

Winter School: **LA PROTEZIONE RENALE ALLA LUCE DELLE NUOVE EVIDENZE SCIENTIFICHE**

Overview delle recenti Linee guida



ADA/EASD Consensus 2022

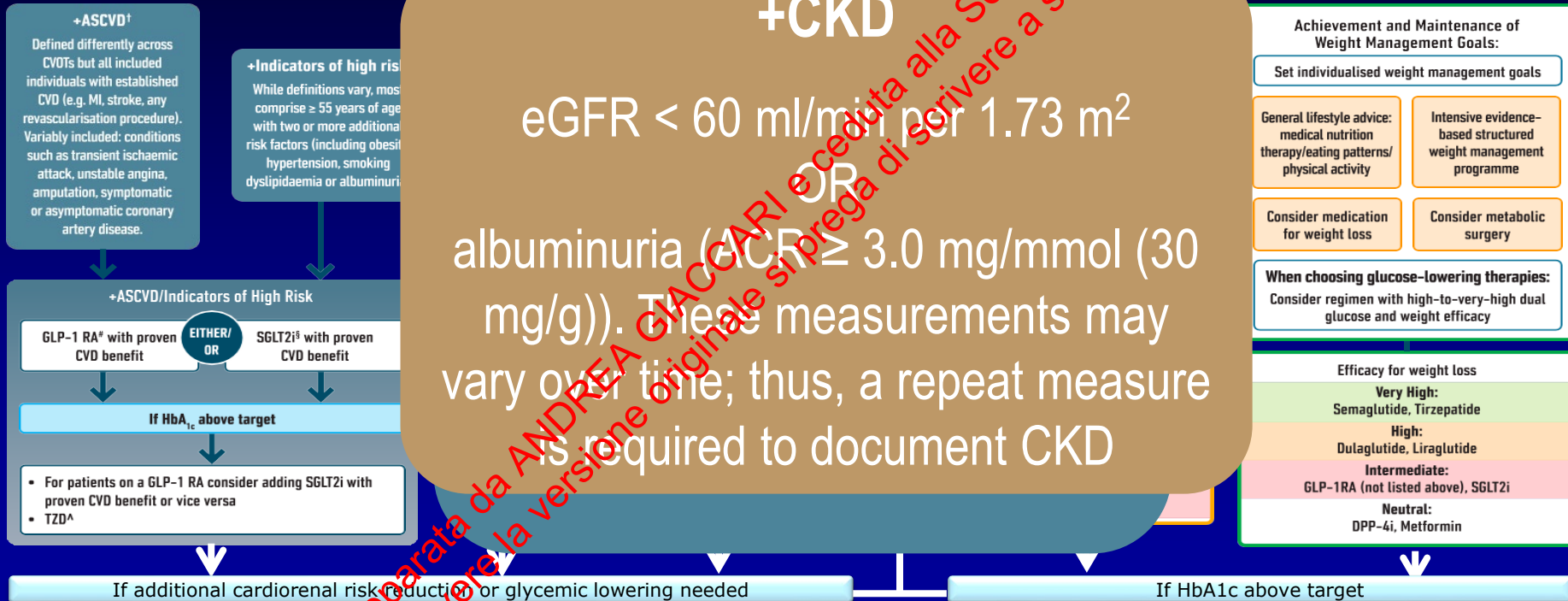
USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)



Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes

Achievement and Maintenance of Glycaemic and Weight Management Goals



linee guida SID/AMD 2022

Nessun evento cardiovascolare, non scompenso cardiaco, eGFR ≥ 60 ml/min	Nessun evento cardiovascolare, non scompenso cardiaco, eGFR < 60 ml/min	Progresso evento cardiovascolare, non scompenso cardiaco	Scompenso cardiaco
Metformin	Metformin ¹	SGLT2i	SGLT2i
SGLT2i	GLP1RA	Met.	Met. ²
GLP1RA		GLP1RA	GLP1RA
DPP4i	Si raccomanda la deprescrizione di sulfoniluree e glinidi		
			Acar.
			Insulin

¹ Se la metformina non è controindicata per ridotto eGFR.

² Se la metformina non è controindicata per ridotta funzione cardiaca.

³ Eccetto saxagliptin che non è indicato in caso di scompenso cardiaco.

La raccomandazione sui pazienti con eGFR < 60 ml/min è debole per carenza di studi clinici effettuati su questa popolazione.

Si raccomanda la deprescrizione di sulfoniluree e glinidi.

what are PICO questions?

P Patient, Population, Problem

I Intervention

C Comparison

O Outcome

literature search
evidence synthesis
(meta-analysis)

La gestione del paziente adulto con diabete o con iperglicemia ricoverato in setting clinico non critico: Le raccomandazioni 4

in soggetti che richiedono un trattamento insulinico è preferibile avviare una terapia insulinica basale o una terapia insulinica multiiniettiva?

- non sono disponibili dati su mortalità, durata della degenza e re-ospedalizzazioni
- con sola basale:
 - riduzione significativa dei valori medi di glicemia
 - riduzione significativa degli episodi di ipoglicemia

si suggerisce di avviare una terapia insulinica basale rispetto ad una terapia insulinica multiiniettiva.

Raccomandazione condizionata a favore dell'intervento
Qualità delle prove: bassa



La gestione del paziente adulto con diabete o con iperglicemia ricoverato in setting clinico non critico: Le raccomandazioni 5

con necessità di terapia insulinica è preferibile il trattamento insulinico strutturato oppure il trattamento "sliding scale"?

- trattamento strutturato è associato a riduzione della glicemia media e durata della degenza
- sliding scale riduce il numero di episodi di ipoglicemia

è possibile utilizzare sia un trattamento insulinico strutturato che un trattamento di tipo "sliding scale".

Raccomandazione condizionata di non differenza fra l'intervento e il confronto
Qualità delle prove: molto bassa



what GRADE means?

