Starting therapy:
cosa dicono le linee guida e cosa pensa il medico

Edoardo Mannucci

Diabetologia e Malattie Metaboliche, AOU Careggi
Endocrinologia, Università di Firenze

Conflitti di interesse

Negli ultimi due anni, E. Mannucci ha ricevuto compensi per relazioni e/o consulenze da

Boehringer Ingelheim, Dexcom, Eli Lilly, MSD, Novo Nordisk, Sanofi

La struttura di appartenenza di E. Mannucci ha ricevuto :

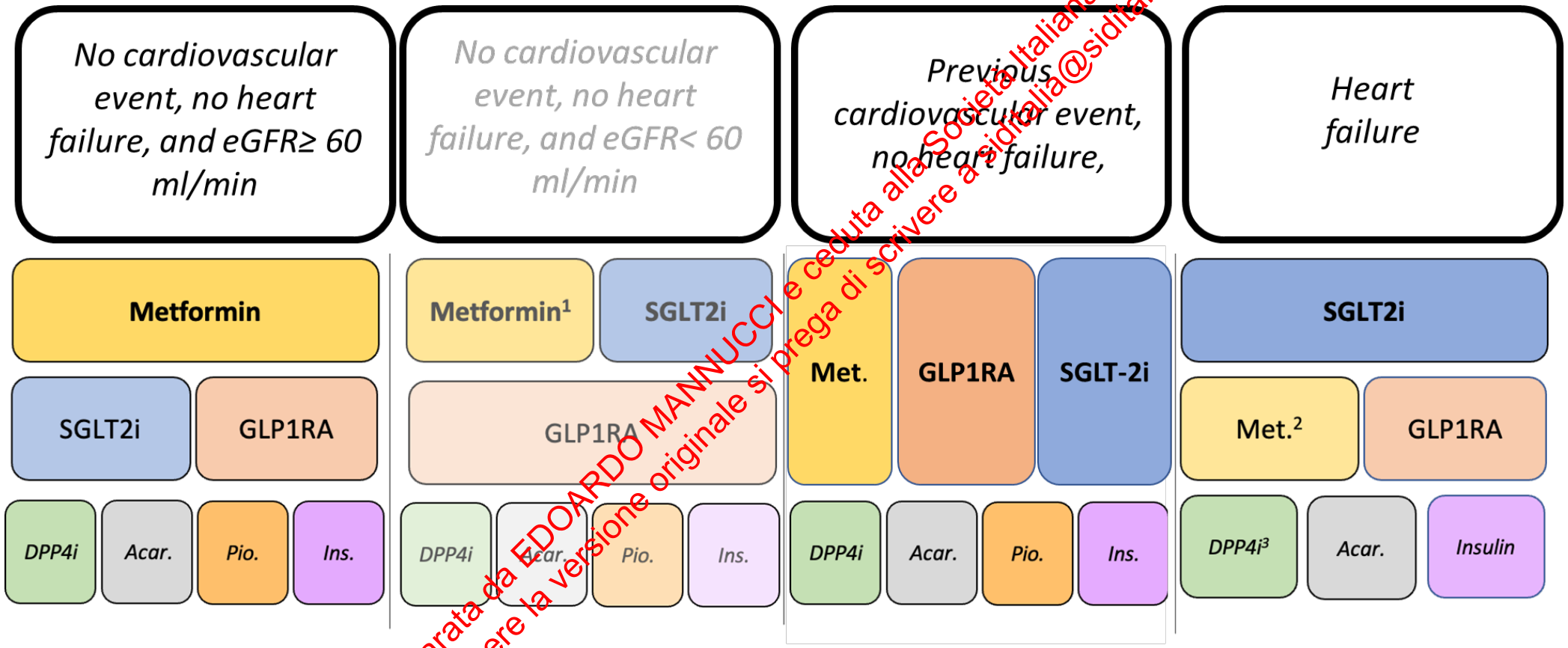
- Finanziamenti per ricerca indipendente non condizionata da ***Abbott***
- Compensi per studi clinici sponsorizzati da ***Boehringer Ingelheim, Daiichi Sankyo, Eli Lilly, Molteni, Novo Nordisk***

Starting therapy

- Cosa dicono le linee guida?
- Cosa pensa il medico?

Italian guidelines for the treatment of T2DM, 2023

Drug therapy



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[3] *With the exception of saxagliptin which is not indicated for patients with heart failure.*

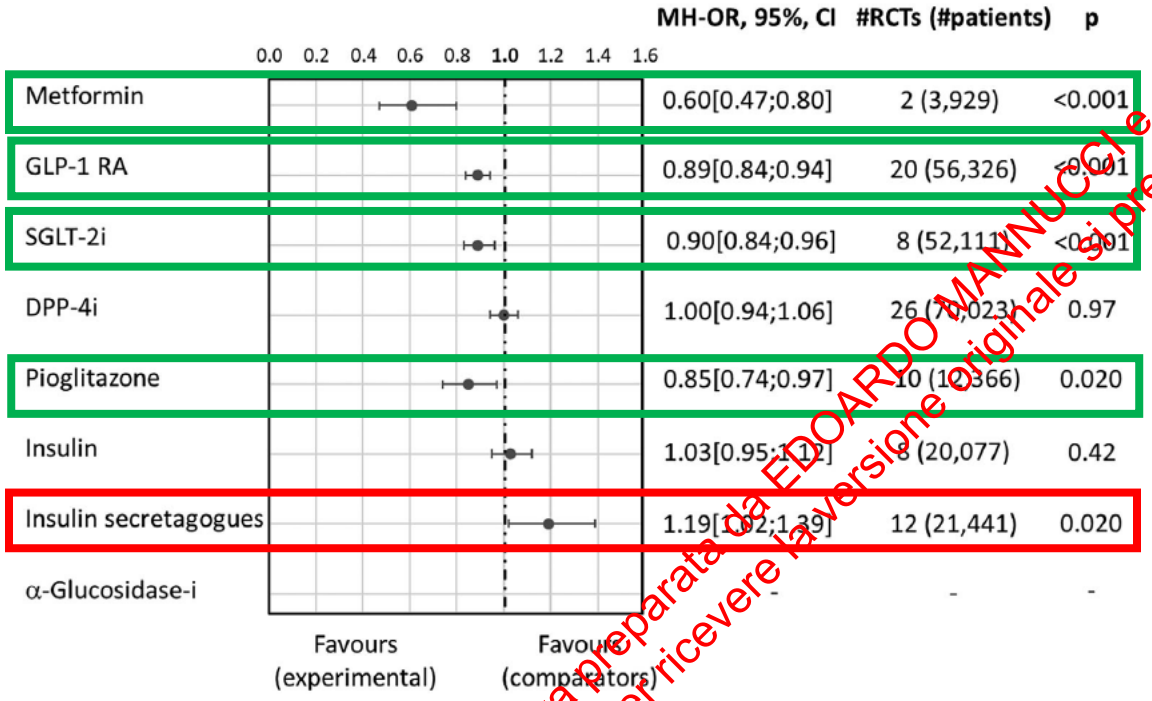
The recommendation for patients with eGFR< 60ml/min is weak (few studies on this population) and therefore is written with a lighter type

We recommend to deprescribe sulfonylureas and glinides.

