 [0.63, 0.97]
VADT 15-years 2019	-0.1045	0.1074	703	688	5.9%	0.90 [0.73, 1.11]
Total (95% CI)			**18369**	**18341**	**100.0%**	**0.98 [0.93, 1.03]**

Heterogeneity: Chi² = 6.49, df = 4 (P = 0.17); I² = 38%
Test for overall effect: Z = 0.79 (P = 0.43)



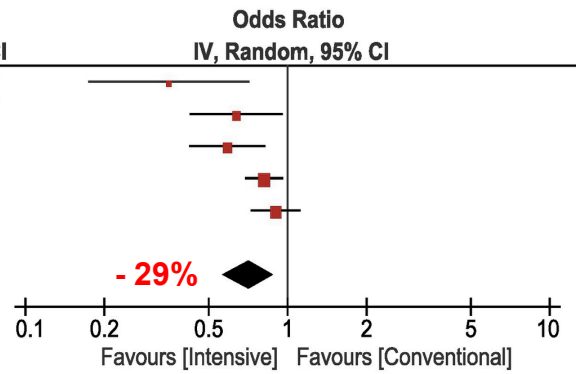
Prattichizzo et al., Metab Clin Exp 2020

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A LUNGO TERMINE SU COMPLICANZE M-VASCOLARI (IV)

A) Only trials with follow-up >10 years

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Random, 95% CI
DCCT EDIC 2005	-1.0436	0.3574	593	589	7.5%	0.35 [0.17, 0.71]
DCCT EDIC 2016	-0.4509	0.2047	630	607	16.0%	0.64 [0.43, 0.95]
UKPDS* Metformin group 2008	-0.5301	0.1668	279	309	19.7%	0.59 [0.42, 0.82]
UKPDS* Sulphonylurea/Insulin group 2008	-0.2068	0.0804	2118	880	30.1%	0.81 [0.69, 0.95]
VADT 15-years 2019	-0.1045	0.1074	703	688	26.7%	0.90 [0.73, 1.11]
Total (95% CI)			**4323**	**3073**	**100.0%**	**0.71 [0.57, 0.88]**

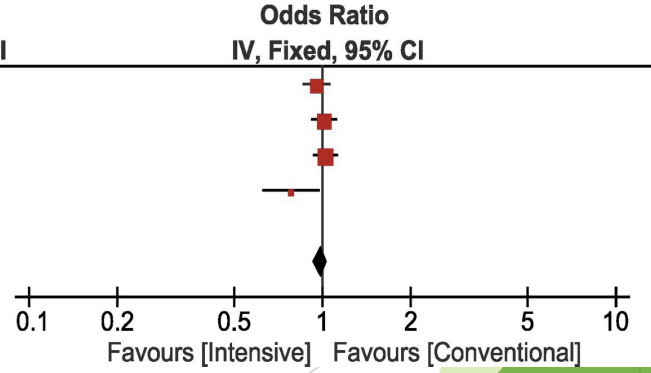
Heterogeneity: Tau² = 0.03; Chi² = 10.83, df = 4 (P = 0.03); I² = 63%
Test for overall effect: Z = 3.13 (P = 0.002)



B) Trials with follow-up < 10 years

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Fixed, 95% CI
ACCORD ON 2016	-0.0465	0.0516	5128	5123	27.4%	0.95 [0.86, 1.06]
ADVANCE ON 2014	0.0133	0.0479	5571	5569	31.8%	1.01 [0.92, 1.11]
ORIGINALE 2016	0.0227	0.0458	6264	6273	34.8%	1.02 [0.94, 1.12]
VADT 10-years 2015	-0.2474	0.1102	703	688	6.0%	0.78 [0.63, 0.97]
Total (95% CI)			**17666**	**17653**	**100.0%**	**0.98 [0.93, 1.04]**

Heterogeneity: Chi² = 5.85, df = 3 (P = 0.12); I² = 49%
Test for overall effect: Z = 0.57 (P = 0.57)



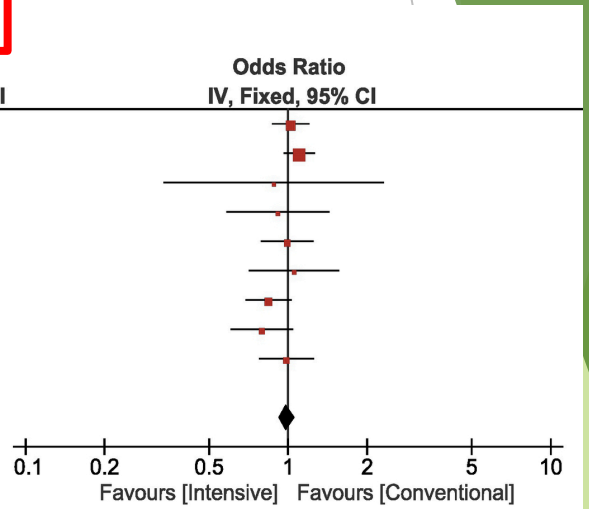
Prattichizzo et al., Metab Clin Exp 2020

TRATTAMENTO INTENSIVO DELL'IPERGLICEMIA: EFFETTI A LUNGO TERMINE SU COMPLICANZE M-VASCOLARI (V)

A) Only events recorded during the observational, post-active phases of the trials (all studies)

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Fixed, 95% CI
ACCORD ON 2016	0.0217	0.079	4270	4331	21.5%	1.02 [0.88, 1.19]
ADVANCE ON 2014	0.0969	0.0658	5571	5569	31.0%	1.10 [0.97, 1.25]
DCCT EDIC 2005	-0.1264	0.4894	593	589	0.6%	0.88 [0.34, 2.30]
DCCT EDIC 2016	-0.091	0.2261	630	607	2.6%	0.91 [0.59, 1.42]
ORIGINALE 2016	-0.0081	0.1138	2016	2037	10.4%	0.99 [0.79, 1.24]
UKPDS* Metformin group 2008	0.0521	0.1989	279	309	3.4%	1.05 [0.71, 1.56]
UKPDS* Sulphonylurea/Insulin group 2008	-0.1719	0.0986	2118	880	13.8%	0.84 [0.69, 1.02]
VADT 10-years 2015	-0.2305	0.1364	703	688	7.2%	0.79 [0.61, 1.04]
VADT 15-years 2019	-0.0156	0.1196	703	688	9.4%	0.98 [0.78, 1.24]
Total (95% CI)			**16883**	**15698**	**100.0%**	**0.99 [0.92, 1.06]**

