
# "Casi Clinici e sondaggio con QNOW"



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# Disclosures

***Il dott. Mario Luca Morieri negli ultimi 2 anni ha ricevuto lecture fee, advisory fee, o research grants da:***

***Amarin, Amgen, AstraZeneca, Boehringer Ingelheim, Daichi, Eli Lilly, Merck Sharp & Dohme, Novo Nordisk, Novartis, Servier***

# Caso clinico 1 (Claudio)

Claudio, 69 aa, inviato dal MMG (prima visita)
***An. patologica:*** Diabete da 5-7 anni, HbA1c 6.8% (in metformina 850 BID)
Ipertensione in terapia da 10 anni con ACEi (ramipril 5 mg) e discreto controllo (PA 135/80 domicilio); Nessuna storia di malattia cerebro-cardiovascolare

***An. familiare:*** madre diabetica, padre deceduto per ictus a 88 aa (iperteso), nonno paterno IMA non precoce, non dislipidemia o altre condizioni di rilievo

***An. fisiologica:*** Stile di vita sedentario + 1 camminata/sett da 30-40 minuti; Non fuma.
Dieta abbastanza varia con qualche extra (dolci). Beve 1 bicch. di vino a cena. Peso: 88 Kg (BMI 29 kg/m2), graduale incremento di 10 kg negli ultimi 10 anni. Ha 2 figli in buona salute.

***Esami***: Hba1c 6.8%, FPG: 142 mg/dl.
Col-Tot 180 mg/dl, ,c-HDL 54 mg/dl , TG 160 mg/dl  c-LDL = 94 mg/dl  Col-nonHDL= 126 mg/dl
Creatinina 1,57 mg/dl -> VFG (CKD-EPI) 44 ml/min  ; UACR = 37 mg/g (spot)
Emocromo n.d.p, AST 23 U/L e ALT 33 U/L

***EO:*** PA 140/85 mmHg, FC 72 bpm R, BMI 28 kg/m2; Addome globoso, fegato a 3-4 cm dall'arco costale in inspirium, per il resto obiettività cardiopolmonare e addominale ndp. Polsi AAII simmetrici, normosfigmici.

# Che altri accertamenti/valutazioni servirebbero per inquadrare meglio il paziente?

# Quale è il rischio cardiovascolare del paziente?

**A. Molto Alto**

**B. Alto**

**C. Moderato**

**D. Non so/non ne sono sicuro**

?

# Cardiovascular risk category in T2D

## EAS – ESC 2019

| | |
|---|---|
| **Very high risk** | Patients with DM **and** established CVD<br>**or** other target organ damage[b]<br>**or** three or more major risk factors[c]<br>**or** early onset T1DM of long duration (>20 years) |
| **High risk** | Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor |
| **Moderate risk** | Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors |

[b]Proteinuria, renal impairment defined as eGFR <30 mL/min/1.73 m$^2$, left ventricular hypertrophy, or retinopathy.



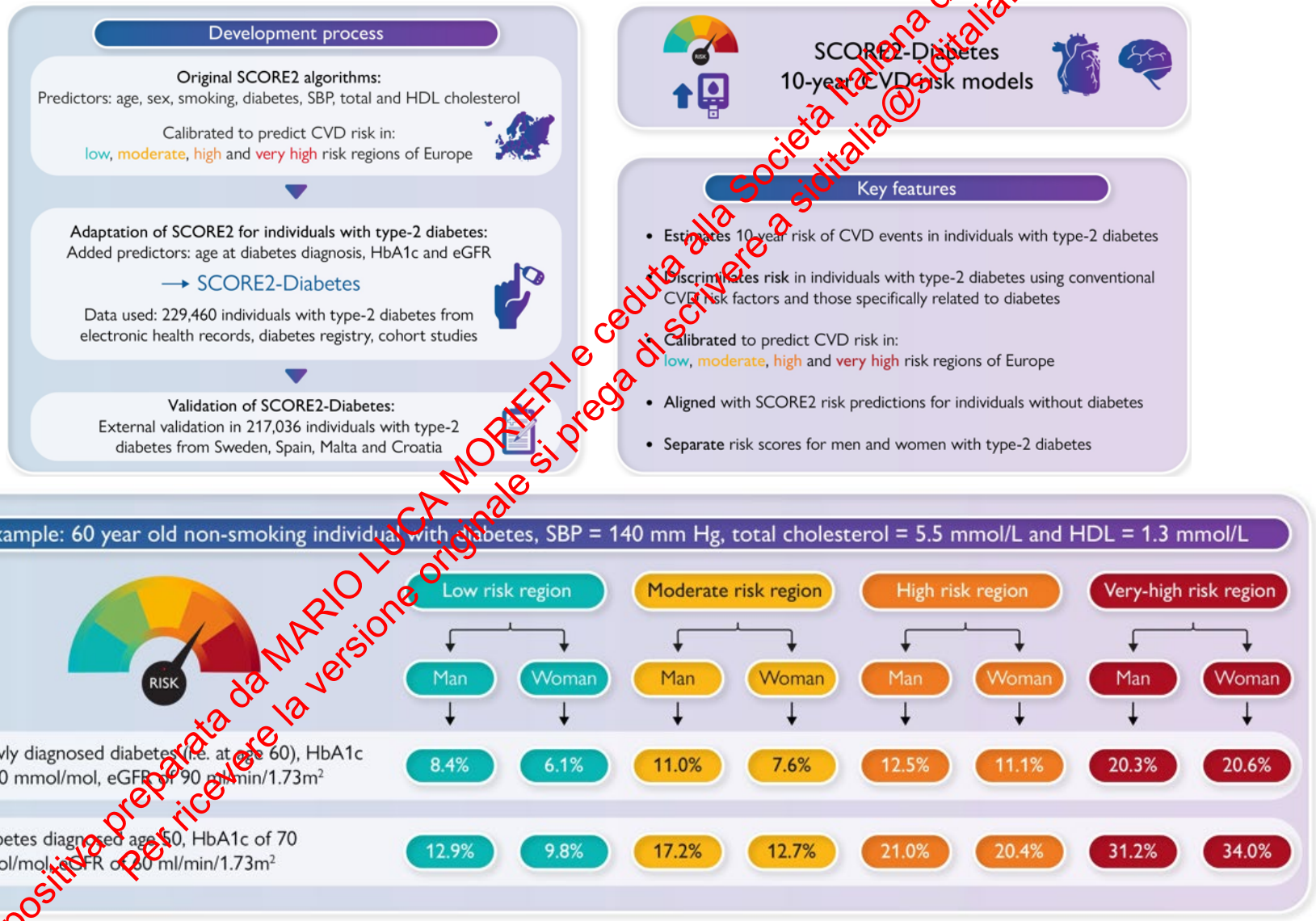
## ESC 2023

| | |
|---|---|
| **Very high CV risk** | Patients with T2DM with:<br>• Clinically established ASCVD or<br>• Severe TOD or<br>• 10-year CVD risk ≥20% using SCORE2-Diabetes |
| **High CV risk** | Patients with T2DM not fulfilling the very high-risk criteria and a:<br>• 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:<br>• 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:<br>• 10-year CVD risk <5% using SCORE2-Diabetes |

Severe TOD defined as eGFR <45 mL/min/1.73 m$^2$ irrespective of albuminuria; or eGFR 45–59 mL/min/1.73 m$^2$ and microalbuminuria (UACR 30–300 mg/g; stage A2); or proteinuria (UACR >300 mg/g; stage A3); or presence of microvascular disease in at least three different sites [e.g. microalbuminuria (stage A2) plus retinopathy plus neuropathy].[43–45]