G Grading of
R Recommendations,
A Assessment,
D Development, and
E Evaluations

Quality (A, B, C, D)

rate down:

- Risk of bias
- Imprecision
- Inconsistency
- Indirectness
- Publication bias

rate up:

- Large magnitude of effect
- Dose-response gradient
- Reduced confounders

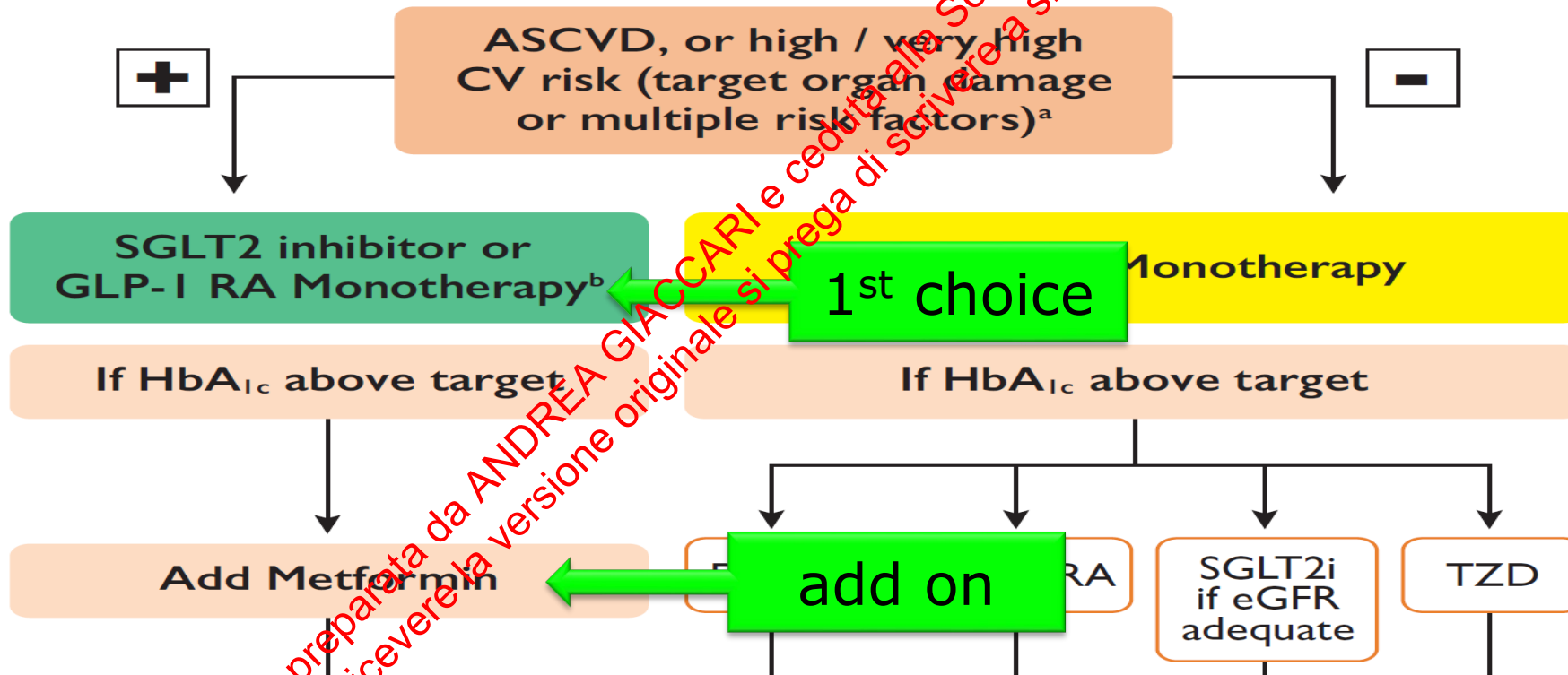
Strength of the recommendation – “We recommend” or “We suggest”

ESC 23 class of evidence

Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

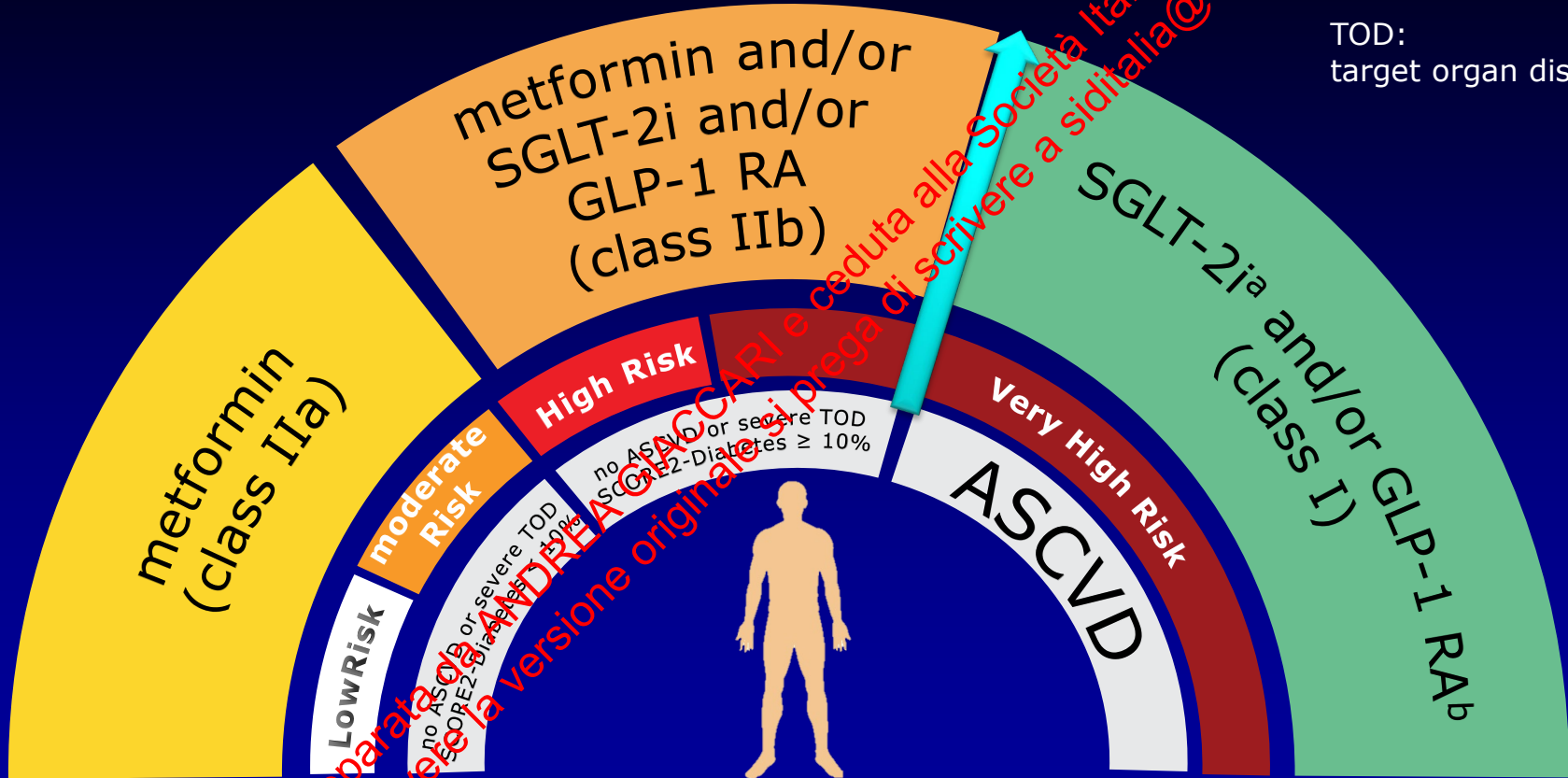
ESC 2019 treatment algorithm in patients with T2DM