Heterogeneity: Chi² = 8.39, df = 8 (P = 0.40); I² = 5%
Test for overall effect: Z = 0.25 (P = 0.80)

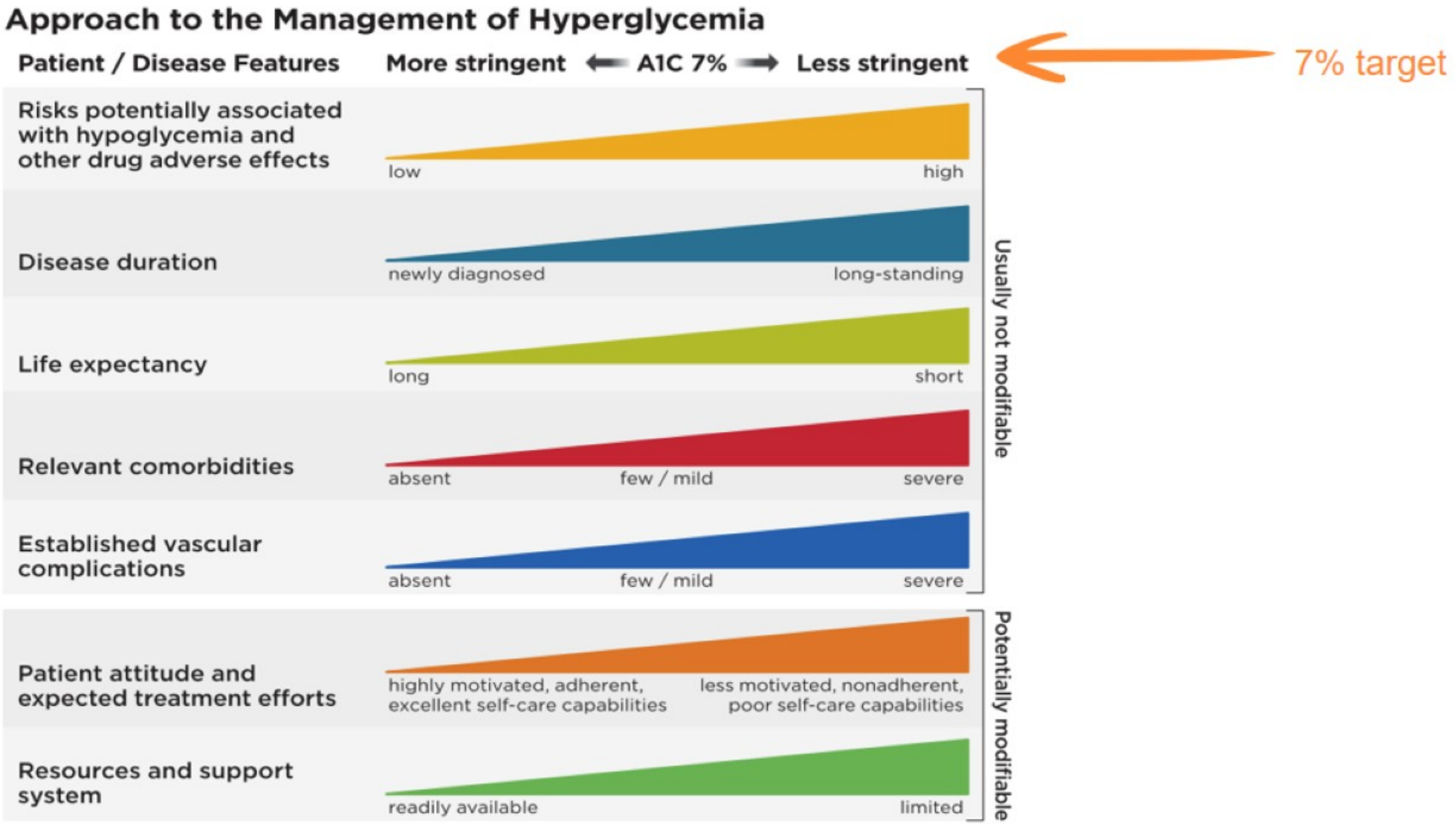


- Intensive glycaemic control reduces the incidence of late MACEs in DM patients.
- The protective effect is more relevant in patients with short diabetes duration, no prevalent cardiovascular diseases, and followed-up for more than 10 years
- No protective effect on MACEs beyond the period of intensive glycaemic treatment

LEGACY

Prattichizzo et al., ... Lab Clin Exp 2020

Reassessment of Glycemic Targets Based on Individualized Criteria



ElSayed NA, et al. Diabetes Care. 2023;46(1_suppl):S97-S110.

Table 3 Glucose-lowering and cardioprotective therapies at follow-up[a]

Therapy	ACCORD (n=10,208)		ADVANCE (n=10,973)		UKPDS[b] (n=3,646)		VADT (n=1,745)	
	Less-intensive	More-intensive	Less-intensive	More-intensive	Less-intensive	More-intensive	Less-intensive	More-intensive
Glucose-lowering drugs								
Sulfonylurea, n (%)	2,516 (49.3)	2,304 (45.1)	3,245 (59.1)	4,939 (90.1)	273 (25.6)	1,384 (53.7)	387 (44.1)	461 (53.1)
Metformin, n (%)	3,506 (68.8)	3,784 (74.1)	3,599 (65.6)	3,951 (72.0)	89 (8.3)	203 (7.9)	474 (54.1)	519 (59.8)
Thiazolidinedione, n (%)	1,534 (30.1)	2,814 (55.1)	578 (10.5)	895 (16.3)	N/A	N/A	249 (28.4)	317 (36.5)
Acarbose, n (%)	162 (3.2)	681 (13.3)	640 (11.7)	972 (17.7)	N/A	N/A	20 (2.3)	92 (10.6)
Glinide, n (%)	487 (9.6)	1,280 (25.0)	145 (2.6)	70 (1.3)	N/A	N/A	2 (0.23)	10 (1.2)
Insulin, n (%)	2,603 (51.0)	3,628 (71.0)	1,326 (24.2)	2,205 (40.2)	165 (15.5)	1,006 (39.0)	678 (77.3)	756 (87.2)
Other drugs[c]								