*ESC guidelines 2023*

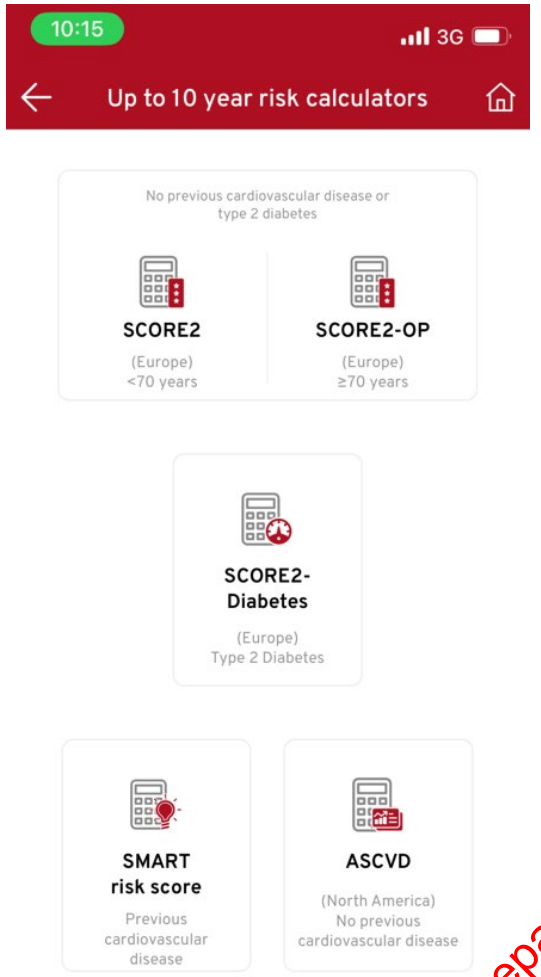
# Cardiovascular risk category in T2D

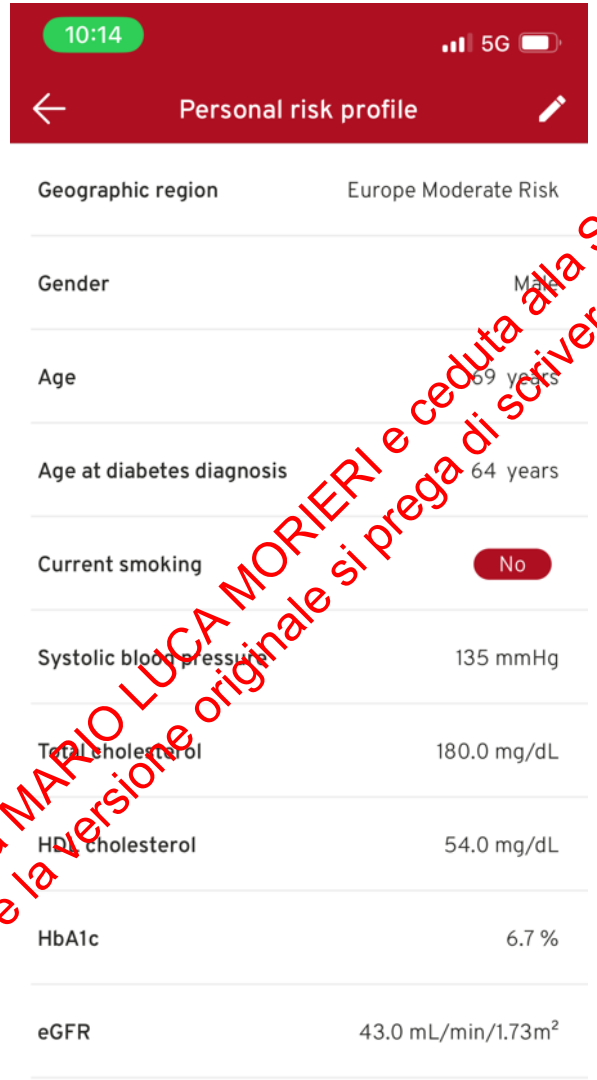


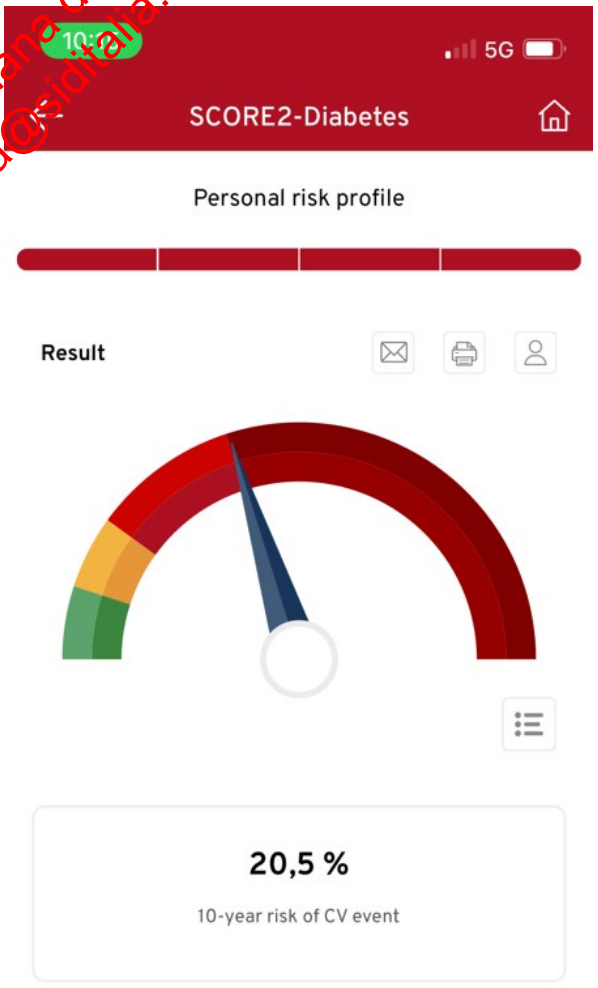



*Score 2 group; Eur Heart Journal – 2023*

# Cardiovascular risk category in T2D






*Score 2 group; Eur Heart Journal – 2023*

# Cardiovascular risk category in T2D

## Predicted 10 year risk of atherosclerotic CVD*

CKD Patch and calibration are based on data from CKD-PC (Chronic Kidney Disease Prognosis Consortium)

| Calibrated Risk | |
|---|---|
| PCE Calibrated 50th Percentile | PCE Calibrated 50th Percentile + CKD Patch |
| 19.5% | 21.7% |

* Atherosclerotic CVD (ASCVD) includes coronary heart disease and stroke

**Kidney Measures**

| | |
|---|---|
| eGFR (estimated glomerular filtration rate) (mL/min/1.73m²) | 45 |
| Urine Albumin to Creatinine Ratio (mg/g) click on units to change between mg/g and mg/mmol Convert Urine Protein-Creatinine to Albumin-Creatinine | 25 |

**PCE Variables**

| | |
|---|---|
| Age (18-80yrs) | 69 |
| Gender | Male |
| Race | White or Other |
| Systolic Blood Pressure (mmHg) | 135 |
| Antihypertensive Medications | Yes |
| HDL Cholesterol (mg/dL) click on units to change between mg/dL and mmol/L | 40 |
| Total Cholesterol (mg/dL) click on units to change between mg/dL and mmol/L | 180 |
| Diabetes | Yes |
| Current Smoker | No |

**Calibration**

| | |
|---|---|
| Calibration | 50th percentile in CKD-PC |

il progetto cuore

Epidemiologia e prevenzione delle malattie cerebro e cardiovascolari

Valutazione del rischio

Home page

### Calcolo del punteggio individuale

| | |
|---|---|
| Sesso: | uomo |
| Età: | 69 |
| Abitudine al fumo di sigaretta: | no |
| Pressione sistolica: | 138 mmHg |
| Colesterolemia totale: | 180 mg/dl |
| Colesterolemia HDL: | 54 mg/dl |
| Diabete: | sì |
| Presenza di ipertensione arteriosa: | sì |

Lei si trova all'interno di una soglia attualmente considerata a rischio elevato.