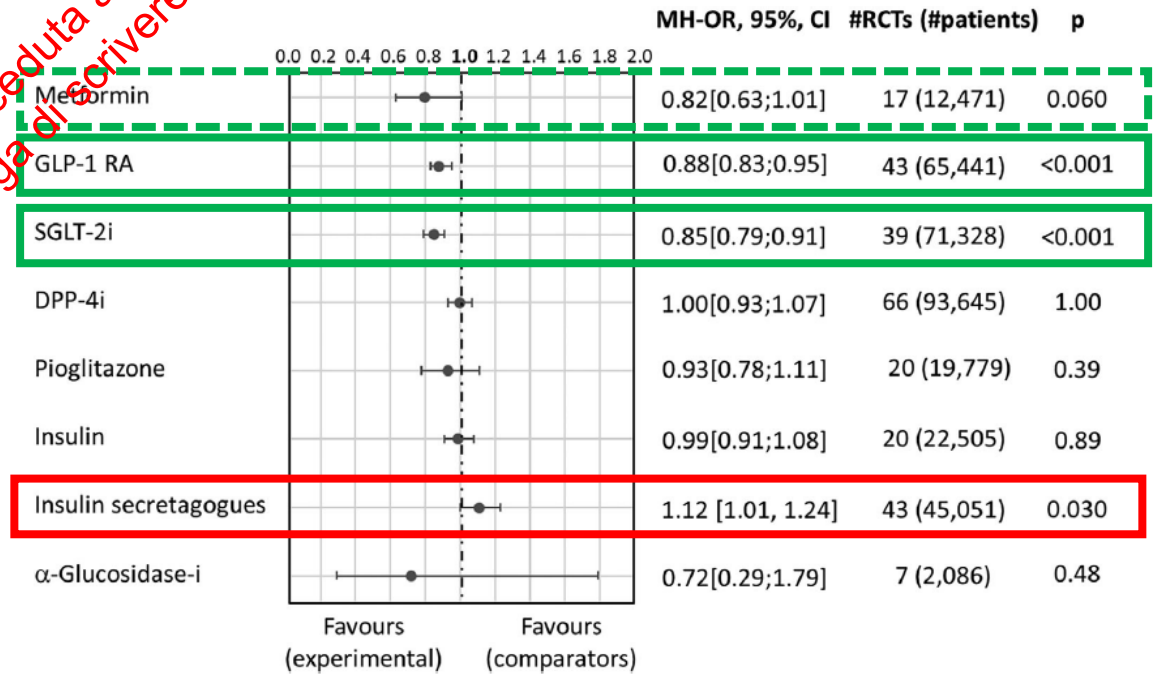
Mannucci E et al. for SID and AMD. *Acta Diabetol*, 2023

Italian guidelines for the treatment of T2DM
Evidence base for 2023 update

Major Cardiovascular Events



All-cause mortality



Mannucci E et al. for SID-AMD T2DM Guideline Panel. *Diabetes Obes Metab* 25:444-53, 2023

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TABLE 1 Effects of different classes of drugs on renal endpoints

Outcome	Glucose-lowering agents MH-OR [95% CI]							
	Metformin	GLP-1 RA	SGLT-2i	DPP-4i	Pioglitazone[a]	Insulin	Insulin secretagogues[a]	α-Glucosidase-i
Renal outcomes								
Worsening albuminuria[c]	[b]	0.81 [0.66; 1.00]*	0.67 [0.55; 0.80]	0.85 [0.76,0.95]	[b]	[b]	[b]	[b]
No. of studies (patients)	[b]	5 (42 093)	5 (42 837)	2 (23 471)	[b]	[b]	[b]	[b]
Doubling of creatinine[d]	[b]	0.92 [0.74; 1.14]	0.58 [0.44; 0.79]	1.30 [0.67; 2.53]	[b]	1.34 [0.95; 1.90]*	[b]	[b]
No. of studies (patients)	[b]	4 (19 277)	4 (29 809)	3 (17 104)	[b]	1 (577)	[b]	[b]
Renal death	2.14 [0.86;9.94]	1.19 [0.53, 2.66]	0.43 [0.15; 1.24]	0.87 [0.39,1.93]	[b]	[b]	2.02 [0.97;4.21]*	[b]
No. of studies (patients)	1 (3625)	4 (26 025)	3 (17 449)	8 (32 368)	[b]	[b]	3 (10 472)	[b]

Abbreviations: CI, confidence intervals; CV, cardiovascular; DPP-4i, dipeptidyl-peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonists; i, inhibitors; MH-OR, Mantel-Haenzel odds ratio. SGLT-2i, sodium-glucose co-transporter-2 inhibitor.

[a]One study reported the following renal outcome: 'new or worsening CKD' comparing pioglitazone vs. sulphonylureas: (MH-OR: 0.98 [0.82; 1.18]).

[b]Unknown effect.

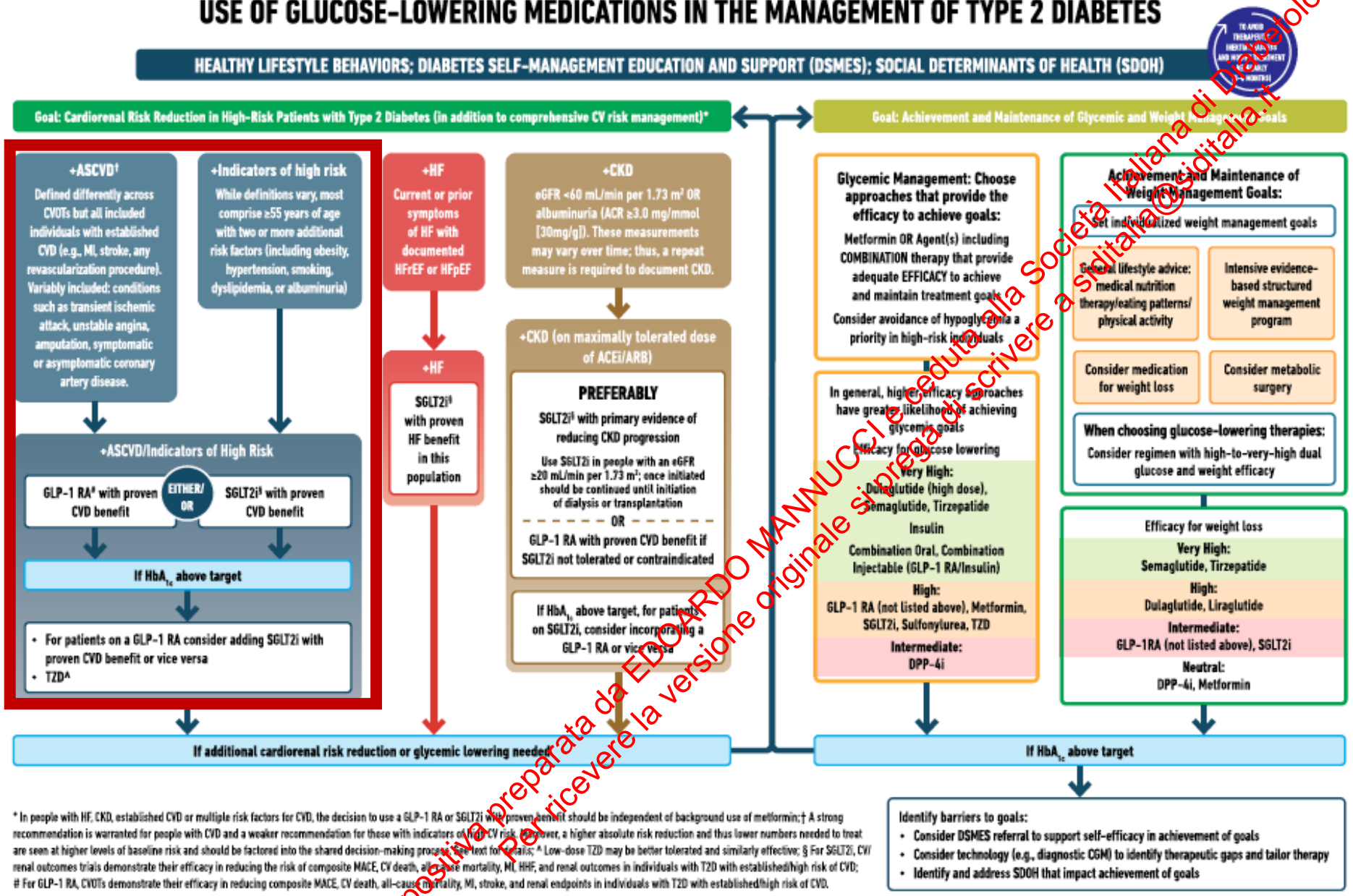
[c]Worsening albuminuria: incident microalbuminuria in normoalbuminuric subjects or incident macroalbuminuria in microalbuminuric subjects.