Turnbull FM et al.; Diabetologia 2009;52:2288–2298

Reduction in CV Outcomes Risk With SGLT2 Inhibitors and GLP-1 RA *Meta-Analyses*

Outcome	SGLT2 Inhibitors Meta-Analysis of 6 Outcomes Trials[1] Risk vs Placebo (Range)	GLP-1 RA Meta-Analysis of 7 Trials (Excluding ELIXA)[2] Risk vs Placebo (Range)
MACE	-10% (-5 to -15%)	-15% (-10 to -20%)
CV death	-15% (-7 to -22%)	-15% (-7 to -22%)
MI	- 9% (-1 to -16%)	-12% (-4 to -19%)
Stroke	-4% (-13 to +7%)	-19% (-10 to -26%)
Hospitalization for HF	**-32% (-24 to -39%)**	**-12% (-2 to -21%)**
CKD	-38% (-30 to -44%)	- 18% (-2 to -31%)

1. McGuire DK, et al. JAMA Cardiol. 2021;6:148-158. 2. Sattar N, et al. Lancet Diabetes Endocrinol. 2021;9:653-662.

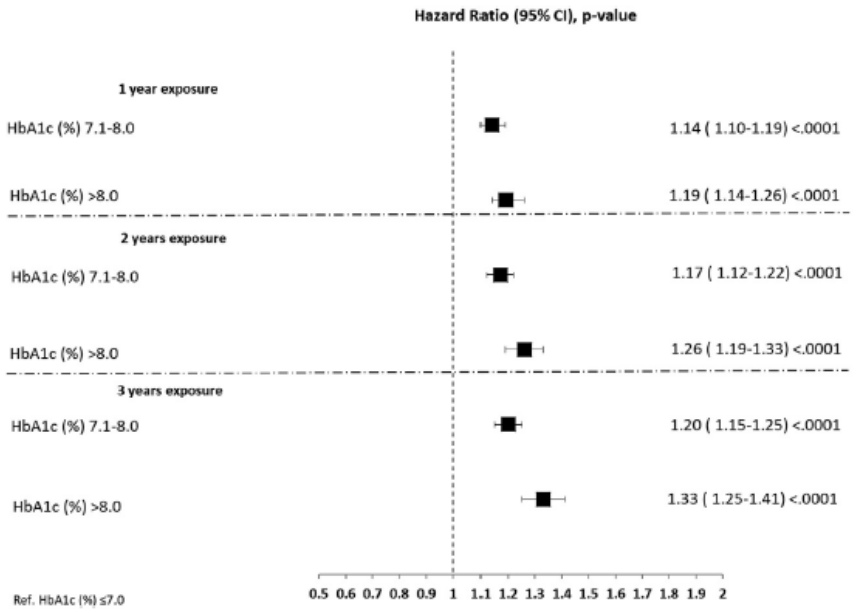
- **CVOTs were not designed to test higher versus lower A1C (equipoise!!);**
- **Cardiorenal benefits SGLT2-I or GLP-1RA are not contingent upon A1C lowering;**
- **Initiation can be considered in people with type 2 diabetes and CVD/CKD independent of the current A1C or A1C goal or metformin background**

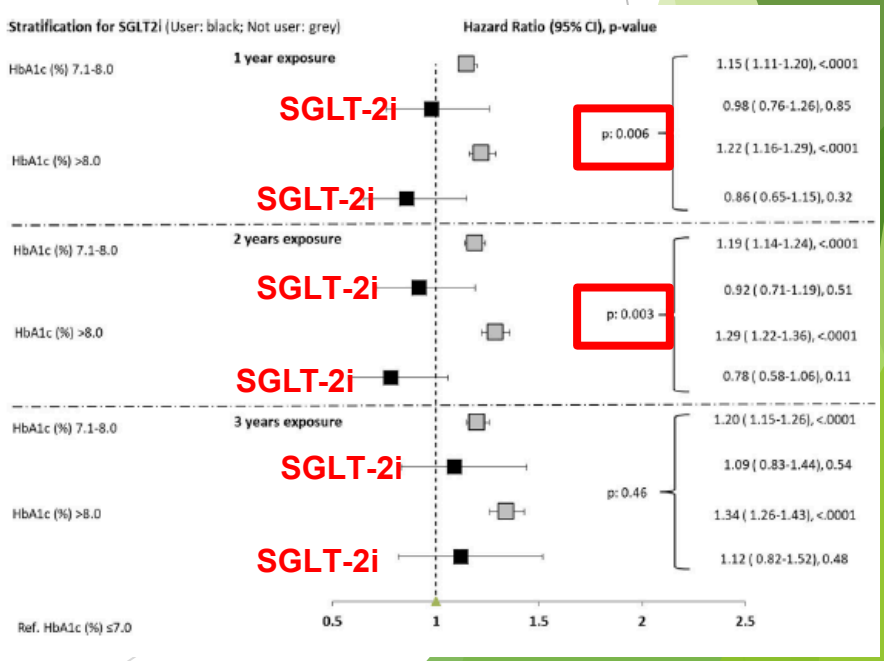
The legacy effect of hyperglycemia and early use of SGLT-2 inhibitors: a cohort study with newly-diagnosed people with type 2 diabetes