La probabilità di andare incontro a un primo evento cardiovascolare maggiore è pari a:
**24,9% nei prossimi 10 anni**

# Quale è il rischio di progressione del danno renale?

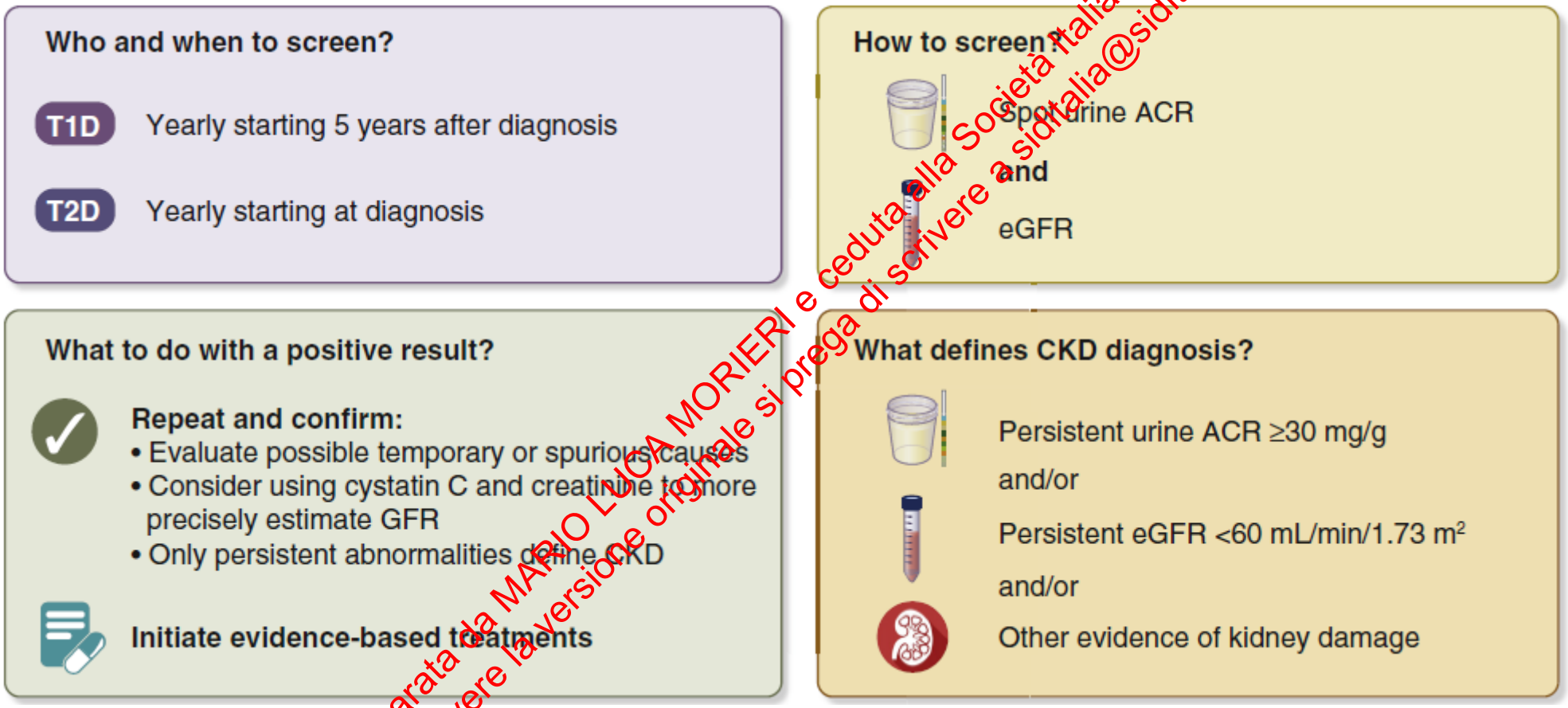
**A. Molto Alto**

**B. Alto**

**C. Moderato**

**D. Non so/non sono sicuro**

# Come si definisce la nefropatia diabetica






*De Boer et al, ADA-KDIGO consensus*
*Kindey Intern 2022*

# Risk of chronic kidney disease (CKD) progression by CKD classification

| CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A) | | | | Albuminuria categories Description and range | | |
|---|---|---|---|---|---|---|
| | | | | A1 | A2 | A3 |
| | | | | Normal to mildly increased | Moderately increased | Severely increased |
| | | | | <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 m²) Description and range | G1 | Normal or high | ≥90 | Screen 1 | Treat 1 | Treat and refer 3 |
| | G2 | Mildly decreased | 60–89 | Screen 1 | Treat 1 | Treat and refer 3 |
| | G3a | Mildly to moderately decreased | 45–59 | Treat 1 | Treat 2 | Treat and refer 3 |
| | G3b | Moderately to severely decreased | 30–44 | Treat 2 | Treat and refer 3 | Treat and refer 3 |
| | G4 | Severely decreased | 15–29 | Treat and refer* 3 | Treat and refer* 3 | Treat and refer 4+ |
| | G5 | Kidney failure | <15 | Treat and refer 4+ | Treat and refer 4+ | Treat and refer 4+ |

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



*De Boer et al, ADA-KDIGO consensus Kindey Intern 2022*

Quale è la probabilità che Claudio abbia una riduzione del 40% della VFG nei prossimi 3 anni?

**A. <= 2 %**

**B. 2-5%**

**C. 5-10%**

**D. >10%**

# Quale è la probabilità di ESRD (dialisi o trapianto) a 5 anni?

**A. <= 0.5%**

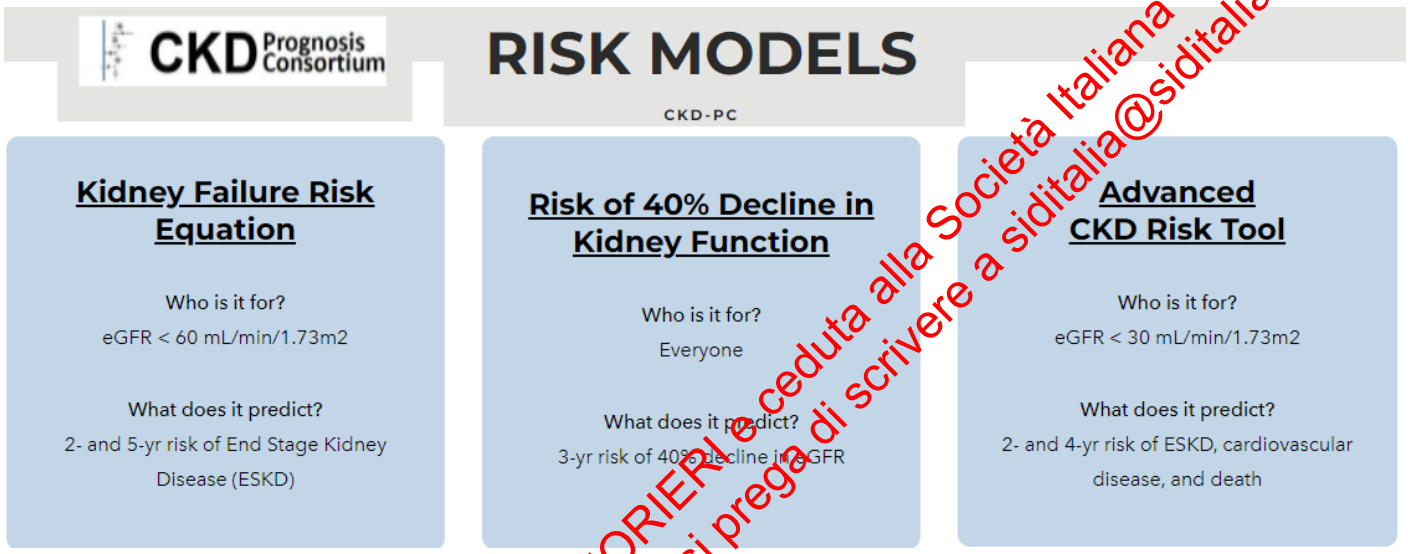
**B. 0.5-1.5%**

**C. 1.5-2.5%**

**D. >2.5%**

?