A Type 2 DM - Drug naïve patients



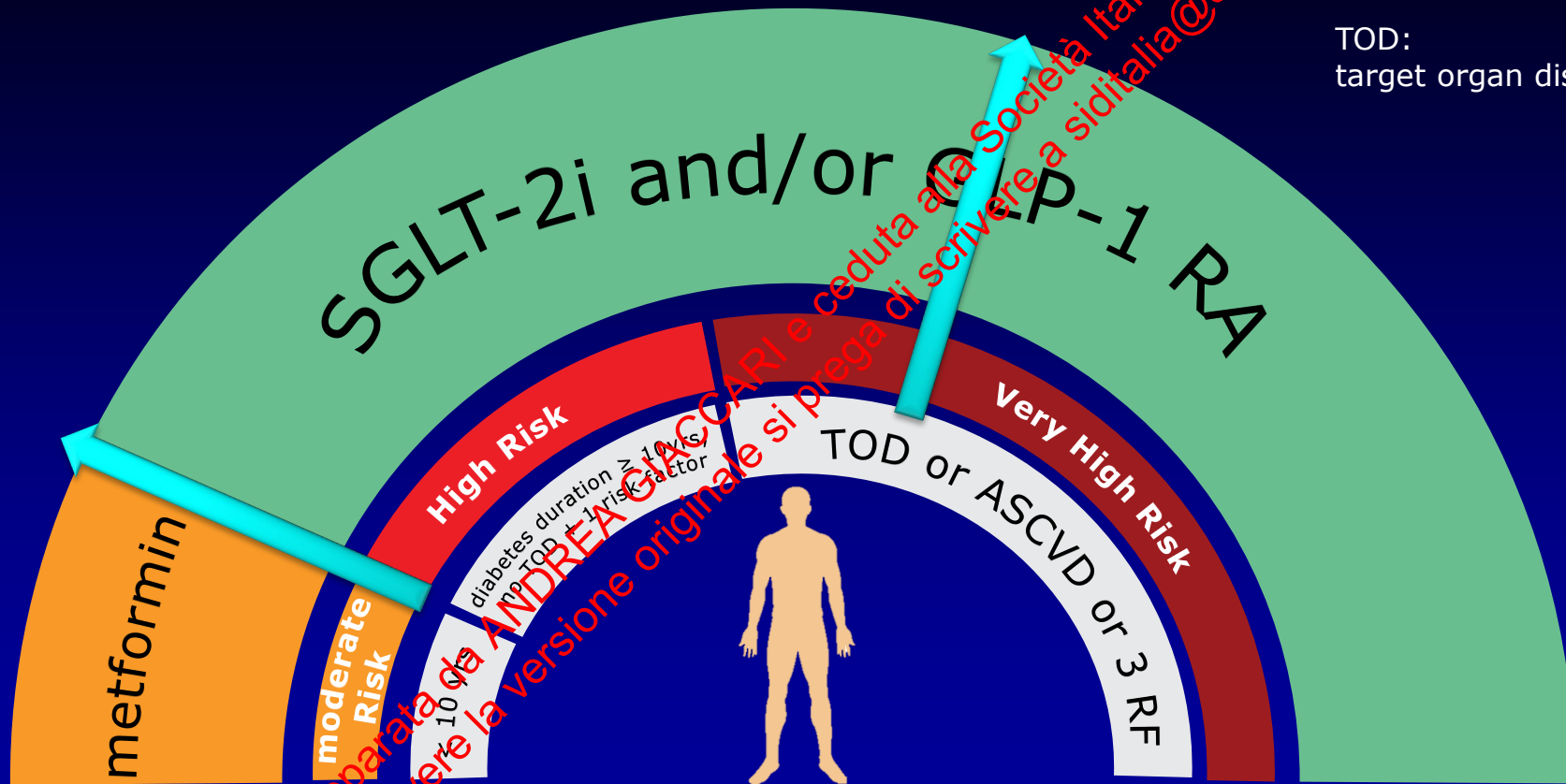
ESC 23: diabetes drug according to risk

TOD:
target organ disease



ESC 19: diabetes drug according to risk

TOD:
target organ disease



ESC 23 diabetes risk categories

Very high CV risk

Patients with T2DM with:

- Clinically established ASCVD or
- Severe TOD or
- 10-year CVD risk $\geq 20\%$ 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

ESC scores

a diabetic patient with 20 yrs of diabetes, HbA1c 10, Chol 180, HDL 50, SBP 130, non-smoking
69 yrs old

70 yrs old

SCORE2-Diabetes

Personal risk profile

180.0

HDL cholesterol (mg/dL)

Min Max

19.0 175.0

50

HbA1c (%)

Min Max

2.0 21.0

10.0

Calculate



SCORE2-OP

Personal risk profile

Total cholesterol (mg/dL)

Min Max

116.0 348.0

180

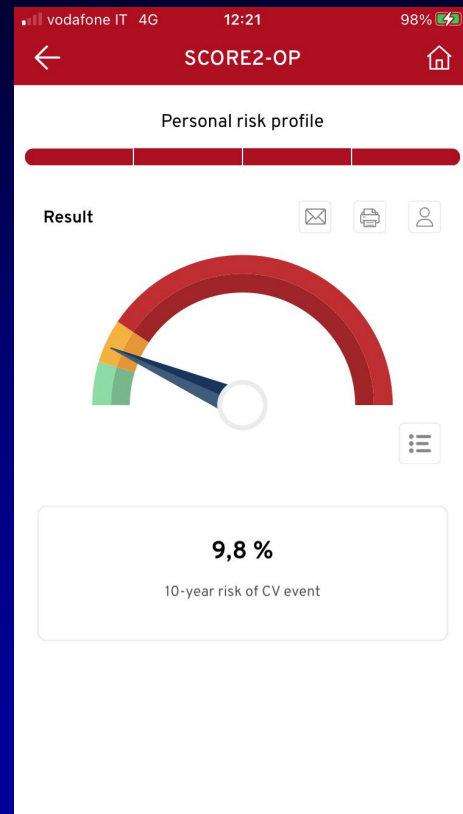
HDL cholesterol (mg/dL)