Lancet Reg Health Eur. 2023

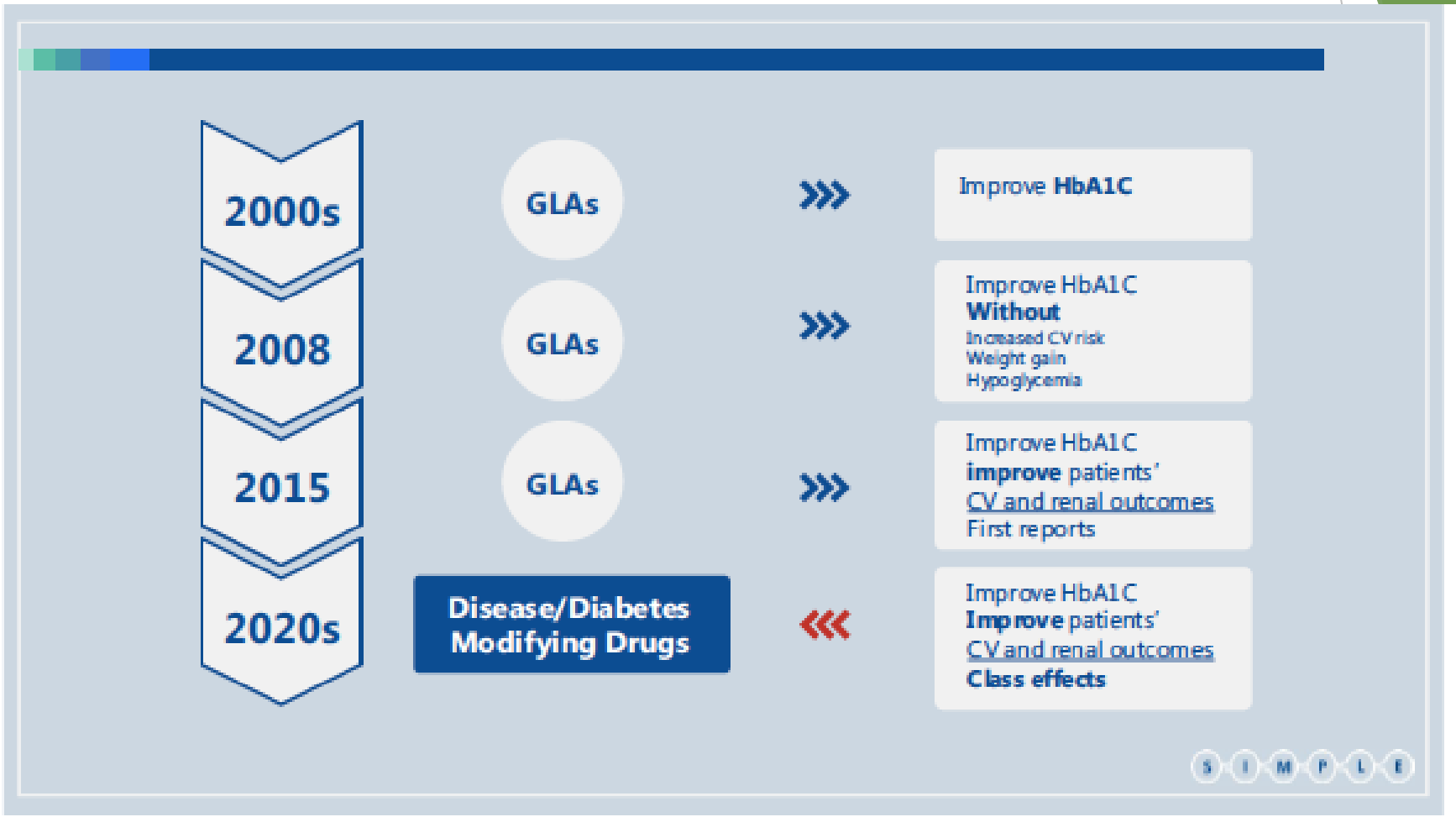
Antonio Ceriello,[a,*] Giuseppe Lucisano,[b] Francesco Prattichizzo,[a,**] Rosalba La Grotta,[a] Chiara Frigé,[a] Salvatore De Cosmo,[c] Paolo Di Bartolo,[d] Graziano Di Cianni,[e] Paola Fioretto,[f] Carlo Bruno Giorda,[g] Roberto Pontremoli,[h] Giuseppina Russo,[i] Francesca Viazzi,[h] and Antonio Nicolucci,[b] AMD Annals study group,[j]

- Dati Annali AMD di 251.339 pz con T2D nuova diagnosi e no CVD al base-line;
- Effetto di HbA1c 7-8 o > 8 vs HbA1c <7 in 3 periodi di esposizione precoce ad iperglicemia (0-1, 0-2, 0-3 aa) su CVD incidente;
- Introduzione precoce SGLT-2i nei 3 periodi di esposizione modifica CVD incidente?



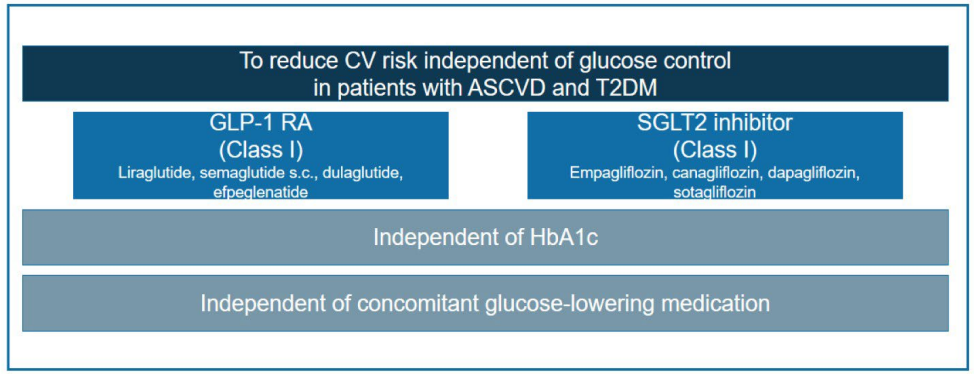


TRATTAMENTO DEL T2D: UN CAMBIO DI PARADIGMA



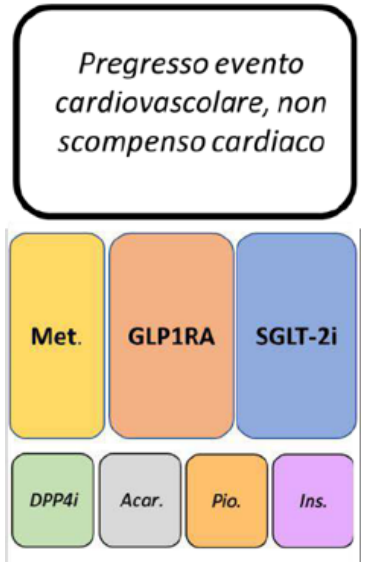
Mosenzon O., et al. Cardiovasc Diabetol 2021