# Rischio di progressione della nefropatia






*CKD prognosis Consortium*

# Rischio di progressione della nefropatia

**3 Year Probability of 40% decline in GFR**

**4.8%**

Reset Print Summary

**Diabetes Status**

| | |
|---|---|
| Diabetes | Yes |

**Patient Characteristics**

| | |
|---|---|
| Age (20-80yrs) | 70 |
| Gender | Male |
| eGFR (mL/min/1.73m²) What's my eGFR? | 45 |
| Urine Albumin to Creatinine (mg/g) click on units to change between mg/g and mg/mmol | 30 |
| SBP | 135 |
| Antihypertensive Medication Use | Yes |
| HF | No |
| CHD | No |
| Afib | No |
| BMI (kg/m²) What's my BMI? | 30 |
| Smoking History | Never Smoked |
| DM Medication | Oral Meds Only |
| HbA1c | 7 |

## Risk of Decline in Kidney Function

**3 Year Probability of 40% decline in GFR**

**2.4%**

Reset Print Summary

**Diabetes Status**

| | |
|---|---|
| Diabetes | No |

**Patient Characteristics**

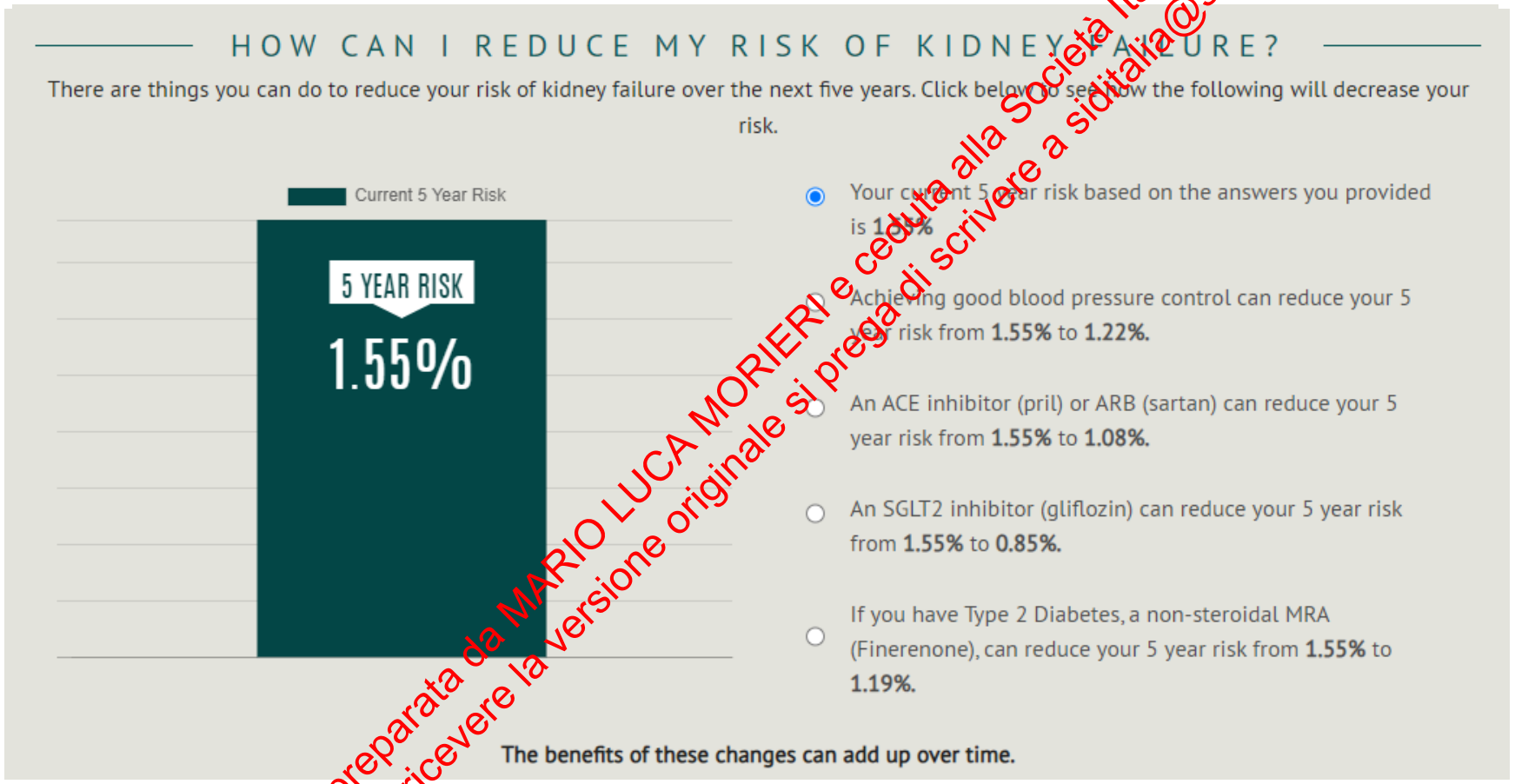
| | |
|---|---|
| Age (20-80yrs) | 70 |
| Gender | Male |
| eGFR (mL/min/1.73m²) What's my eGFR? | 60 |
| Urine Albumin to Creatinine (mg/g) click on units to change between mg/g and mg/mmol | 30 |
| SBP | 135 |
| Antihypertensive Medication Use | Yes |
| HF | No |
| CHD | No |
| Afib | No |
| BMI (kg/m²) What's my BMI? | 30 |
| Smoking History | Never Smoked |

Patient risk of progression to kidney failure requiring dialysis or transplant:

| AT 2 YEARS | AT 5 YEARS |
|---|---|
| 0.4 % | 1.55 % |

*CKD prognosis Consortium*

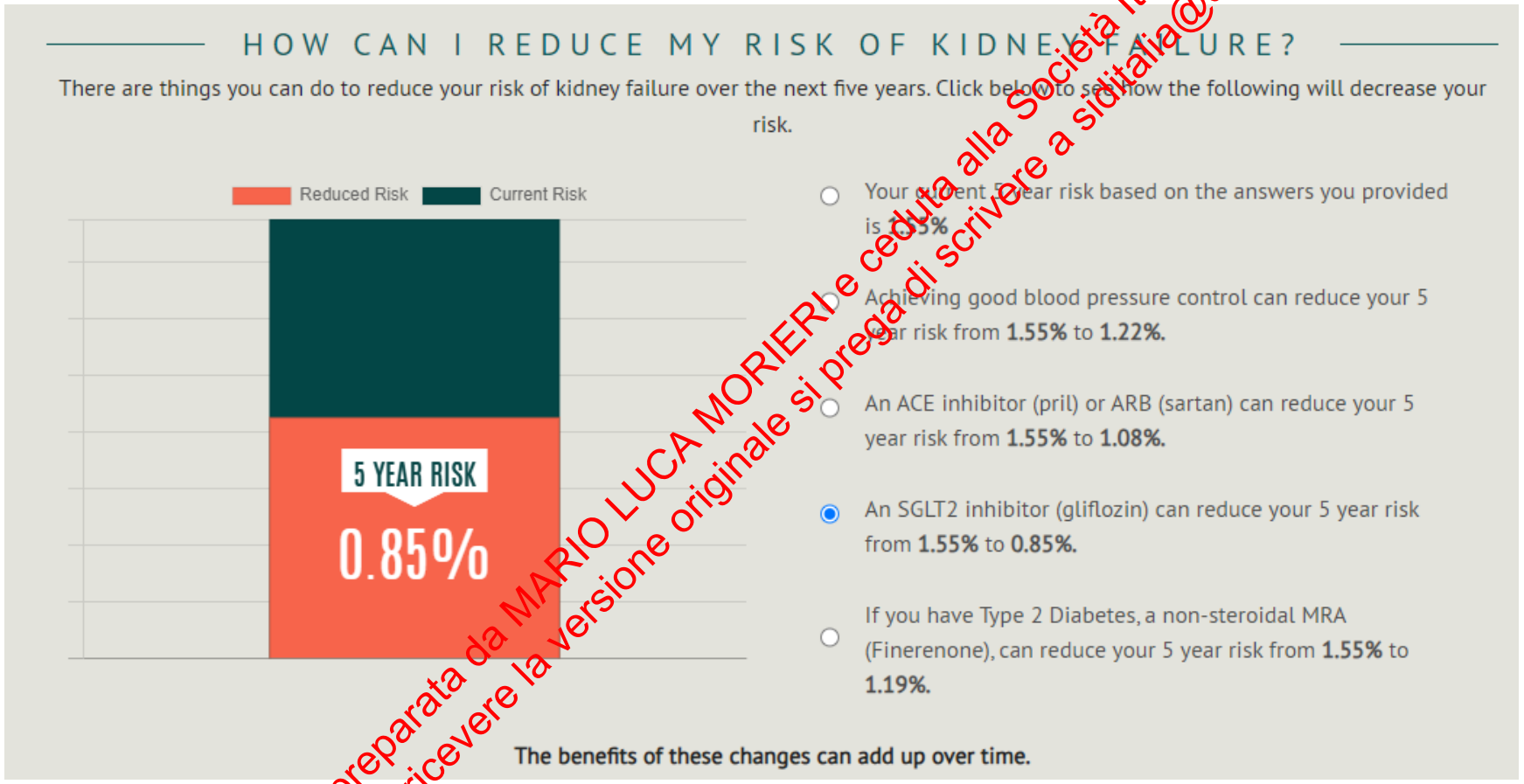
# Rischio di progressione della nefropatia