[d]From baseline.

*$P < .10$.

Mannucci E et al. for SID-AMD T2DM Guideline Panel. *Diabetes Obes Metab* 25:444-53, 2023

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES



* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

American Diabetes Association®

EASD
European Association for the Study of Diabetes

Consensus Report on the management of hyperglycemia in type 2 diabetes

2022 Edition

Diabetes Care 2022;45:2753–2786

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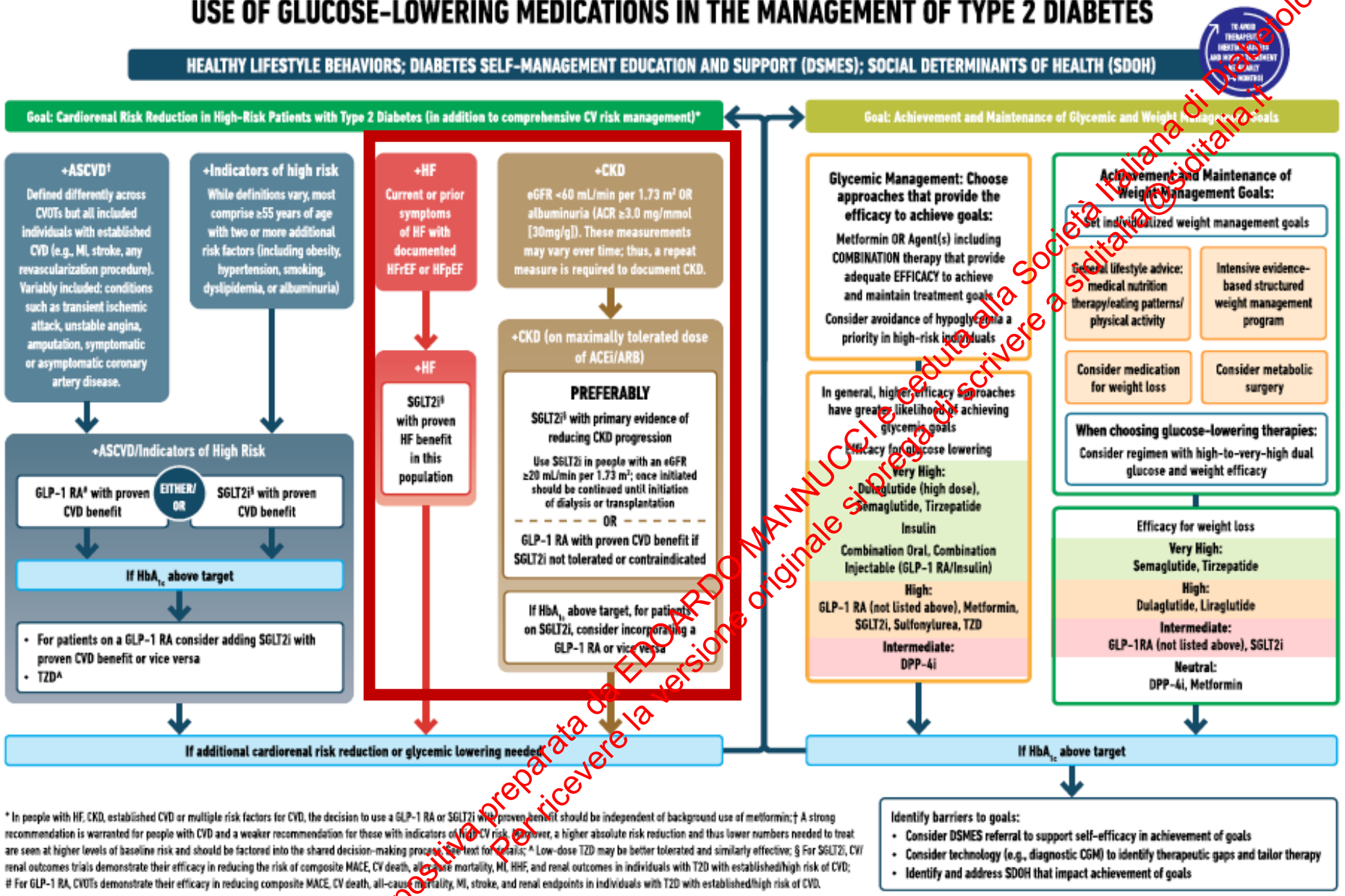

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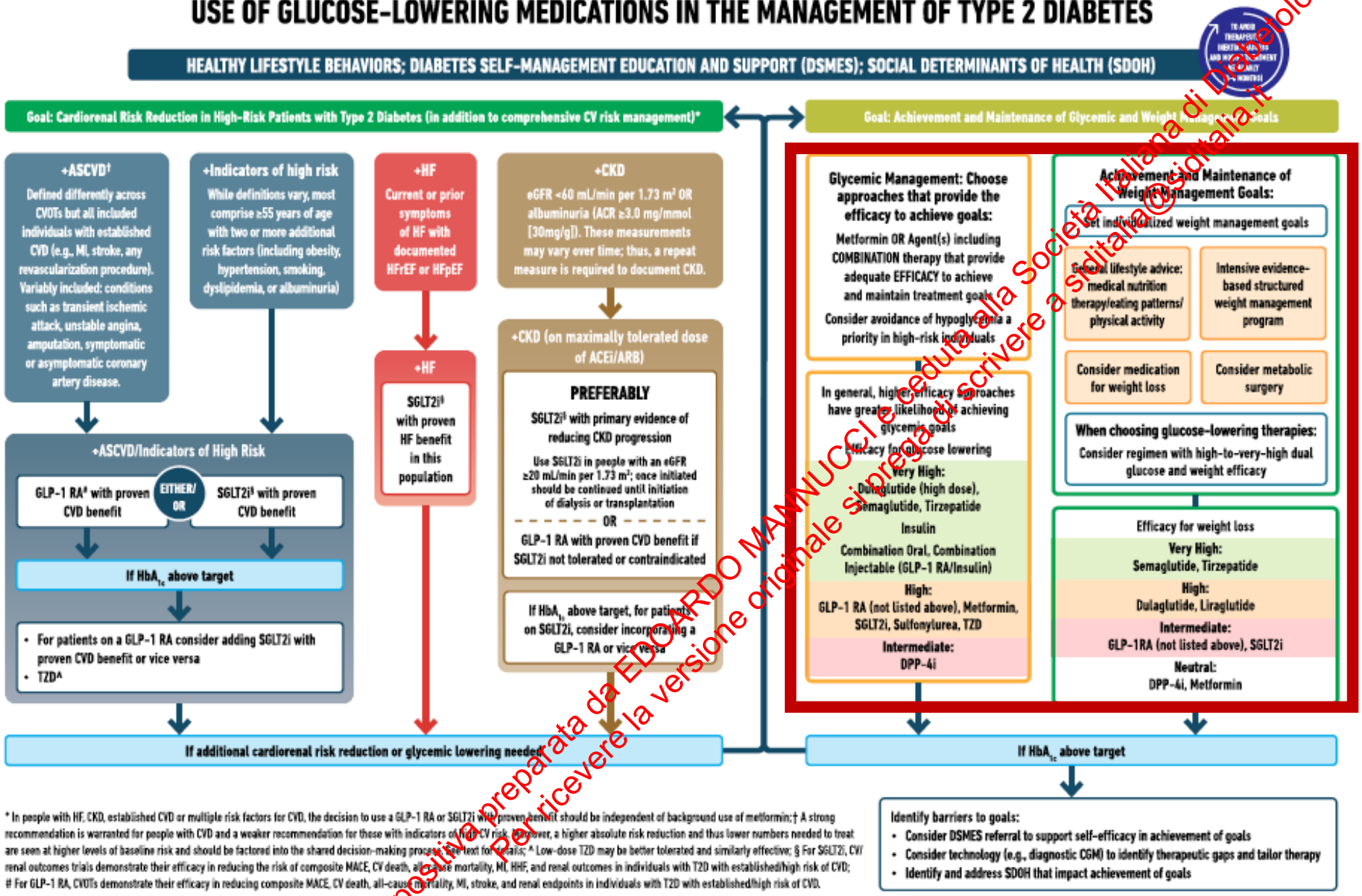