Min Max

27.0 97.0

50

Calculate



ESC 23: pharmacological management to reduce cardiovascular or kidney failure risk in patients with type 2 diabetes and CKD

to reduce cardiovascular risk

statin-based regimen
class I

to reduce kidney failure risk

ACE-I or ARB
class I

to reduce cardiovascular and kidney failure risk

SGLT-2 inhibitor
class I

BP control
class I

finerenone
class I

for additional glucose control

glucose-lowering medications with suggested cardiovascular benefit

GLP-1 RA

glucose-lowering medications with neutral or no proven cardiovascular benefit

metformin (if eGFR >30 mL/min/1.73 m²)

DPP-4 inhibitor

insulin

KDIGO 2020 Clinical Practice Guideline for Diabetes Management in CKD

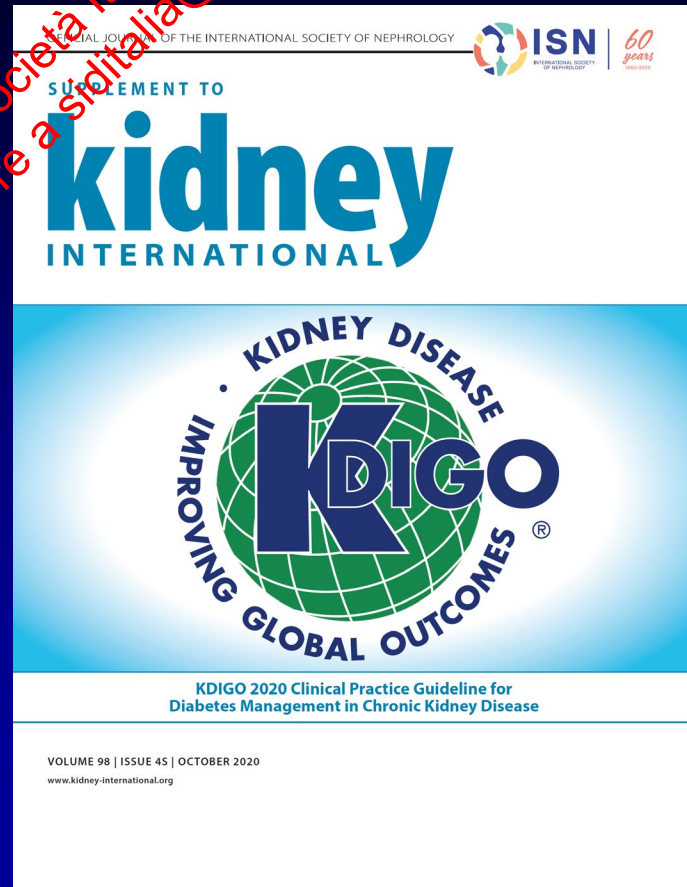
October 2020

Topics:

- Ch 1. Comprehensive care
- Ch 2. Glycemic monitoring and targets
- Ch 3. Lifestyle interventions
- Ch 4. Antihyperglycemic therapies in T2D
- Ch 5. Approaches to management

Published as a Supplement

Executive Summary published in Kidney International





Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO)

<https://doi.org/10.2337/dci22-0027>

Ian H. de Boer,¹ Kamlesh Khunti,²
Tami Sadusky,³ Katherine R. Tuttle,⁴
Joshua J. Neumiller,⁵ Connie M. Rhee,⁶
Sylvia E. Rosas,⁷ Peter Rossing,^{8,9} and
George Bakris¹⁰

¹Kidney Research Institute, University of Washington, Seattle, WA

²Diabetes Research Centre, University of Leicester, Leicester, U.K.

CKD screening and diagnosis for people with diabetes

who and when to screen?

T1D Yearly starting 5 years after diagnosis

T2D Yearly starting at diagnosis

how to screen?



Spot urine ACR

and



eGFR

what defines CKD diagnosis?



persistent urine ACR ≥ 30 mg/g
and/or



persistent eGFR < 60 mL/min/1.73 m²
and/or



other evidence of kidney damage

what to do with a positive result?



Repeat and confirm:

- Evaluate possible temporary or spurious causes
- Consider using cystatin C and creatinine to more precisely estimate GFR
- Only persistent abnormalities define CKD



Initiate evidence-based treatments

risk of CKD progression, visit frequency, and referral to nephrology

CKD is classified based on:

- Cause (C)
- GFR (G)
- Albuminuria (A)

			albuminuria categories		
			A1	A2	A3
			<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m ²)	G1	≥90	screen	treat	treat and refer 3
	G2	60-89			treat and refer 3
	G3a	45-59			treat and refer 3
	G3b	30-44			treat and refer 4+
	G4	15-29	treat and refer 3	treat and refer 3	treat and refer 4+
	G5	<15	treat and refer 4+	treat and refer 4+	treat and refer 4+

refer if:

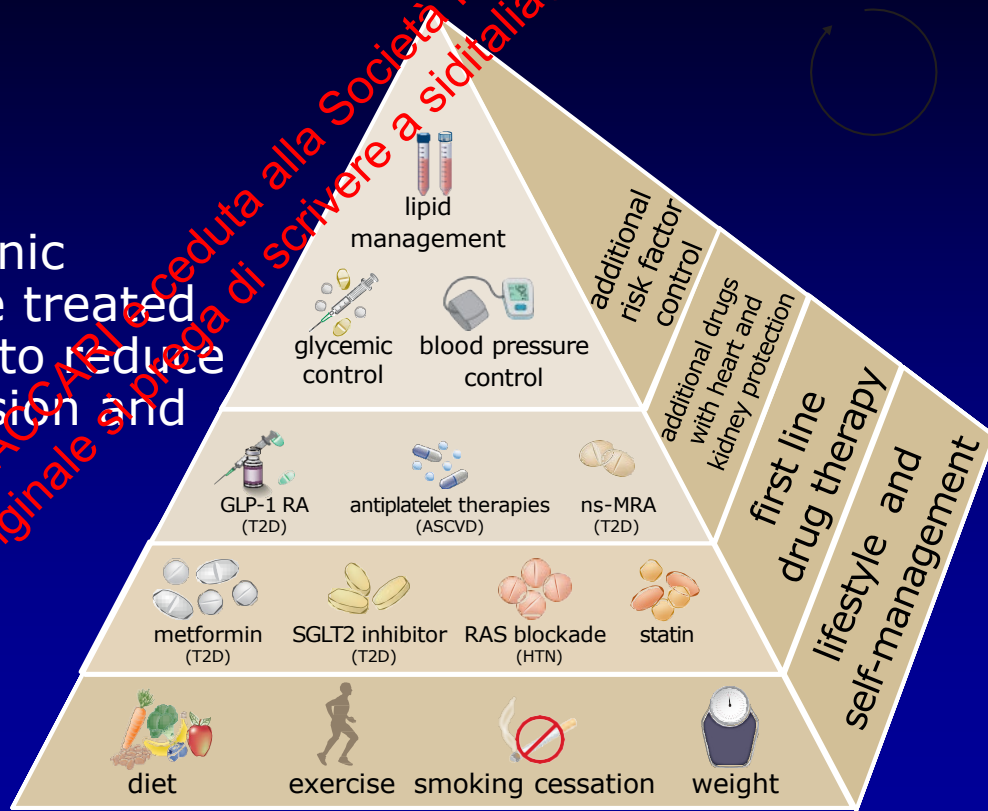
- eGFR < 30
- eGFR < 45 and micro
- macro