2023 ESC Guidelines: Glucose-Lowering Treatment for Patients With T2D and ASCVD To Reduce CV Risk

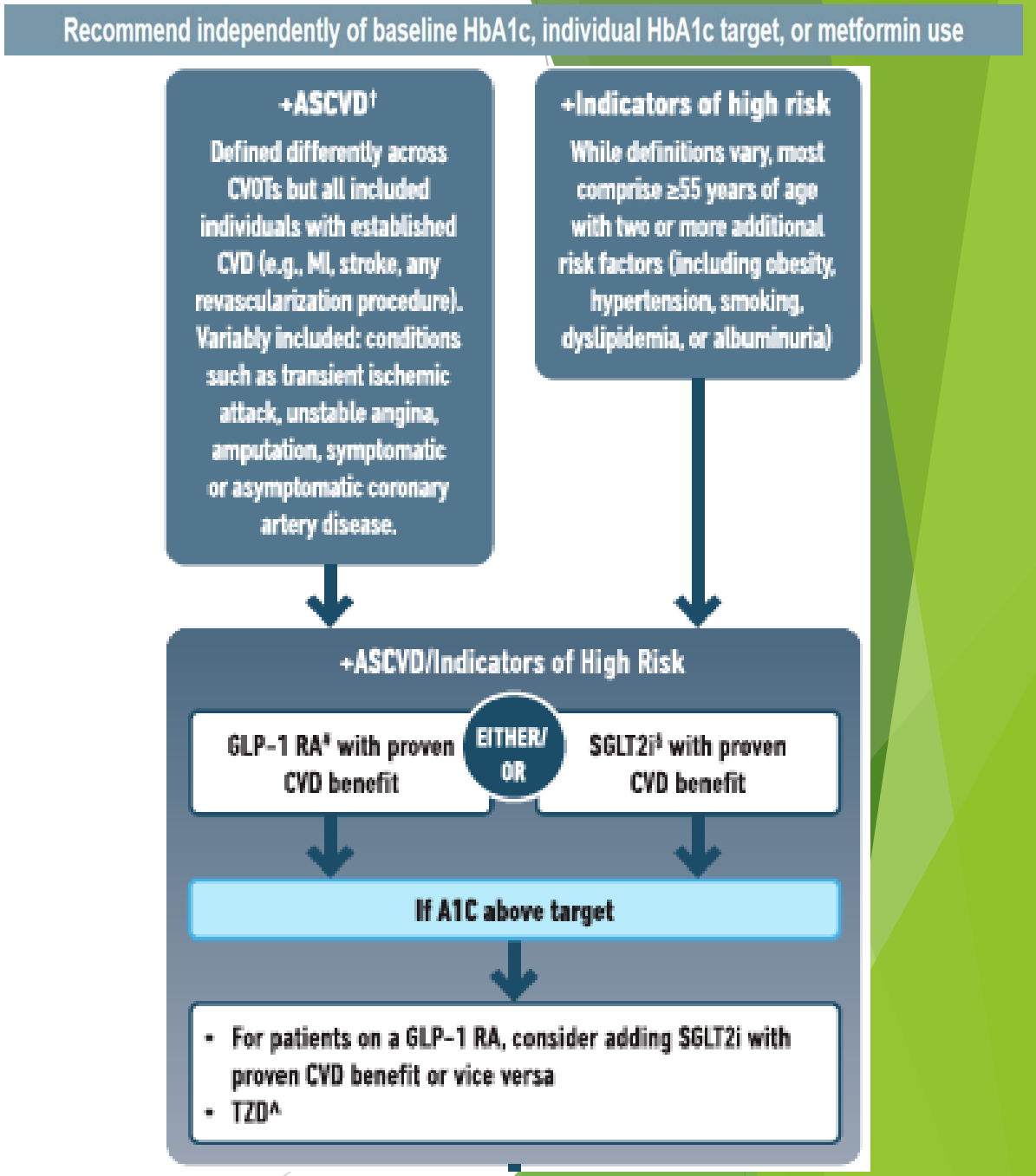


Marx N et al., Eur Heart J 2023

"Linee Guida Italiane per il trattamento del Diabete di Tipo 2 – agg. Febbraio 2023



Si raccomanda l'uso di **metformina**, **SGLT2 e GLP-1 RA** come farmaci di **prima scelta** per il trattamento a lungo termine in pazienti con **TD2 con pregressi eventi cardiovascolari** e senza scompenso cardiaco.
Pioglitazone, DPP-4i, acarbosio ed insulina dovrebbero essere considerati farmaci di seconda scelta. Sulfaniluree e glinidi non sono raccomandati per la terapia del diabete di tipo 2.



Standards of Care in Diabetes—2024

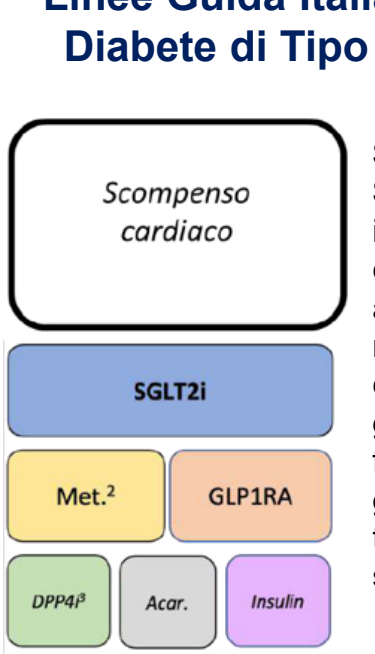
To reduce HF-related outcomes in all patients with T2DM and HF (HFpEF, HFmrEF, HFrEF)

SGLT2 inhibitor (Class I)

Independent of HbA1c

Independent of concomitant glucose-lowering medication

Marx N et al., Eur Heart J 2023



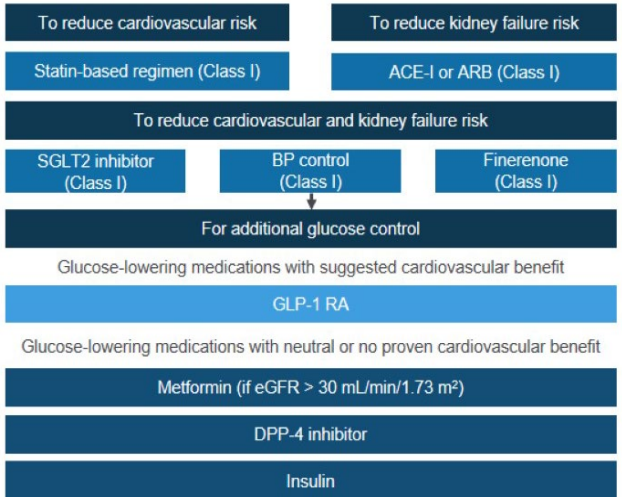
Standards of Care in Diabetes—2024

"Linee Guida Italiane per il trattamento del Diabete di Tipo 2 – agg. Febbraio 2023

Si raccomanda l'uso degli inibitori di **SGLT-2** come farmaci di **prima scelta** per il trattamento a lungo termine di pazienti con **TD2 con scompenso cardiaco**. Gli analoghi recettoriali di GLP-1 e metformina dovrebbero essere considerati come farmaci di seconda scelta, mentre gli DPP-4i,acarbosio ed insulina come farmaci di terza scelta. Sulfaniluree e glinidi non sono raccomandati per la terapia del diabete di tipo 2 associato a scompenso cardiaco.