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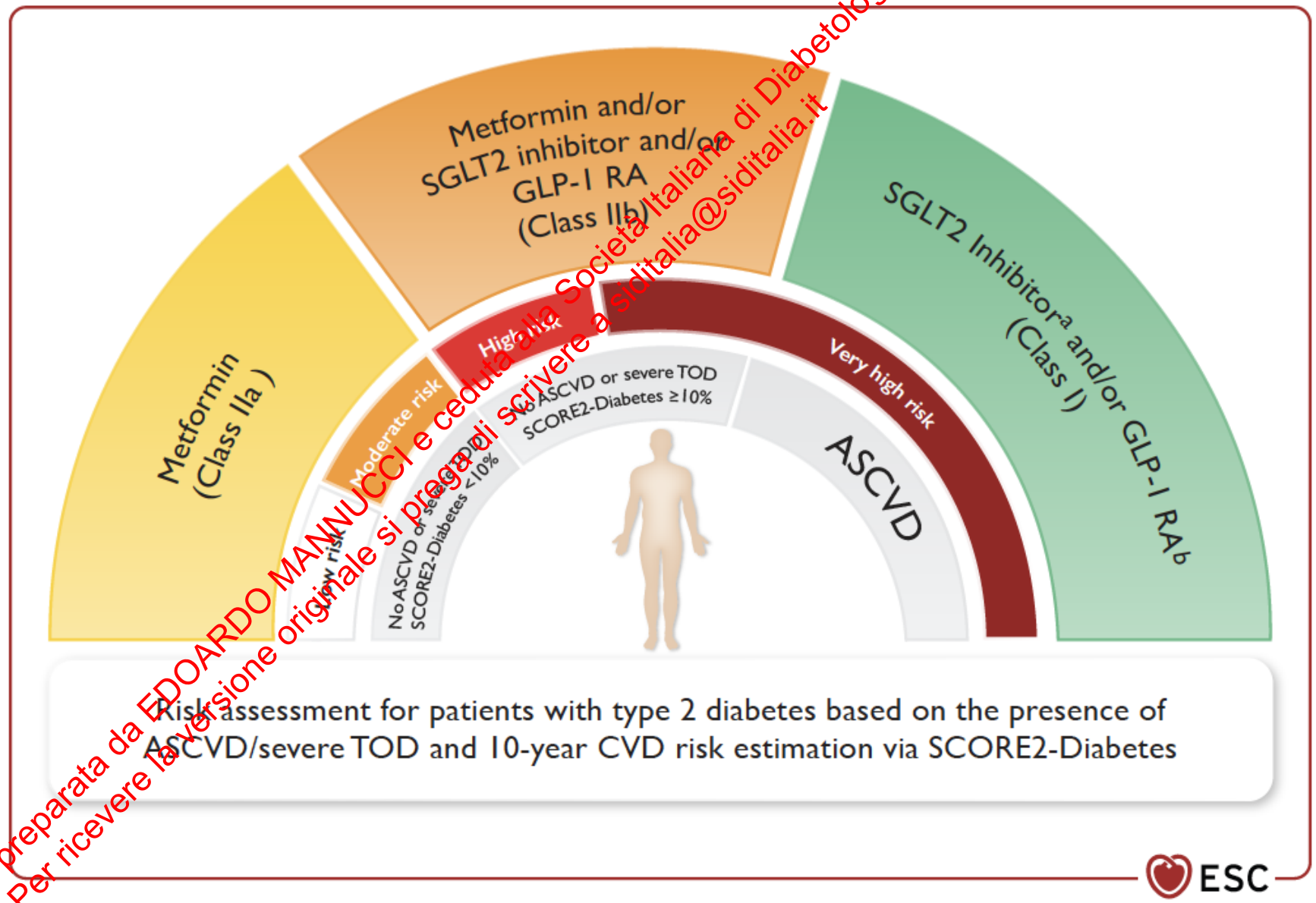
ESC
European Society of Cardiology

ESC Guidelines on diabetes, 2023

ESC European Society of Cardiology
European Heart Journal (2023) 00, 1–98
https://doi.org/10.1093/eurheartj/ehad192
ESC GUIDELINES

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

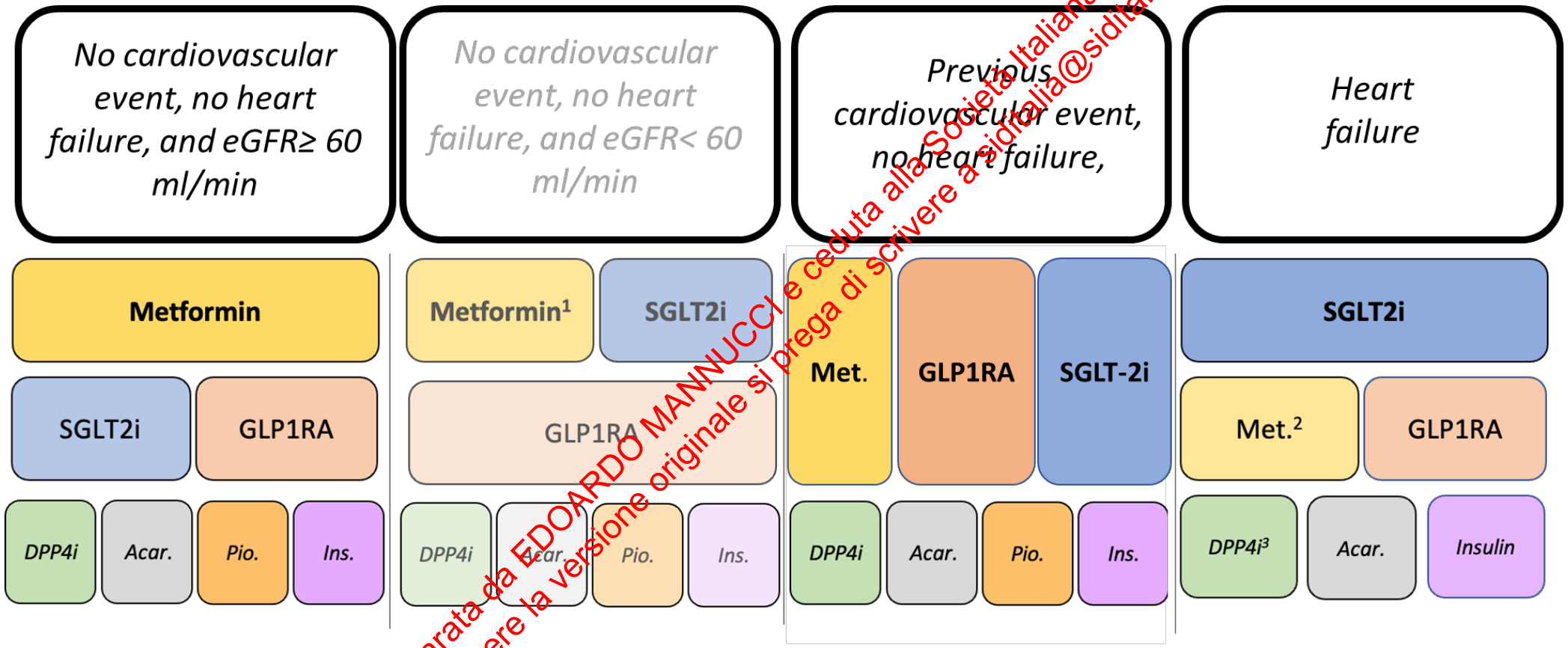


Risk assessment for patients with type 2 diabetes based on the presence of ASCVD/severe TOD and 10-year CVD risk estimation via SCORE2-Diabetes

ESC

Italian guidelines for the treatment of T2DM, 2023

Drug therapy



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Starting therapy

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- Cosa pensa il medico?