*CKD prognosis Consortium*

# Riduzione del rischio di progressione della nefropatia






*CKD prognosis Consortium*

# Quale è l'aspettativa di vita (attesa) di Claudio ?

**A. <7 aa**

**B. 7-12 aa**

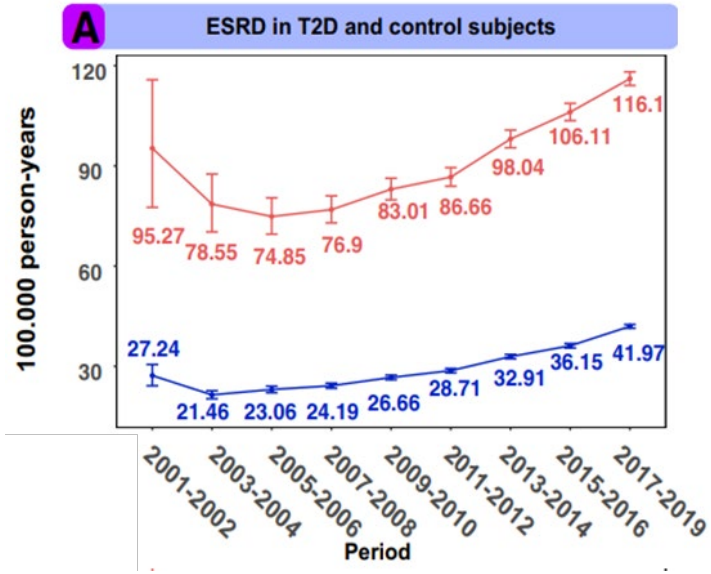
**C. 12-17 aa**

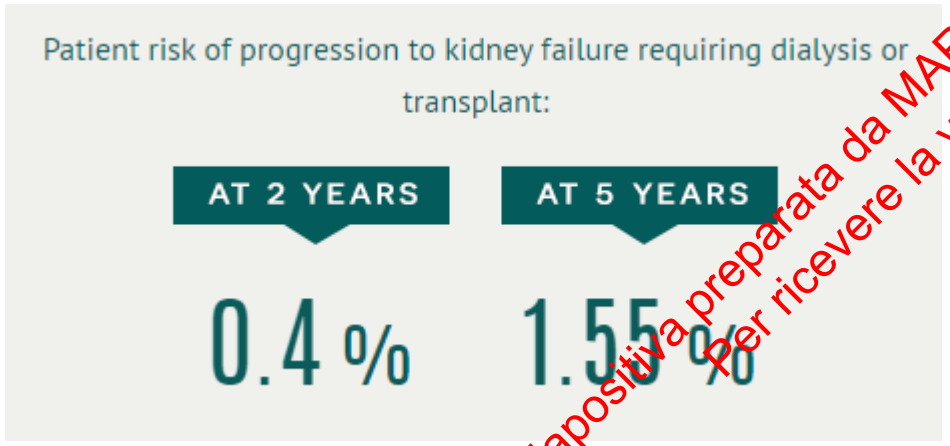
**D. >17 aa**

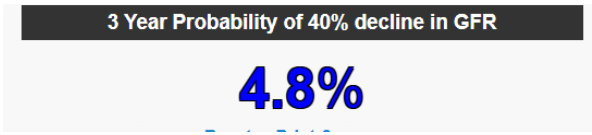
?