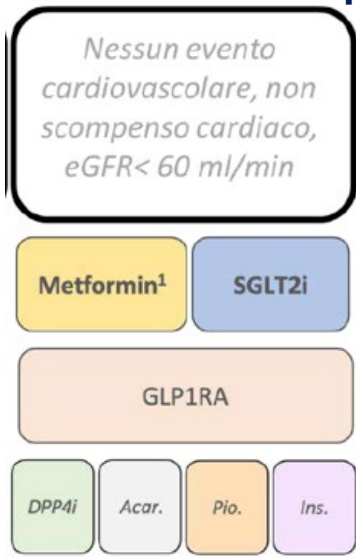
ESC Guidelines 2023

Treatment of patients with T2DM and CKD

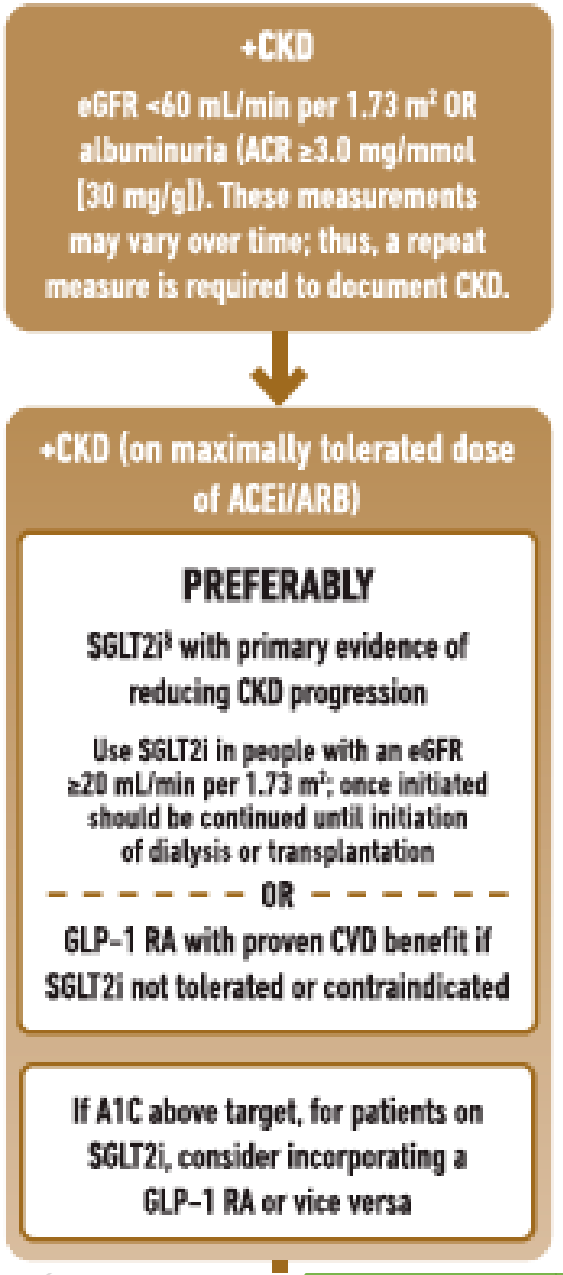


Marx N et al., Eur Heart J 2023

"Linee Guida Italiane per il trattamento del Diabete di Tipo 2 – agg. Febbraio 2023