Annali 2023

Uso dei farmaci (%)

Farmaci per il diabete (%)

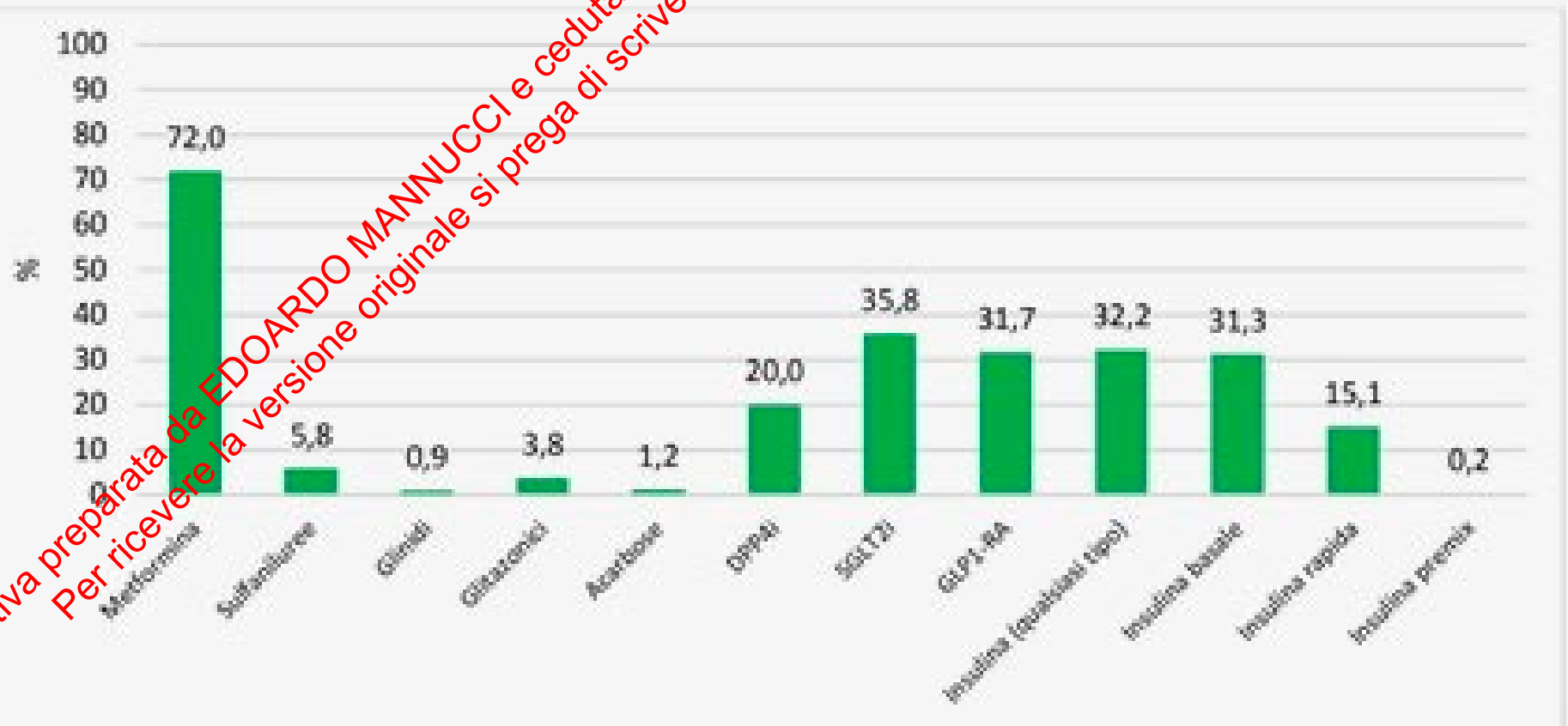
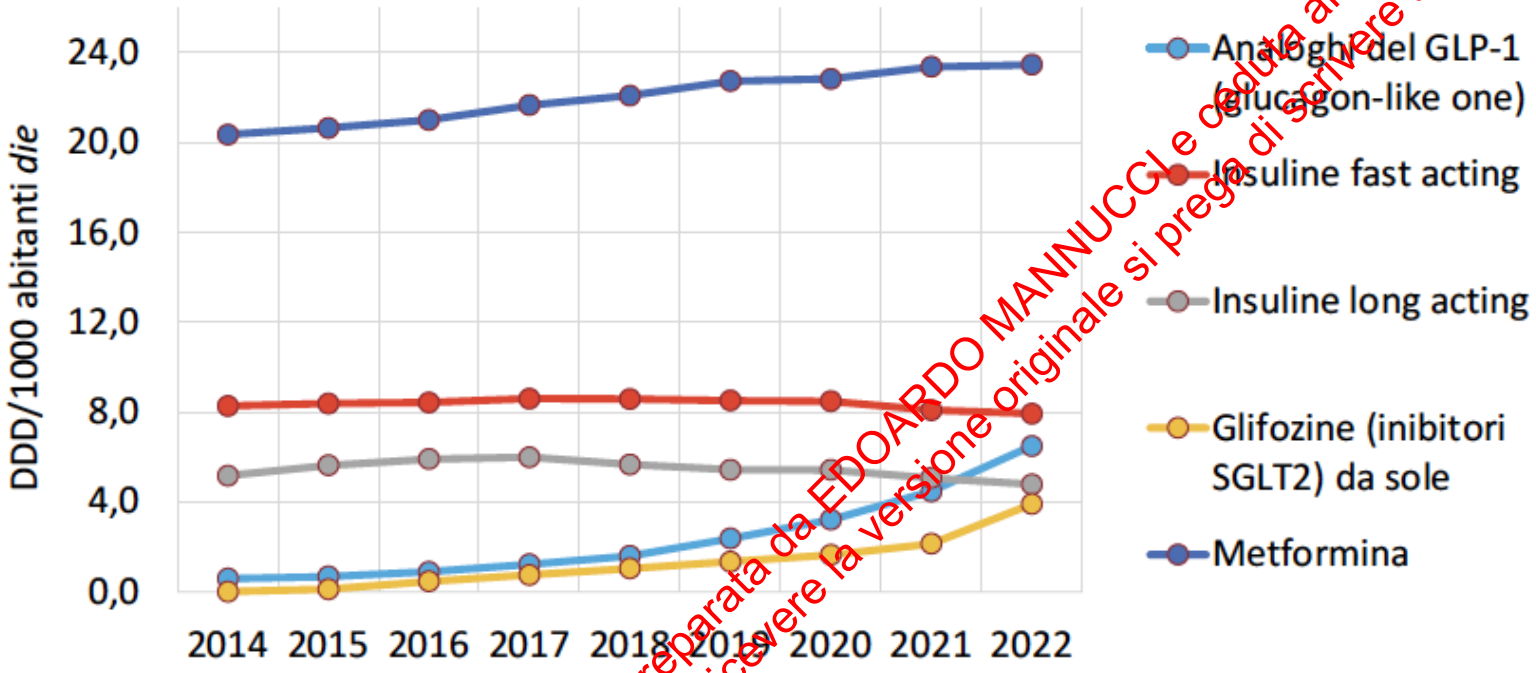


Figura 3.3.1b Antidiabetici, andamento temporale 2014-2022 del consumo (DDD/1000 abitanti *die*) dei sottogruppi a maggior spesa