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk

High risk
Very high risk

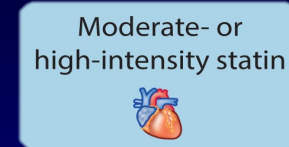
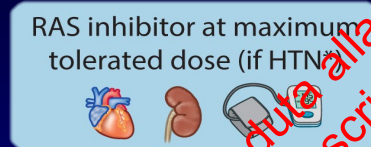
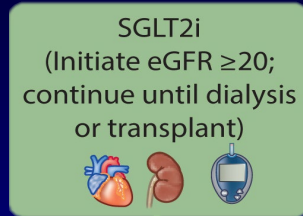
comprehensive care in patients with diabetes and CKD

Practice Point 1.1.1:
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

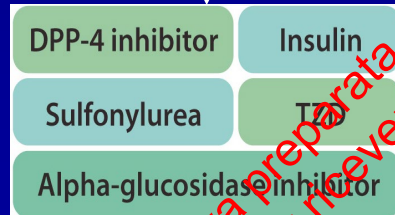
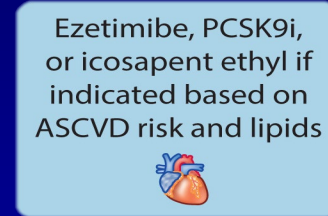
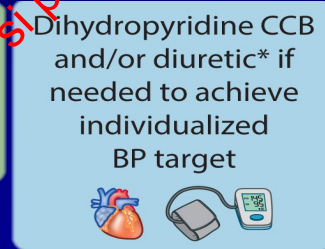
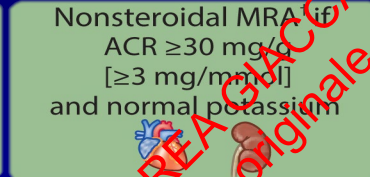
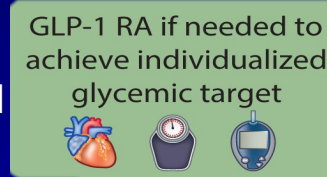


holistic approach for improving outcomes in patients with diabetes and CKD

first line

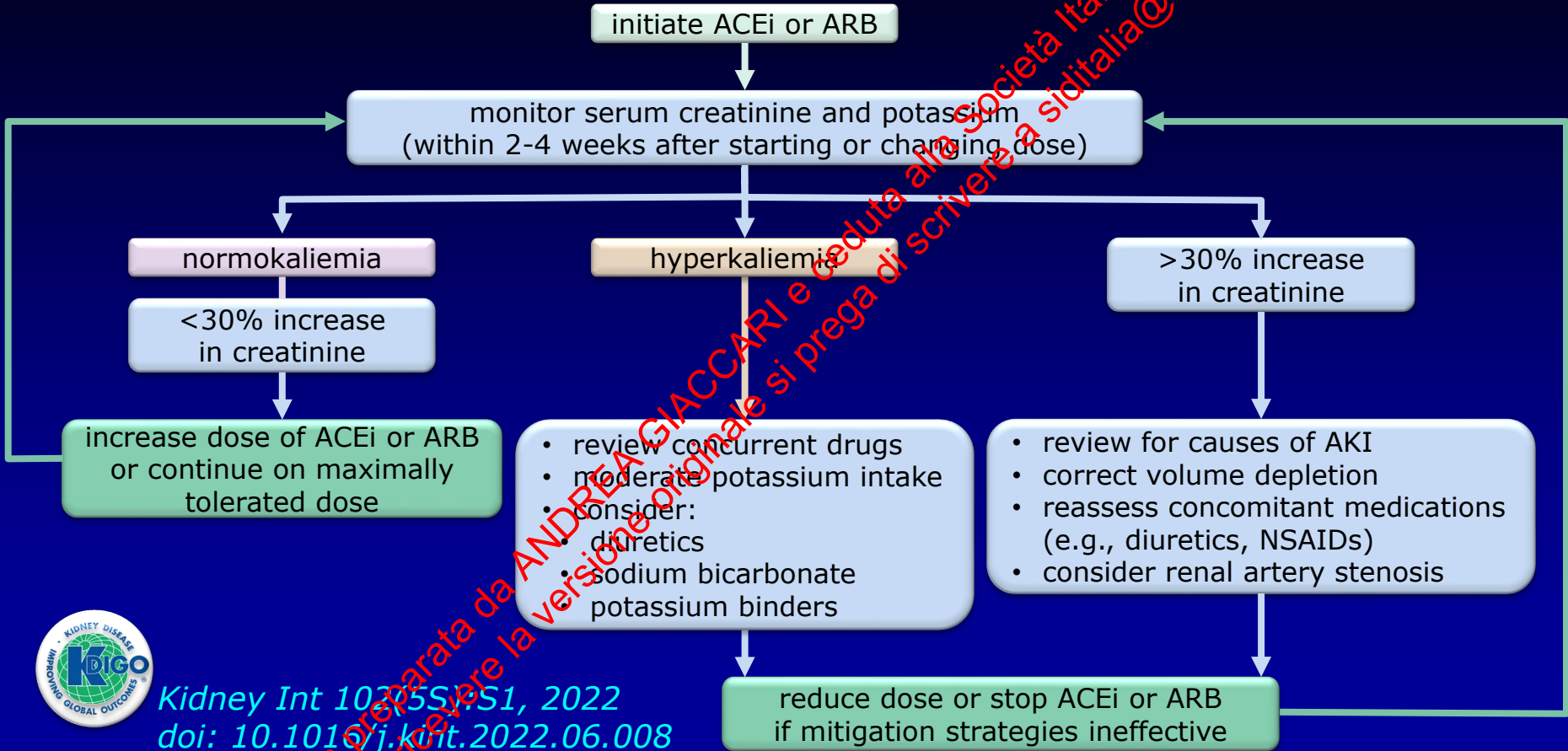


additional
risk-based



Kidney Int 102(5S):S1, 2022
doi: 10.1016/j.kint.2022.06.008

monitoring of creatinine and potassium during ACEi or ARB treatment dose adjustment and monitoring of side effects



practical provider guide to initiating SGLT2 inhibitors

in patients with type 2 diabetes and CKD

assessment intervention follow-up

patient
selection

Eligible patients:

- eGFR ≥ 20 ml/min/1.73 m²

High priority features:

- ACR ≥ 200 mg/g [≥ 20 mg/mmol]
- Heart failure

Potential contraindications:

- Genital infection risk
- Diabetic ketoacidosis
- Foot ulcers
- Immunosuppression

SGLT2 inhibitor

with proven benefits:

- Canagliflozin 100 mg
- Dapagliflozin 10 mg
- Empagliflozin 10 mg

Education:

- Sick day protocol*
- Perioperative care[†]
- Foot care

- Assess adverse effects
- Review knowledge
- Anticipate an acute drop in eGFR, which is generally not a reason to stop the SGLT2 inhibitor

volume

Volume depletion risk?