# Quale è l'aspettativa di vita (attesa) di Claudio ?


**15.7 aa**



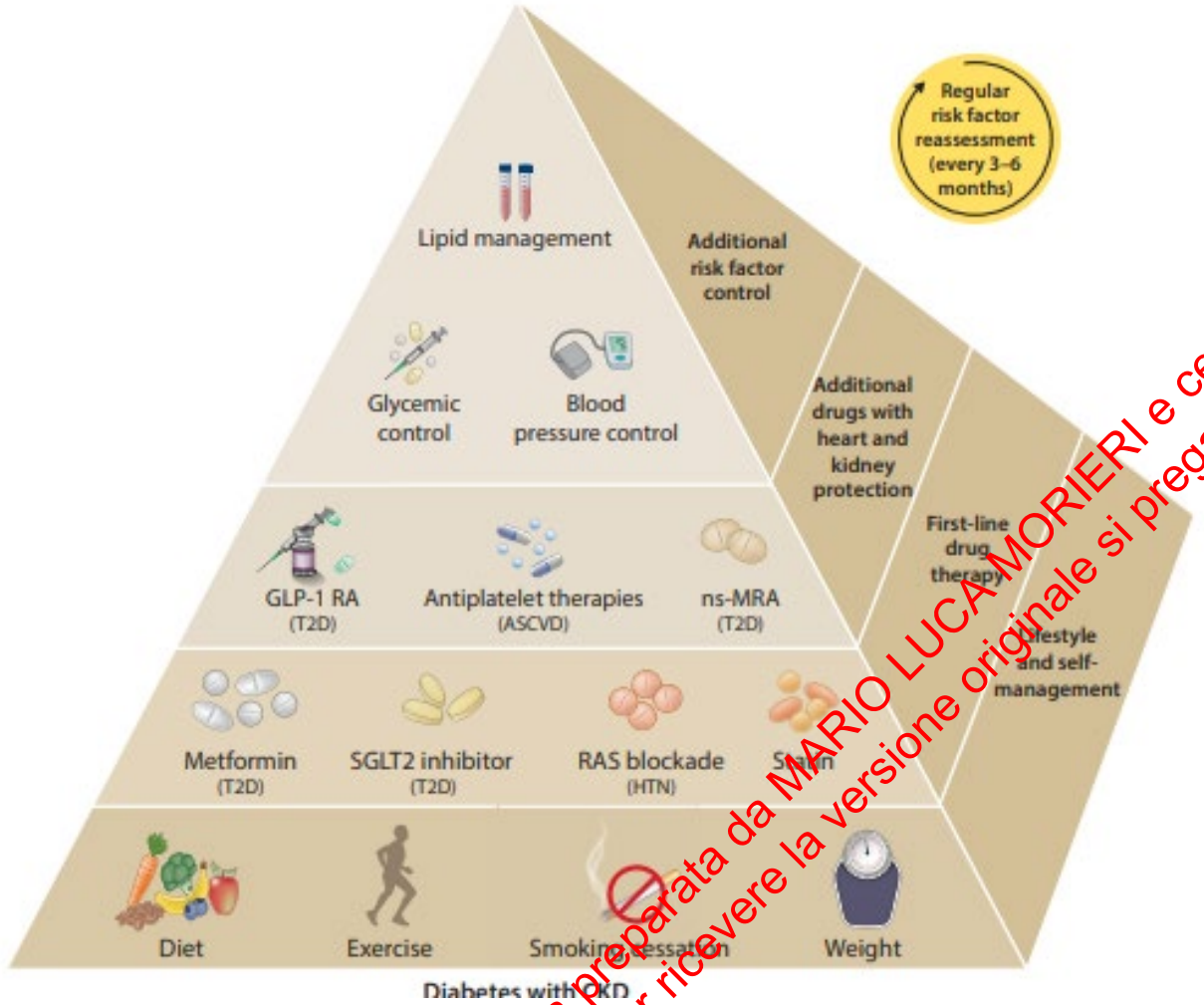






Halmien, Diabetes care Oct 2022

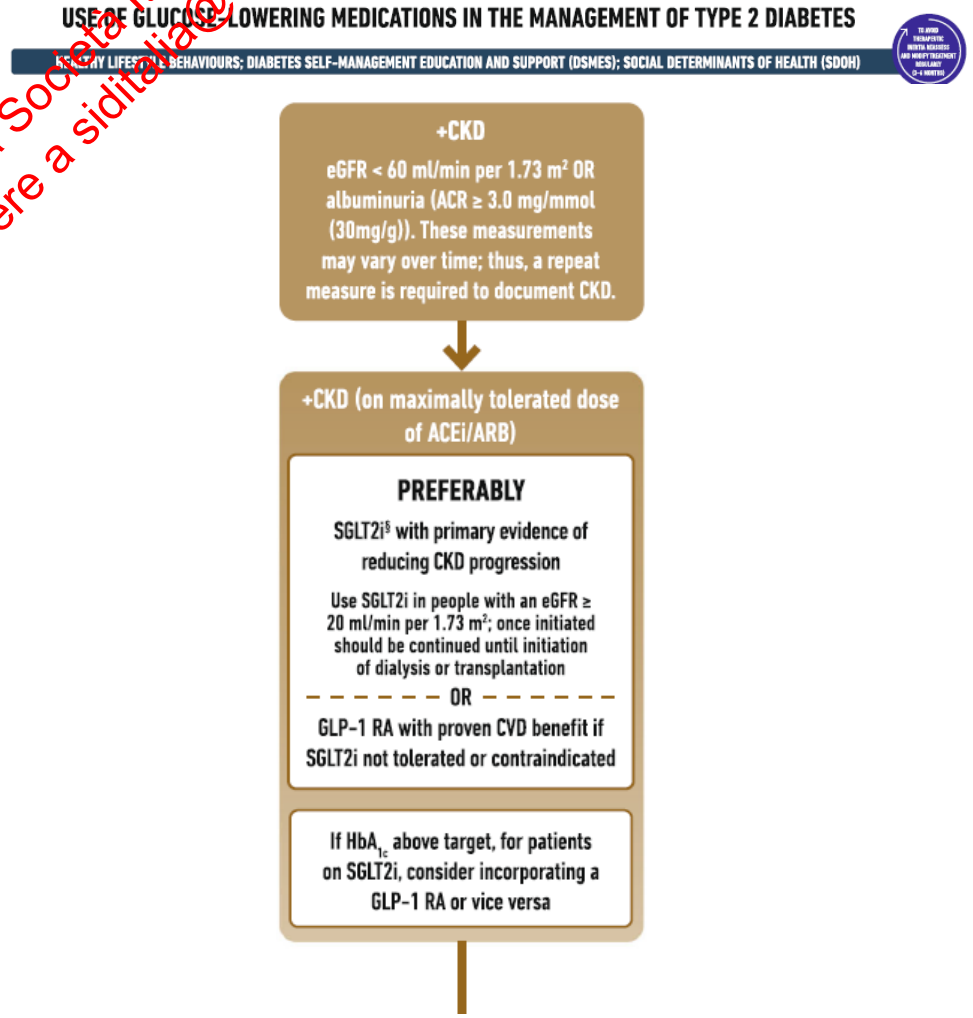
# Quali terapia raccomandereste in questo paziente?

# Diabete e CKD




**Kidney–heart risk factor management**

***ADA-EASD consensus***




***KDIGO guidelines 2022***

# Terapia antidiabetica e DKD

**Table 2 | Considerations for selecting glucose-lowering agents in patients with T2D and CKD** [2,11]

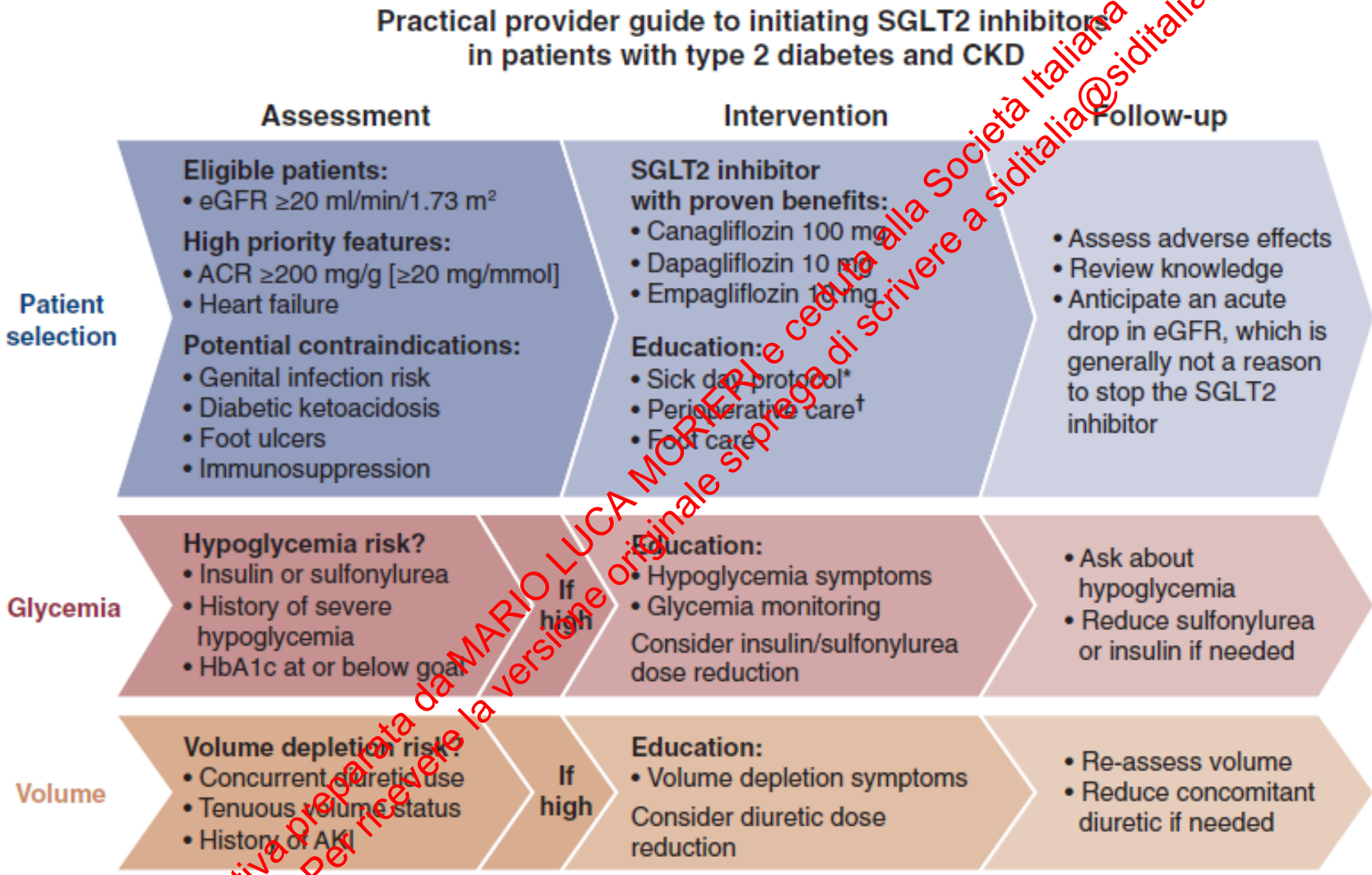
| | Progression of CKD | ASCVD | Heart failure | Glucose-lowering efficacy | Hypoglycemia risk | Weight effects | Cost |
|---|---|---|---|---|---|---|---|
| **Metformin** | Neutral | Potential benefit | Potential benefit | High | Low | Neutral | Low |
| **SGLT2 inhibitors** | Benefit[a] | Benefit[c] | Benefit | Intermediate | Low | Loss | High |
| **GLP-1 receptor agonists** | Benefit[b] | Benefit[c] | Potential benefit | High | Low | Loss | High |
| **DPP-4 inhibitors** | Neutral | Neutral | Potential risk[c] (saxagliptin) | Intermediate | Low | Neutral | High |
| **Insulin** | Neutral | Neutral | Neutral | Highest | High | Gain | High (analogs)<br>Low (human) |
| **Sulfonylureas** | Neutral | Neutral | Neutral | High | High | Gain | Low |
| **Thiazolidinediones** | Neutral | Potential benefit (pioglitazone) | Increased risk | High | Low | Gain | Low |
| **α-Glucosidase inhibitors** | Neutral | Neutral | Neutral | Intermediate | Low | Neutral | Low |