L'uso dei Farmaci in Italia

Rapporto Nazionale
Anno 2022

OSSERVATORIO NAZIONALE SULL'IMPIEGO DEI MEDICINALI

AIFA
AGENZIA ITALIANA DEL FARMACO

AGENZIA ITALIANA DEL FARMACO

Nota AIFA 100

Analisi a 18 mesi dall'introduzione della Nota

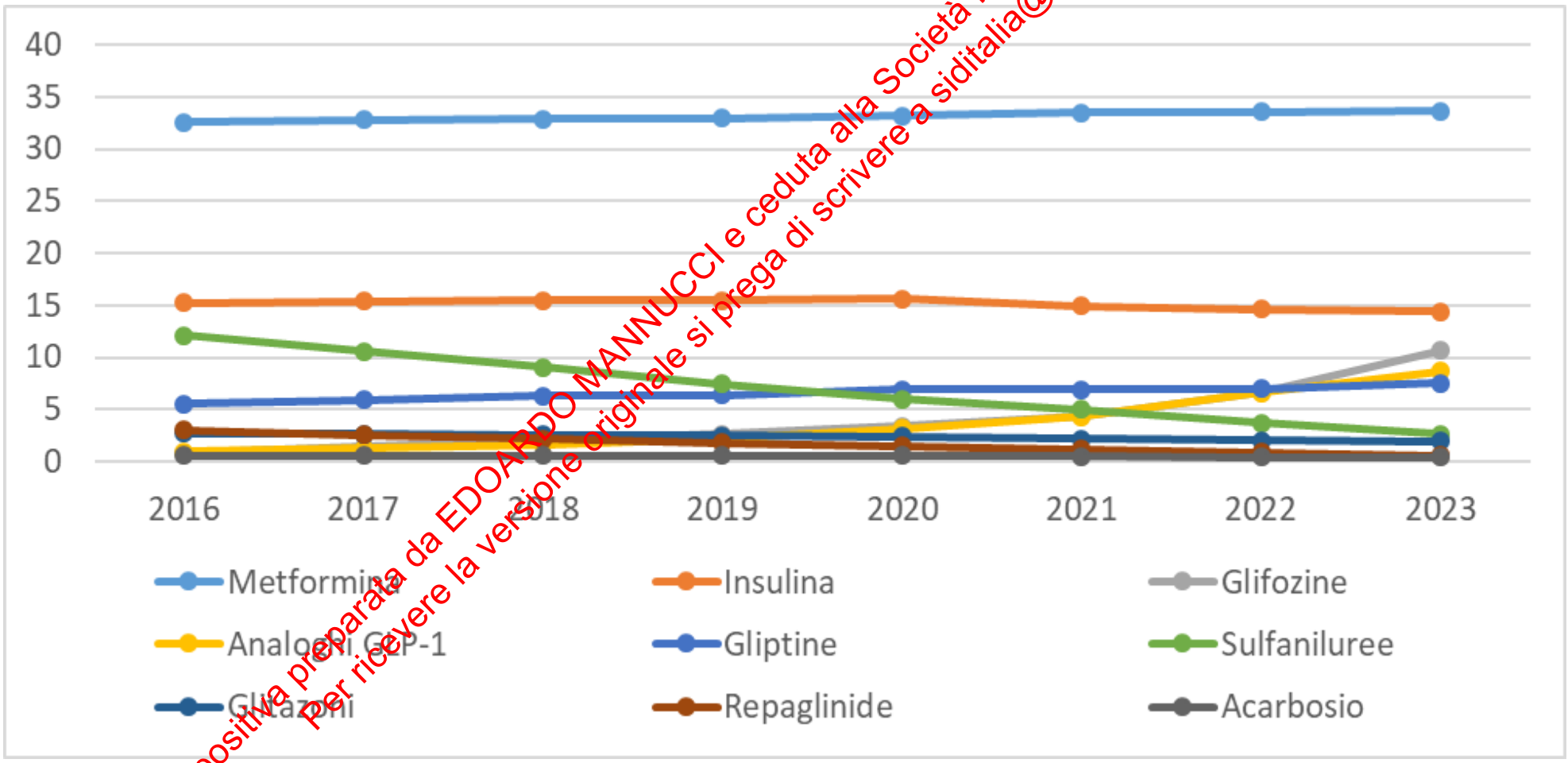
	I semestre 2020	II semestre 2020	I semestre 2021	II semestre 2021	I semestre 2022	II semestre 2022	I semestre 2023
TOTALE categoria A10	3.279.373	3.298.411	3.363.830	3.382.652	3.440.020	3.444.187	3.522.730
delta		1%	2%	1%	2%	0,1%	2%

	I semestre 2020	II semestre 2020	I semestre 2021	II semestre 2021	I semestre 2022	II semestre 2022	I semestre 2023
Categoria GLP1-RA (ATC: A10BJ)	168.625	195.633	236.525	291.615	375.656	433.494	488.807
delta		16%	21%	23%	29%	15%	13%

	I semestre 2020	II semestre 2020	I semestre 2021	II semestre 2021	I semestre 2022	II semestre 2022	I semestre 2023
Categoria SGLT2i (ATC: A10BK)	103.834	117.362	141.258	174.622	251.346	324.020	420.449
delta		13%	20%	24%	44%	29%	30%

ARS TOSCANA
agenzia regionale di sanità

Farmaci per il diabete, 2023



ARS TOSCANA
agenzia regionale di sanità

Farmaci per il diabete, 2023

Tipologia	DDD per 1.000 ab die	Var. % 23-22	Var. media % 23-16
Analoghi del GLP-1	8,7	31,9	110,8
Insulina	14,4	-1,2	-0,8
Glifozine	10,7	59,5	174,3
Metformina	33,7	0,3	0,5
Gliptine	7,6	8,1	5,2
Glitazoni	1,9	-5,5	-4,3
Sulfaniluree	2,6	-30,1	-11,2
Acarbosio	0,4	-9,9	-4,9
Repaglinide	0,6	-31,2	-11,5
Totale	**73,7**	**+5,8**	**+1,5**

Why use a SGLT2 inhibitor rather than a GLP1-RA?

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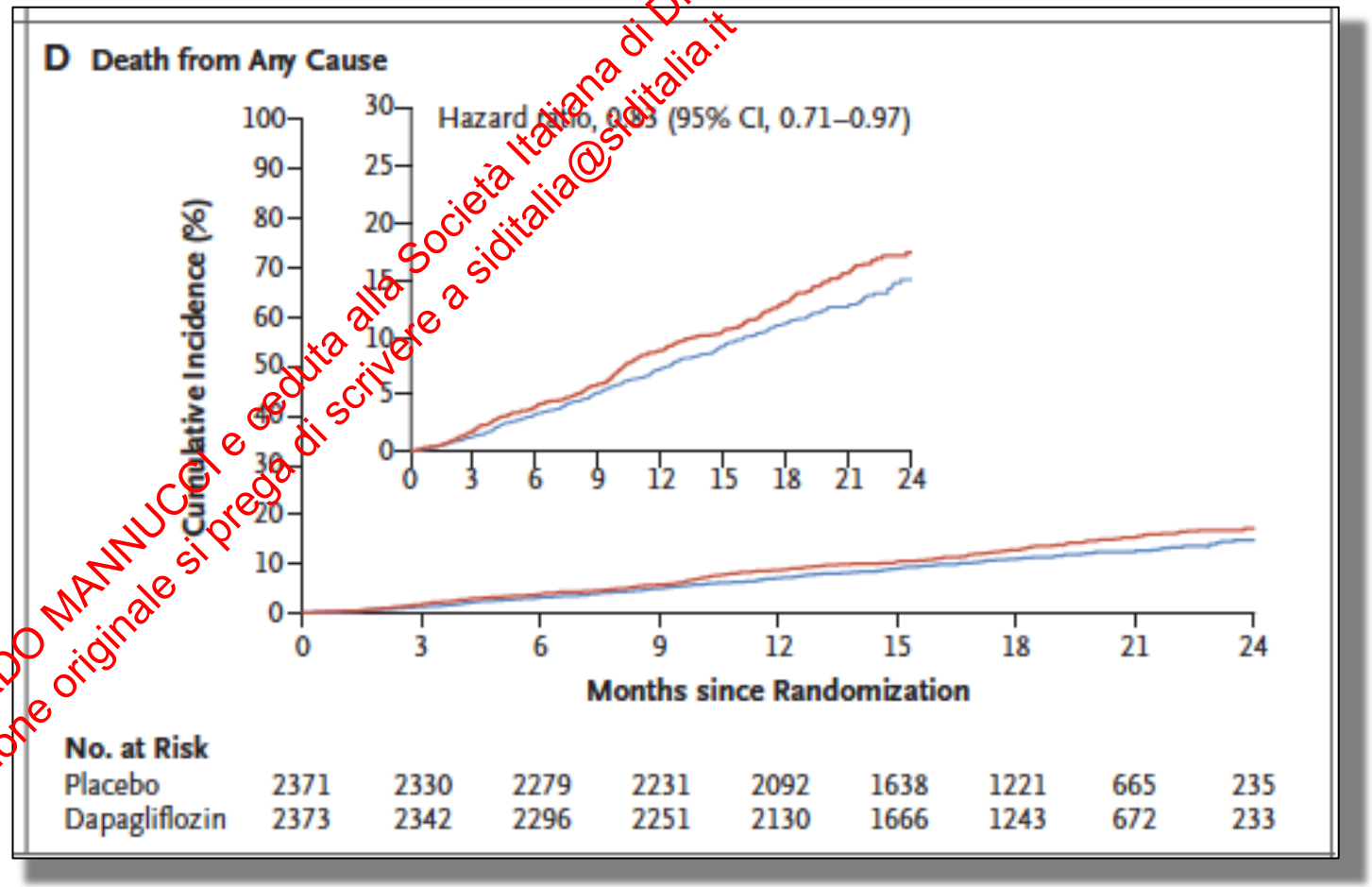
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 21, 2019 VOL. 381 NO. 21