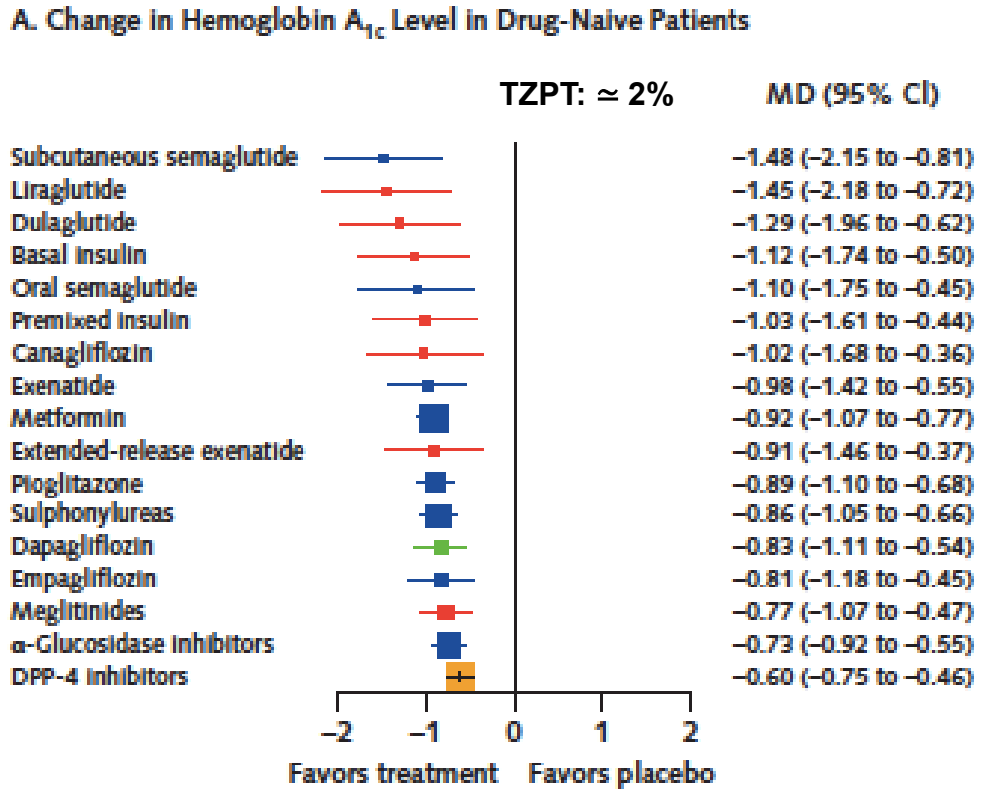


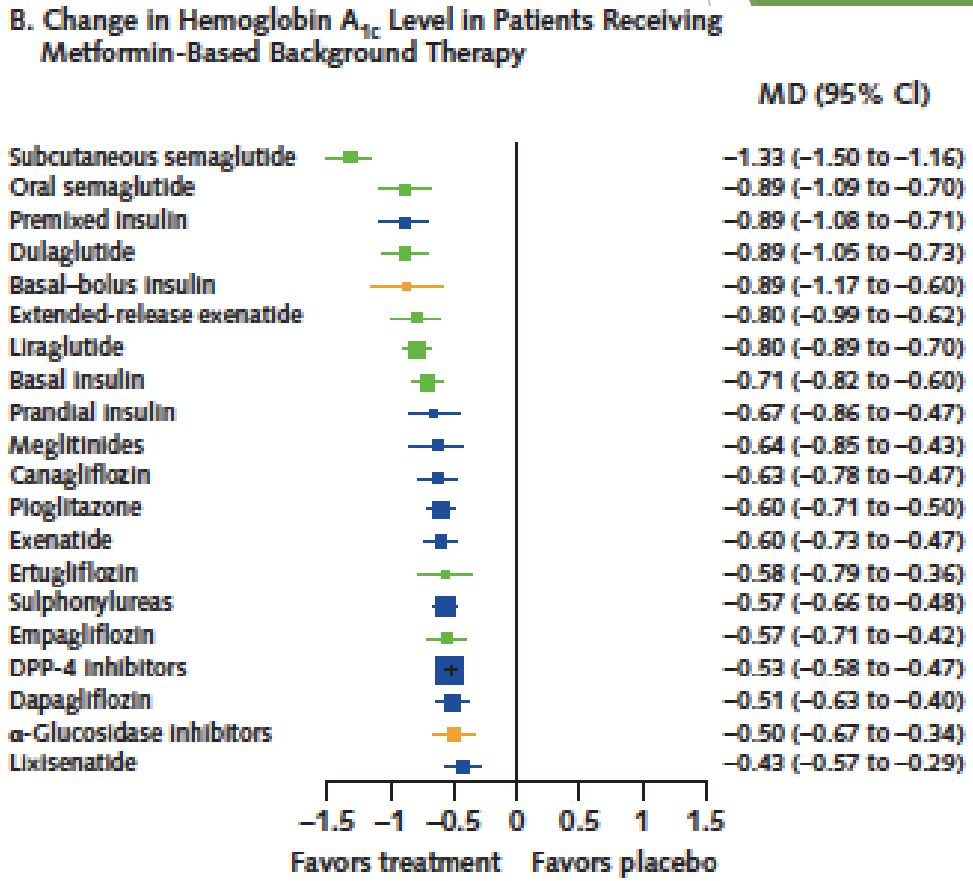
Si suggerisce l'uso di **metformina e SGLT2** inibitori come farmaci di **prima scelta** per il trattamento a lungo termine in pazienti con **TD2 con eGFR<60** ml/min e senza pregressi eventi cardiovascolari o scompenso cardiaco; gli agonisti GLP-1 RA sono raccomandati come farmaci di seconda scelta. Pioglitazone, DPP-4i, acarbosio ed insulina dovrebbero essere considerati farmaci di terza scelta. Sulfaniluree e glinidi non sono raccomandate per la terapia del diabete di tipo 2 associato ad insufficienza renale.



Standards of Care in Diabetes—2024

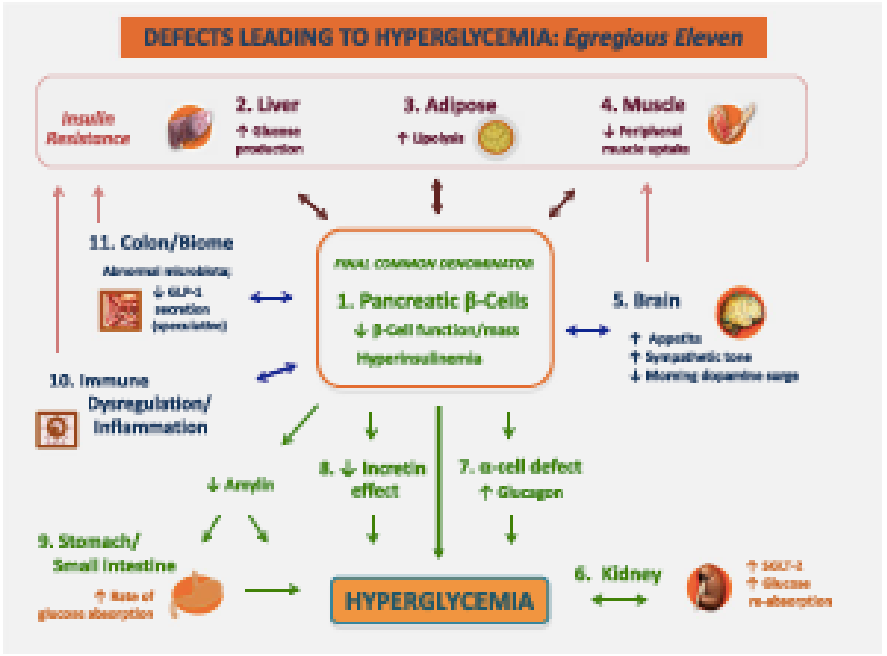
EFFICACIA ANTI-IPERGLICEMICA DEI FARMACI "INNOVATIVI"