Neutral
Potential benefit or intermediate glucose-lowering efficacy
Benefit (organ protection, high efficacy, low hypoglycemia risk, weight loss, or low cost)
Potential risk or high cost to patient
Increased risk for adverse effects



*De Boer et al, ADA-KDIGO consensus*

# SGLT2i






*De Boer et al, ADA-KDIGO consensus*

# SGLT2i effects by KDIGO stages on eGFR



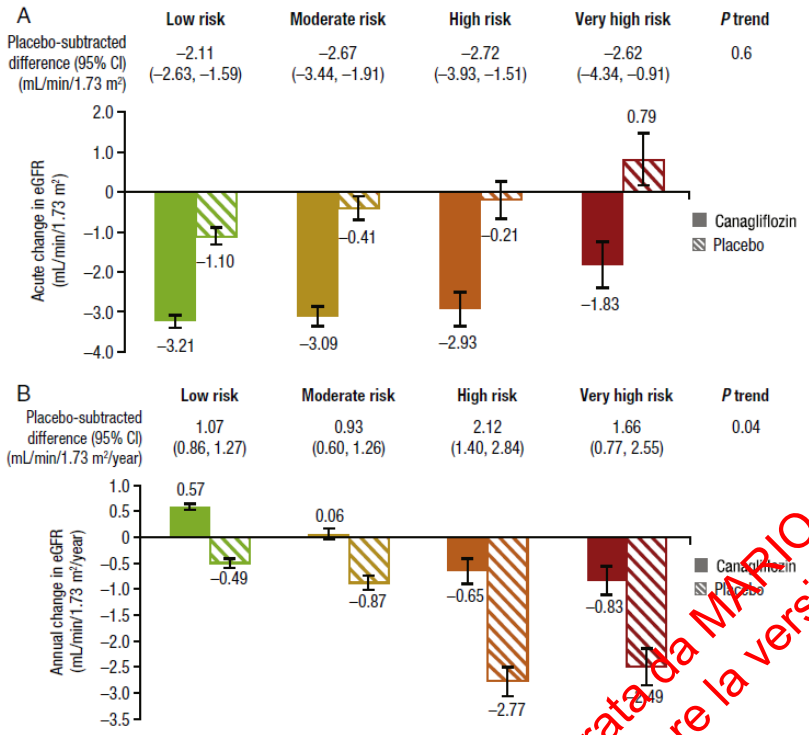
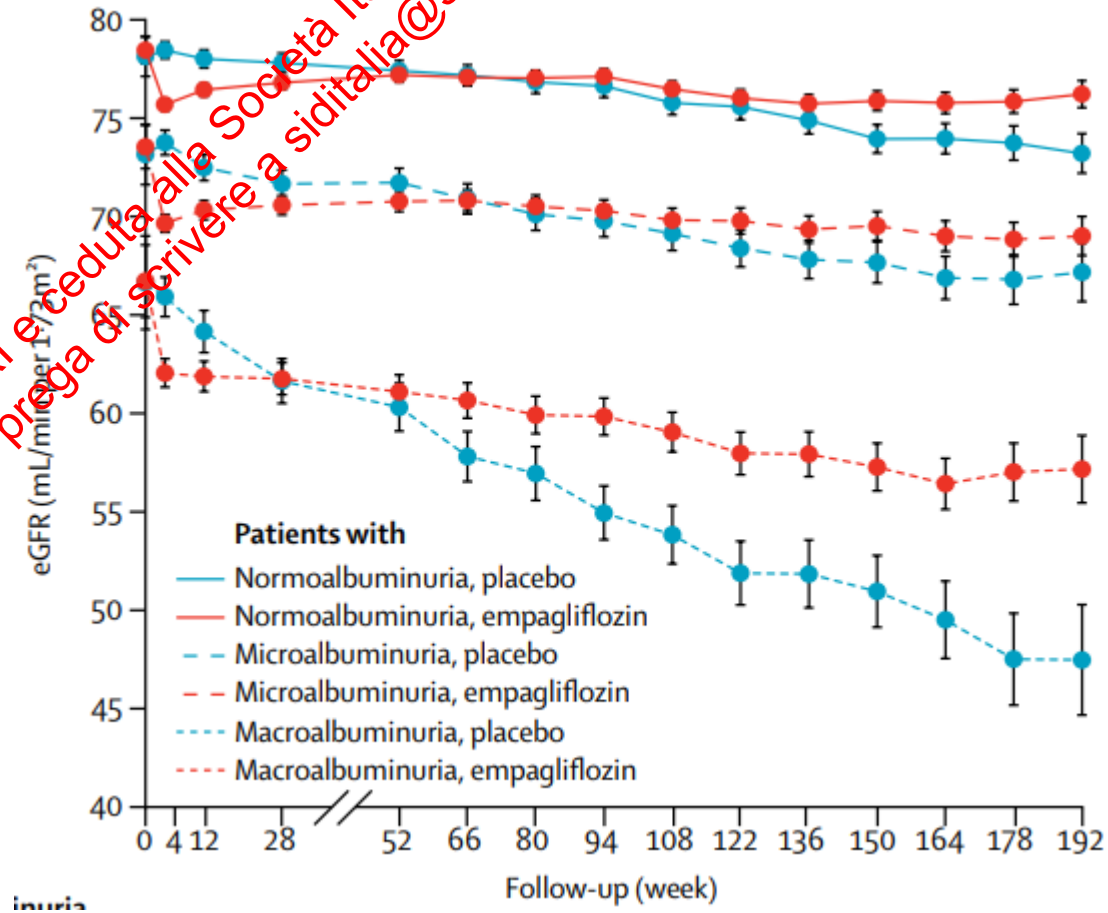



**Figure 3.** Absolute effect of canagliflozin versus placebo on (A) acute change in estimated glomerular filtration rate (eGFR) and (B) chronic eGFR slope (data are reported for week 6 in CANagliflozin cardioVascular Assessment Study (CANVAS) and week 13 in CANVAS-R) in participant subgroups defined by baseline KDIGO (Kidney Disease: Improving Global Outcomes) risk categories (eGFR values shown are mean ± standard error).