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

J.J.V. McMurray, S.D. Solomon, S.E. Inzucchi, L. Køber, M.N. Kosiborod, F.A. Martinez, P. Ponikowski, M.S. Sabatine, I.S. Anand, J. Bělohlávek, M. Böhm, C.-E. Chiang, V.K. Chopra, R.A. de Boer, A.S. Desai, M. Diez, J. Drozdz, A. Dukát, J. Ge, J.G. Howlett, T. Katova, M. Kitakaze, C.E.A. Ljungman, B. Merkely, J.C. Nicolau, E. O'Meara, M.C. Petrie, P.N. Vinh, M. Schou, S. Tereshchenko, S. Verma, C. Held, D.L. DeMets, K.F. Docherty, P.S. Jhund, O. Bengtsson, M. Sjöstrand, and A.-M. Langkilde, for the DAPA-HF Trial Committees and Investigators*



DAPA-HF trial

Treatment: dapagliflozin
Comparator: placebo
Principal outcome: Composite of cardiovascular death or hospitalization for HF
Patients: 4,744 patients with NYHA class II-IV HF and EF<40%
Follow-up: 18 months

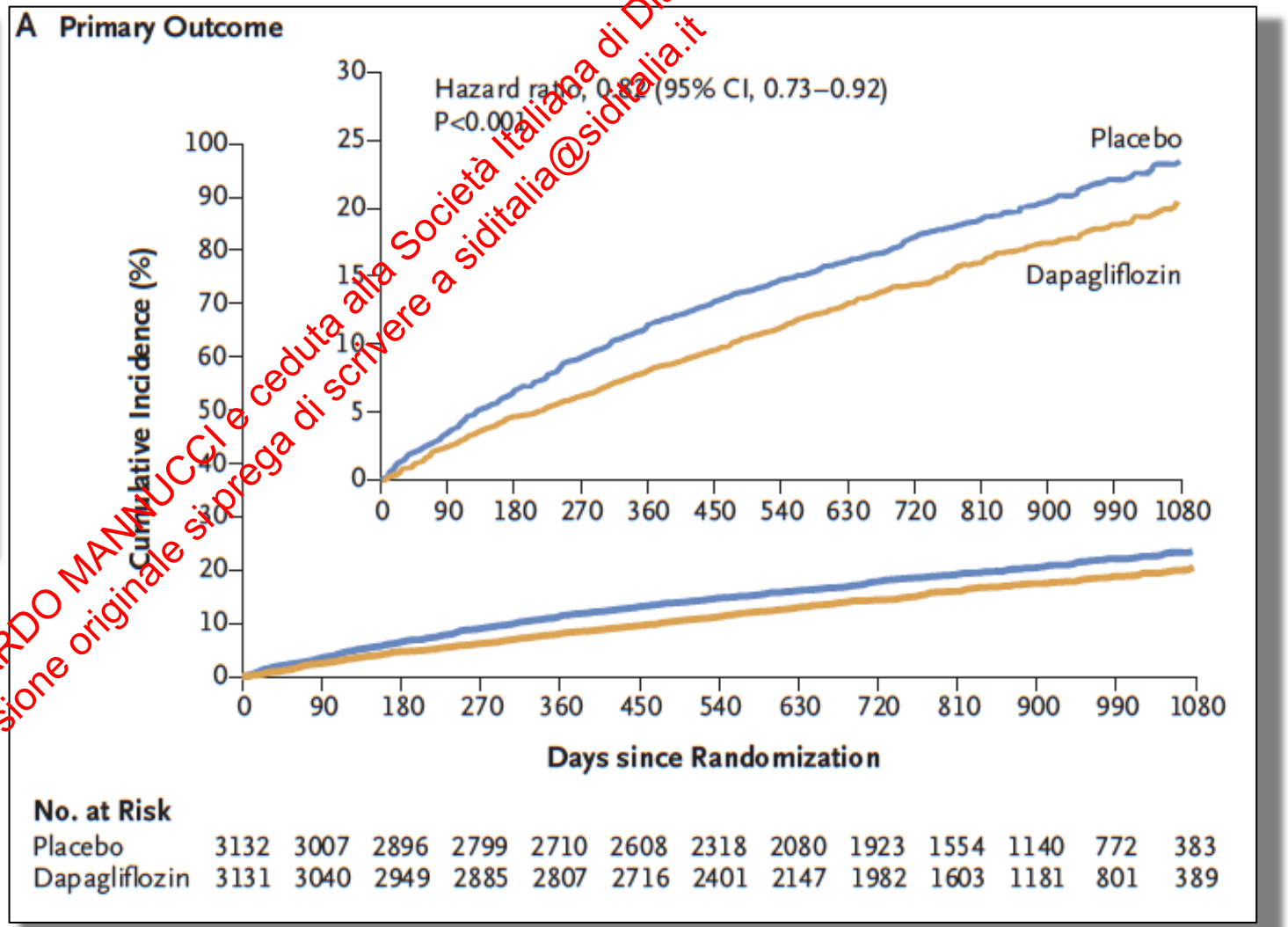
McMurray JJV et al. *N Engl J Med* 381:1995-2008; 2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, B. Claggett, R.A. de Boer, D. DeMets, A.F. Hernandez, S.E. Inzucchi, M.N. Kosiborod, C.S.P. Lam, F. Martinez, S.J. Shah, A.S. Desai, P.S. Jhund, J. Belohlavek, C.-E. Chiang, C.J.W. Borleffs, J. Comin-Colet, D. Dobreanu, J. Drozdz, J.C. Fang, M.A. Alcocer-Gamba, W. Al Habeeb, Y. Han, J.W. Cabrera Honorio, S.P. Janssens, T. Katova, M. Kitakaze, B. Merkely, E. O'Meara, J.F.K. Saraiva, S.N. Tereshchenko, J. Thierer, M. Vaduganathan, O. Vardeny, S. Verma, V.N. Pham, U. Wilderäng, N. Zaozerska, E. Bachus, D. Lindholm, M. Petersson, and A.M. Langkilde, for the DELIVER Trial Committees and Investigators*



DELIVER trial

Treatment: dapagliflozin
Comparator: placebo
Principal outcome: Composite of cardiovascular death or hospitalization for HF
Patients: 6,263 patients with NYHA class II-IV HF and EF>40%
Follow-up: 2.3 years