Tsapas A et al., Ann Int Med 2020

TD2: UN DISORDINE ETEROGENEO



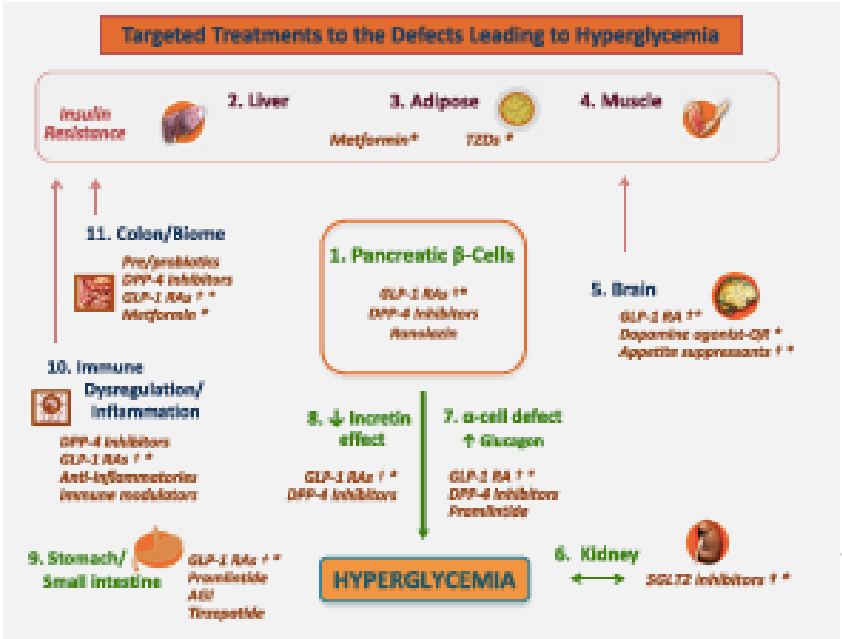
Phenotypic Clustering To Identify Subgroups of Patients With T2D
Swedish All New Diabetics in Scania Cohort

Five replicable clusters in patients with newly diagnosed diabetes (N = 8980) based on age at diagnosis, BMI, HbA1c, GADA, and homoeostatic model assessment 2 estimates of β-cell function and insulin resistance

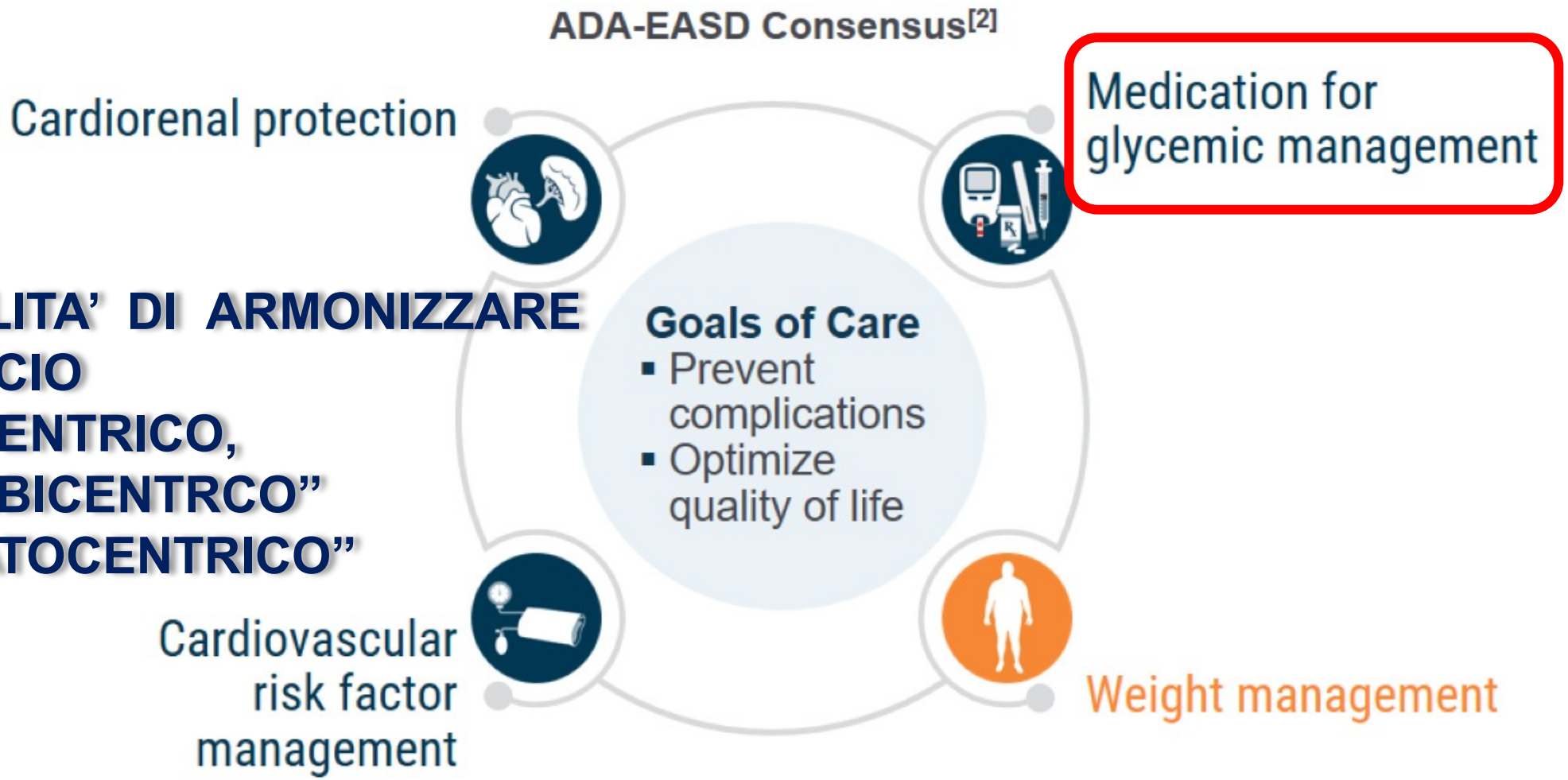
Cluster and Patient Distribution

1	2	3	4	5
Severe Autoimmune Diabetes (6.4%)	Severe Insulin-Deficient Diabetes (17.5%)	Severe Insulin-Resistant Diabetes (15.3%)	Mild Obesity-Related Diabetes (21.6%)	Mild Age-Related Diabetes (39.1%)

BMI, body mass index; GADA, glutamic acid decarboxylase antibodies; HbA1c, glycated hemoglobin.
Ahlqvist E, et al. Lancet Diabetes Endocrinol. 2018;6:361-369.



Holistic Approach to T2D Management Including Weight Loss
2022 ADA-EASD Consensus



POSSIBILITA' DI ARMONIZZARE APPROCCIO GLUCOCENTRICO, "COMORBICENTRCO" "FISIOPATOCENTRICO"

1. Sattar N, et al. Lancet Reg Health Southeast Asia. 2023;9:100111; 2. Davies MJ, et al. Diabetes Care. 2022;45:2753-2786.


Grazie