- Concurrent diuretic use
- Tenuous volume status
- History of AKI

If
high

Education:

- Volume depletion symptoms
- Consider diuretic dose reduction

- Re-assess volume
- Reduce concomitant diuretic if needed

glycemia

Hypoglycemia risk?

- Insulin or sulfonylurea
- History of severe hypoglycemia
- HbA1c at or below goal

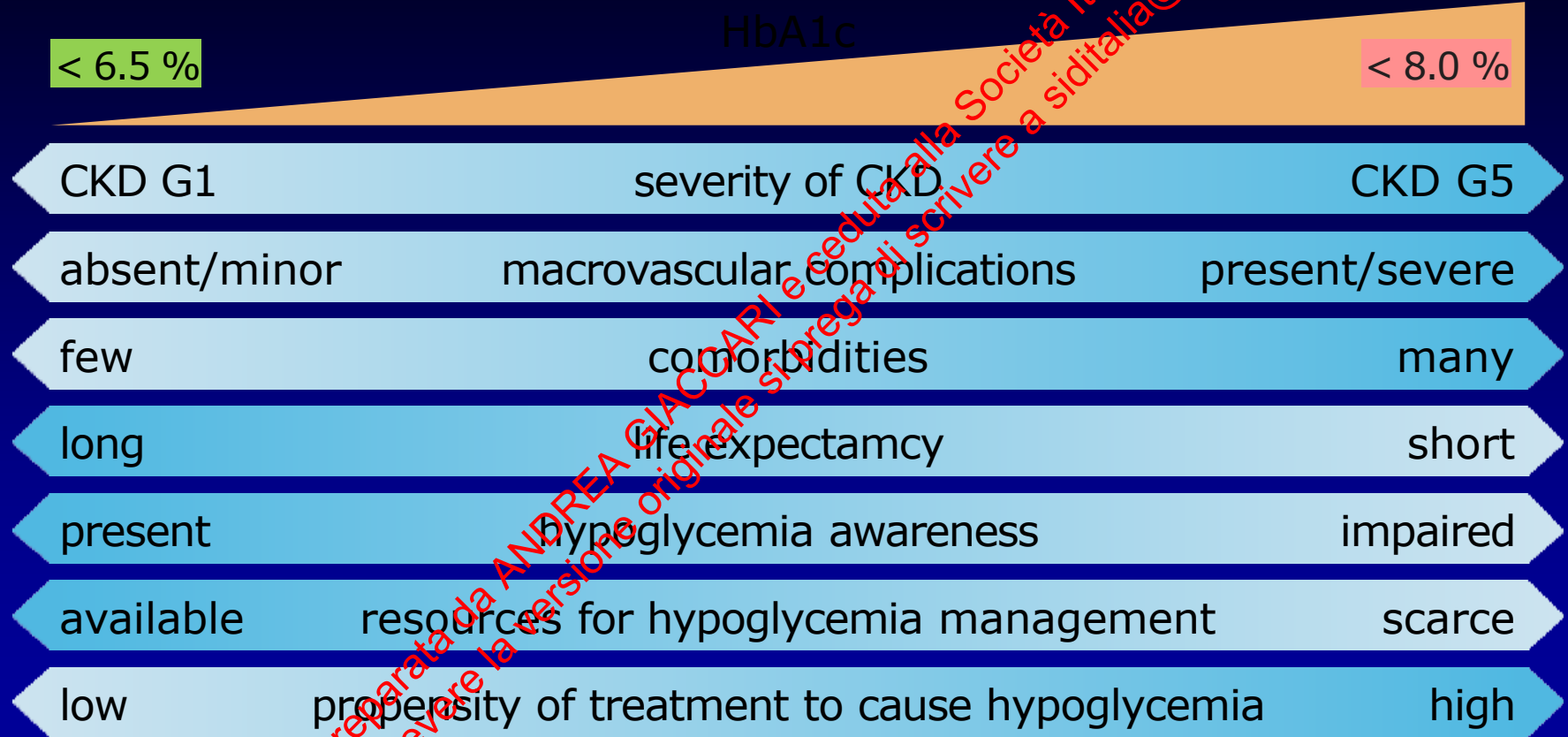
If
high

Education:

- Hypoglycemia symptoms
- Glycemia monitoring
- Consider insulin/sulfonylurea dose reduction