Solomon SD et al. *N Engl J Med* 387:1089-1998; 2022

The NEW ENGLAND JOURNAL of MEDICINE

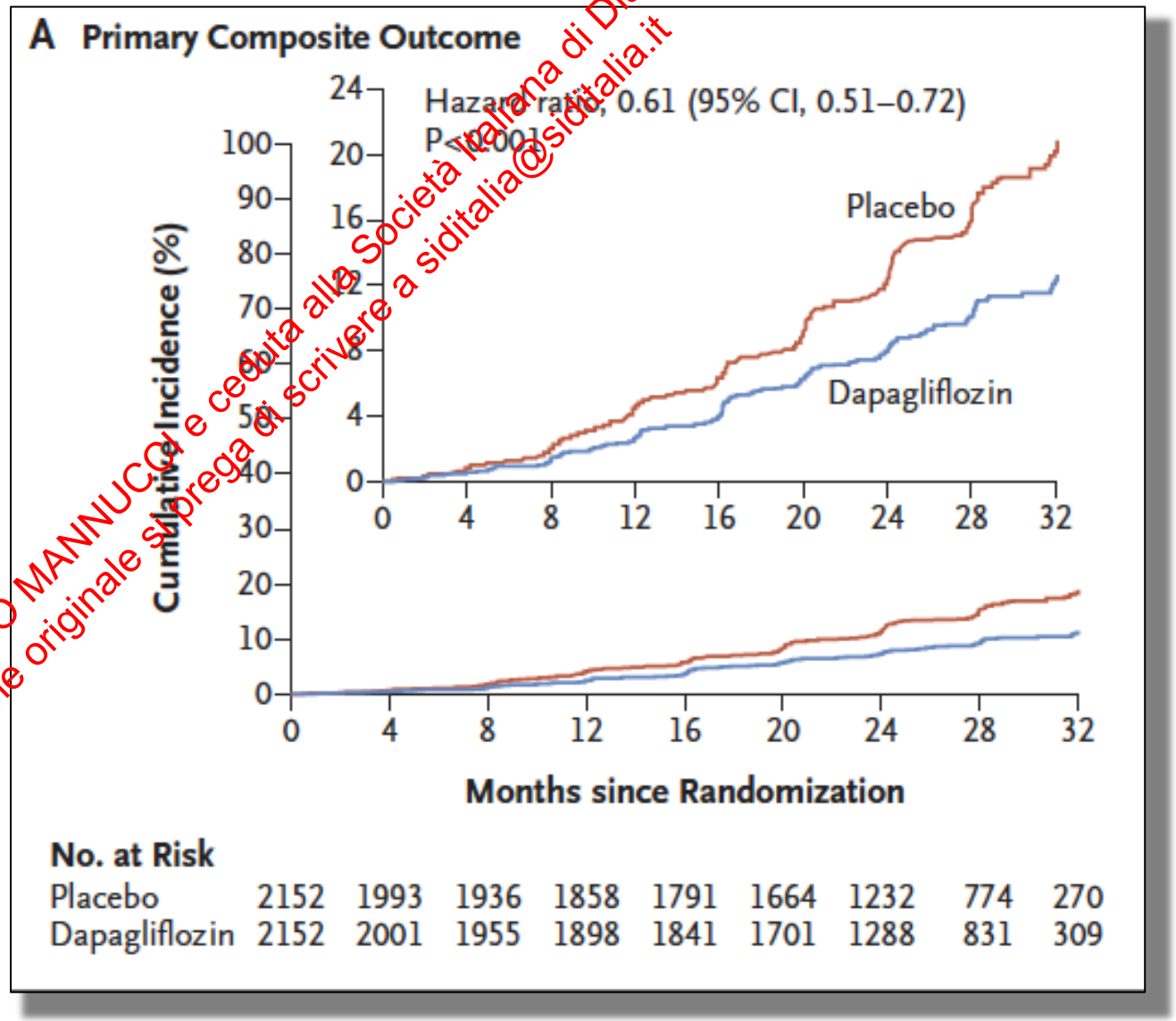
ORIGINAL ARTICLE

Dapagliflozin in Patients with Chronic Kidney Disease

Hiddo J.L. Heerspink, Ph.D., Bergur V. Stefánsson, M.D., Ricardo Correa-Rotter, M.D., Glenn M. Chertow, M.D., Tom Greene, Ph.D., Fan-Fan Hou, M.D., Johannes F.E. Mann, M.D., John J.V. McMurray, M.D., Magnus Lindberg, M.Sc., Peter Rossing, M.D., C. David Sjöström, M.D., Roberto D. Toto, M.D., Anna-Maria Langkilde, M.D., and David C. Wheeler, M.D., for the DAPA-CKD Trial Committees and Investigators*

DAPA-CKD trial

Treatment: dapagliflozin
Comparator: placebo
Principal outcome: Composite of ESRD, CV/renal dearth, eGFR decline>50%
Patients: 4,304 patients with eGFR 25-75 ml/min and ACR >200 mg/g
Follow-up: 2.4 years



Heerspink HJL et al. *N Engl J Med* 383:1436-46; 2022

Italian guidelines for the treatment of T2DM, 2023

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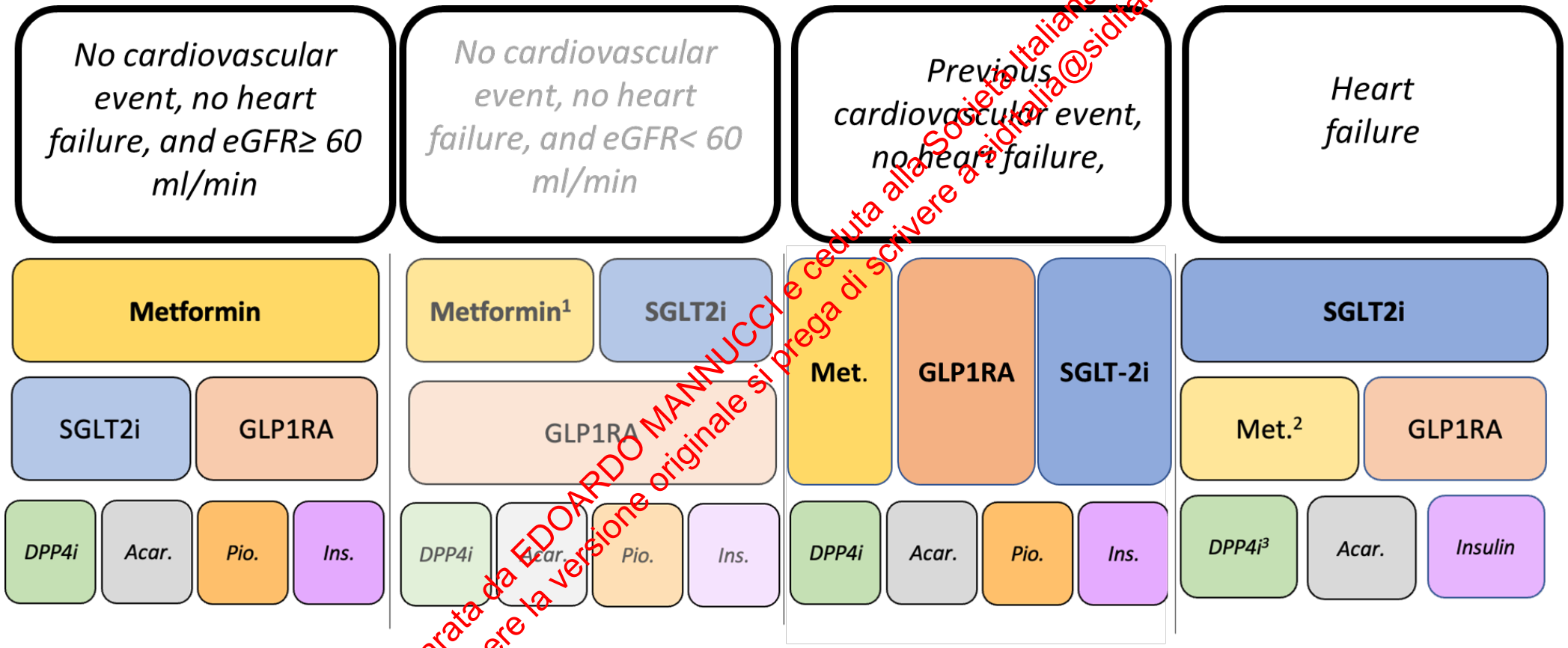

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- Different tolerability profile

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- provided that supply of drug is warranted