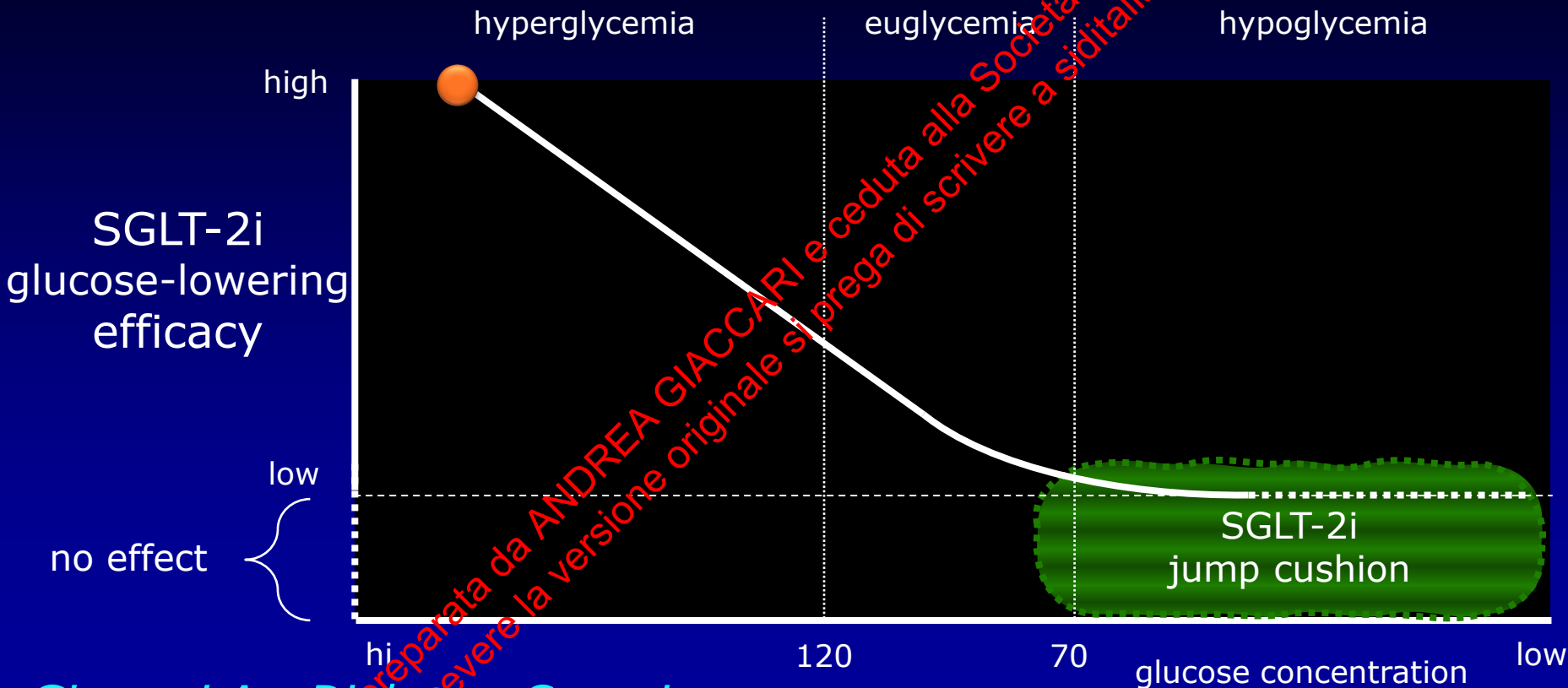
- Ask about hypoglycemia
- Reduce sulfonylurea or insulin if needed

guiding decisions on individual HbA1c targets

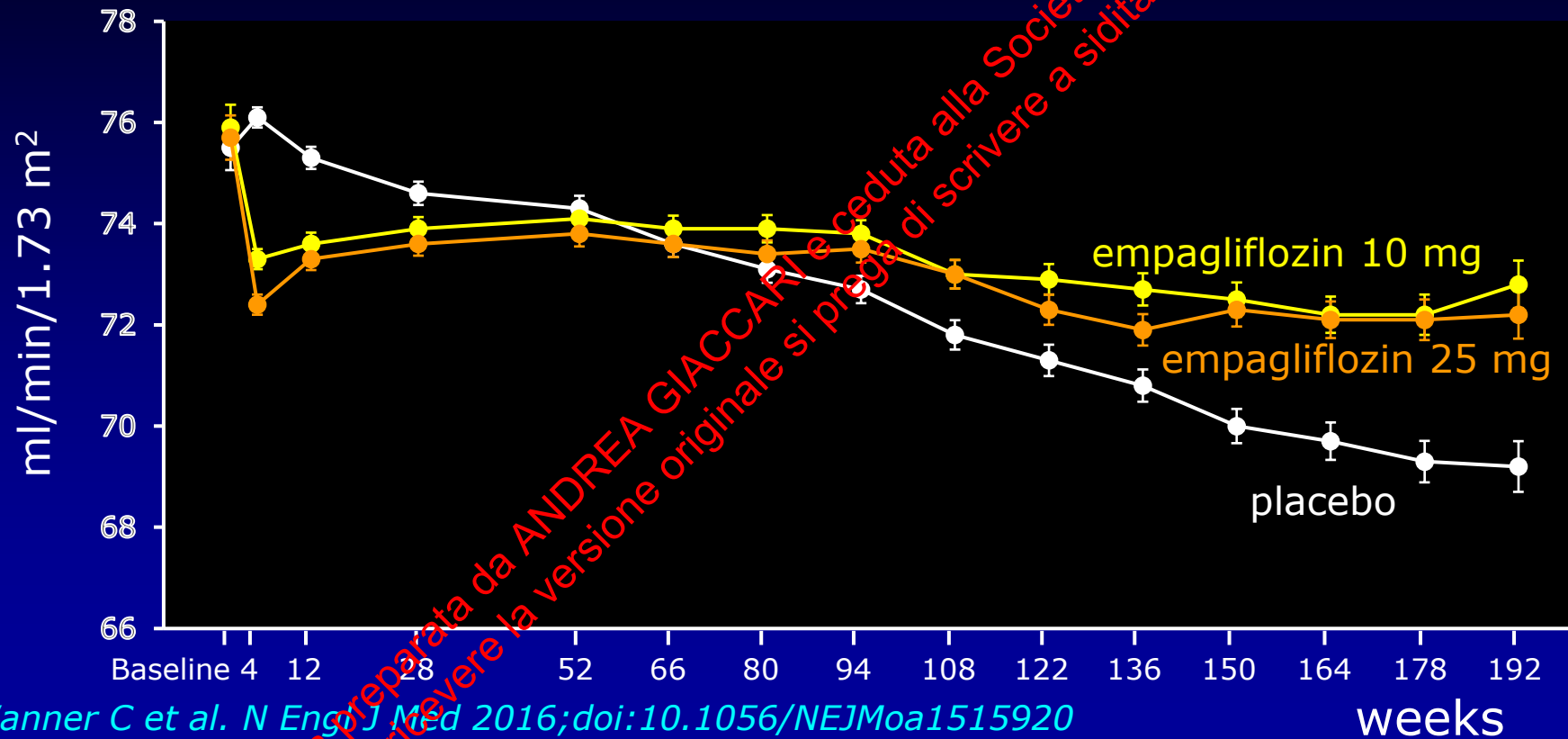


SGLT-2i lose all their efficacy in hypoglycemia

becoming the best companion of insulin treatment

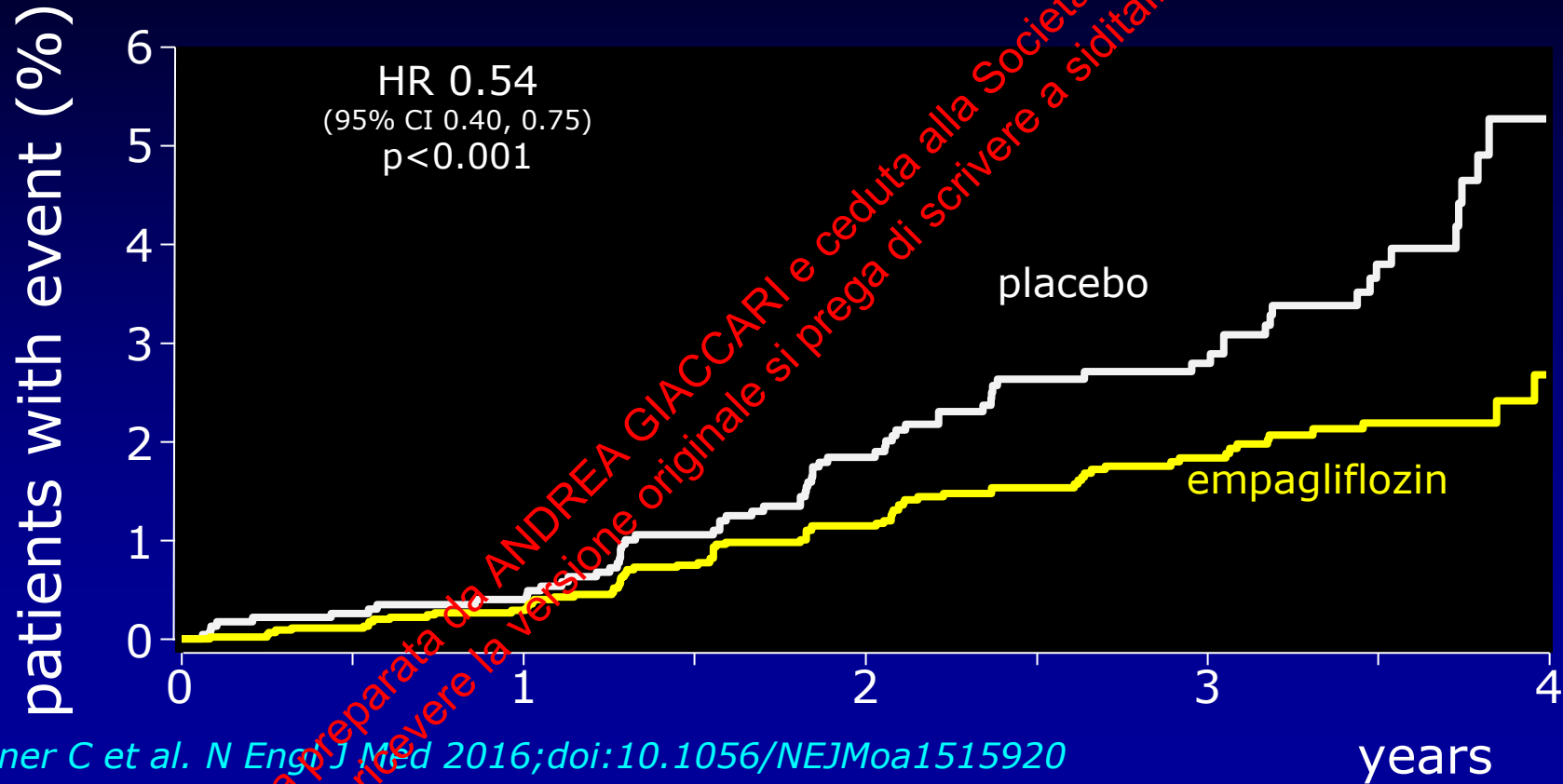


EMPAREG: Kidney function (eGFR) over time



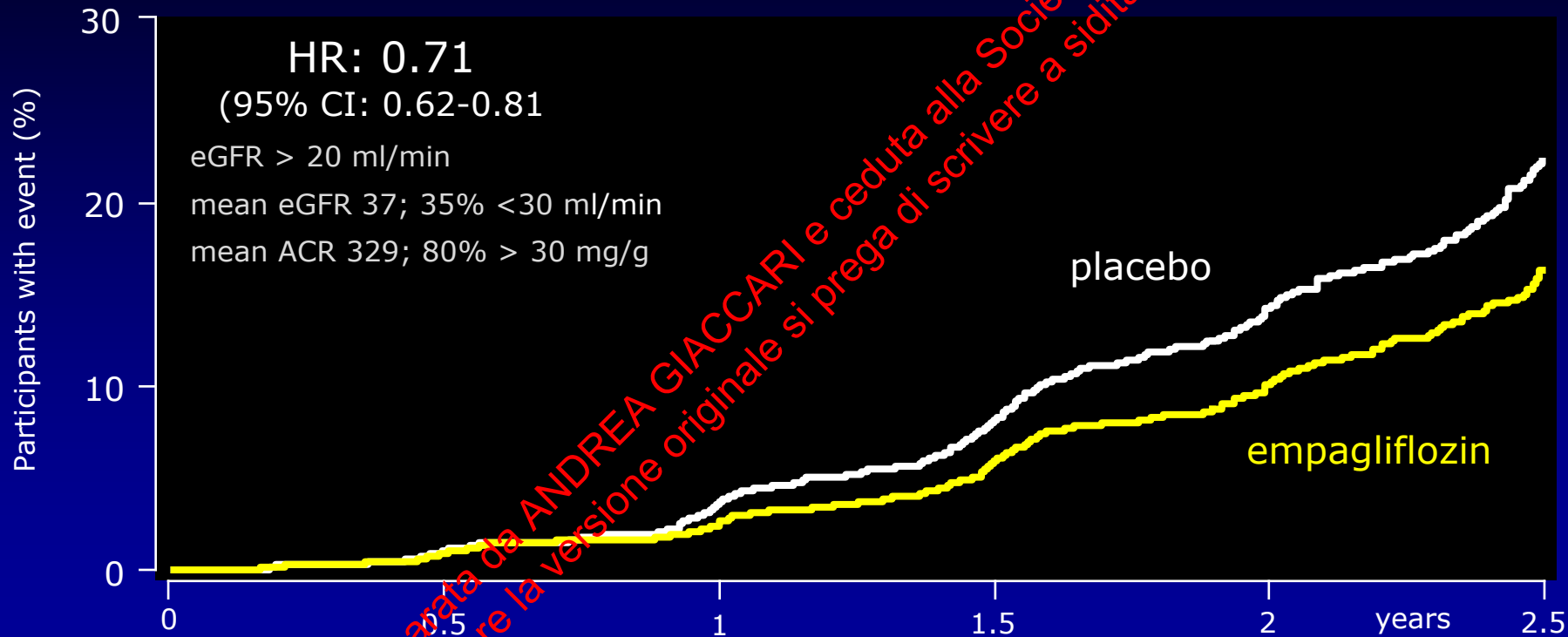
EMPAREG: composite renal

dialysis, transplant, doubling of creatinine, renal death



EMPA-KIDNEY: kidney disease progression

dialysis, transplant, eGFR < 10 ml/min, decline $\geq 40\%$, renal death



when and why we should use SGLT-2i