Cherney Lancet DE 2017

# Cosa fare con la metformina?

A. Sospendo

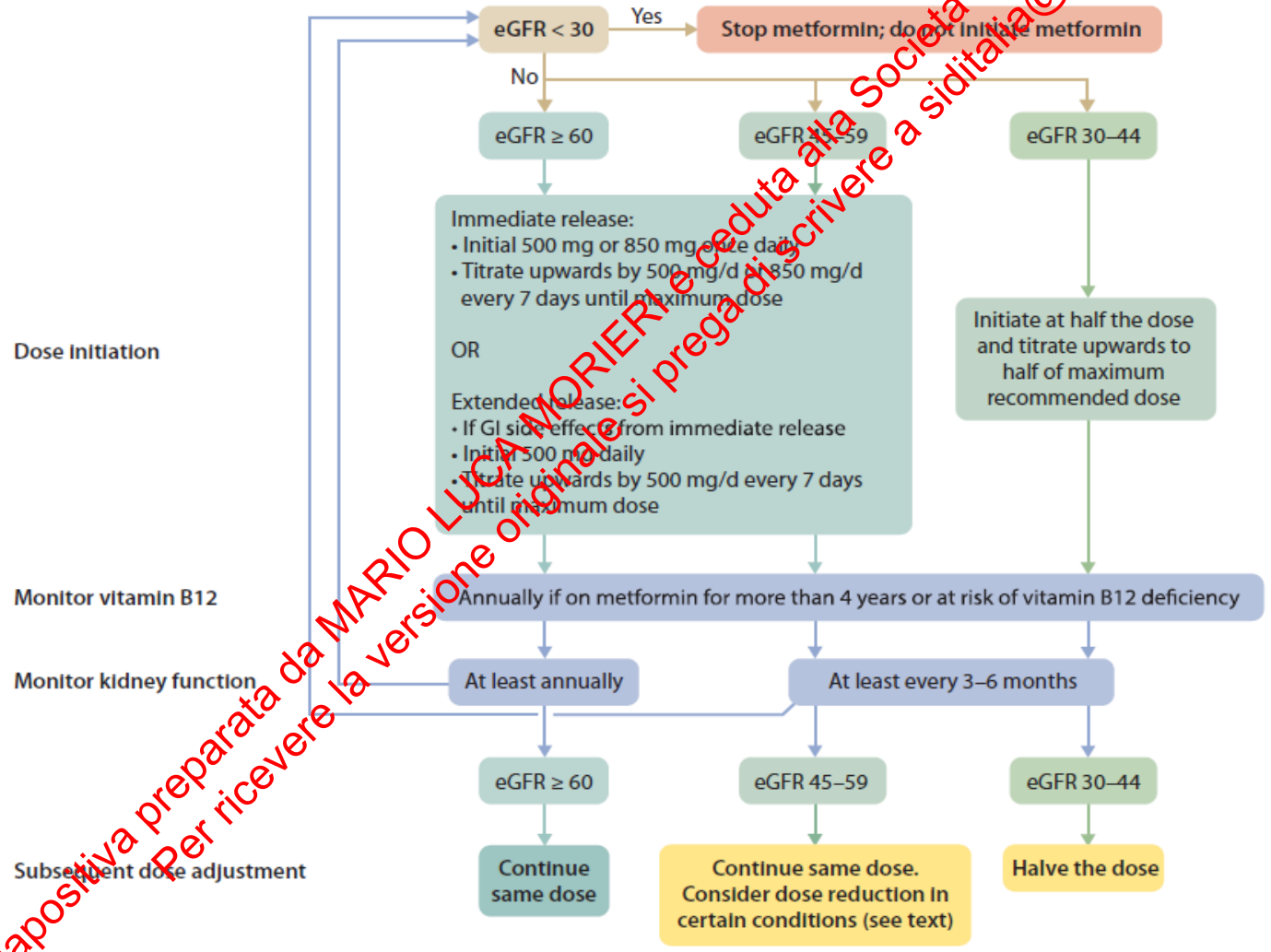
B. Riduco dosaggio

C. Mantengo allo stesso dosaggio

D. Aumento il dosaggio

# Metformin

**Recommendation 4.1.1: We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 $m^2$ with metformin *(1B)*.**






*KDIGO guidelines*

# GLP-1 RAs

| GLP-1 RA | Dose | CKD adjustment |
|---|---|---|
| Dulaglutide | 0.75 mg and 1.5 mg once weekly | No dosage adjustment<br>Use with eGFR >15 ml/min per 1.73 m² |
| Exenatide | 10 µg twice daily | Use with CrCl >30 ml/min |
| Exenatide extended-release | 2 mg once weekly | Use with eGFR >45 ml/min per 1.73 m² |
| Liraglutide | 1.2 mg and 1.8 mg once daily | No dosage adjustment<br>Limited data for severe CKD |
| Lixisenatide | 10 µg and 20 µg once daily | No dosage adjustment<br>Limited data for severe CKD<br>Not recommended with eGFR <15 ml/min per 1.73 m² |
| Semaglutide (injection) | 0.5 mg and 1 mg once weekly | No dosage adjustment<br>Limited data for severe CKD |
| Semaglutide (oral) | 3 mg, 7 mg, or 14 mg daily | No dosage adjustment<br>Limited data for severe CKD |

4.2. Glucagon-like peptide-1 receptor agonists (GLP-1 RA)

**Recommendation 4.2.1: In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications, we recommend a long-acting GLP-1 RA *(1B)*.**

# Quale target consideri adeguati in questo paziente?

| HbA1c | LDL-c | PAS |
|---|---|---|
| A. <6,0 % | A. <116 mg/dl | A. <120 mmHg |
| B. < 6,5 % | B. <100 mg/dl | B. <130 mmHg |
| C. < 7% | C. <70 mg/dl | C. <140 mmHg |
| D. < 7,5% | D. <55 mg/dl | D. <150 mmHg |

# Quali terapia raccomanderesti?

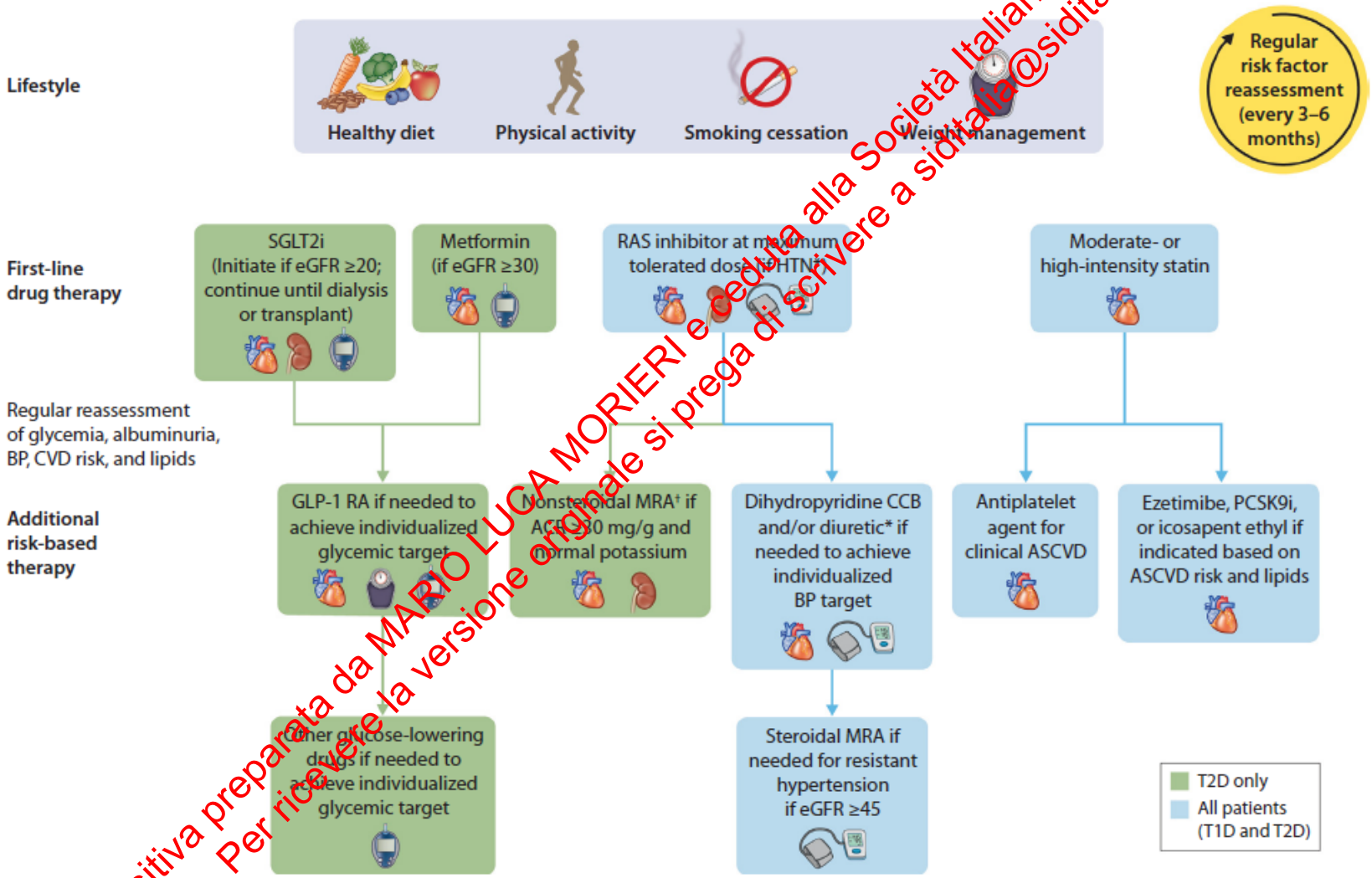
?

# Diabete e CKD


**Kidney–heart risk factor management**

*KDIGO guidelines 2023*

# Holistic approach






*KDIGO guidelines 2023*

# Statins and CVD risk reduction by eGFR in T2D

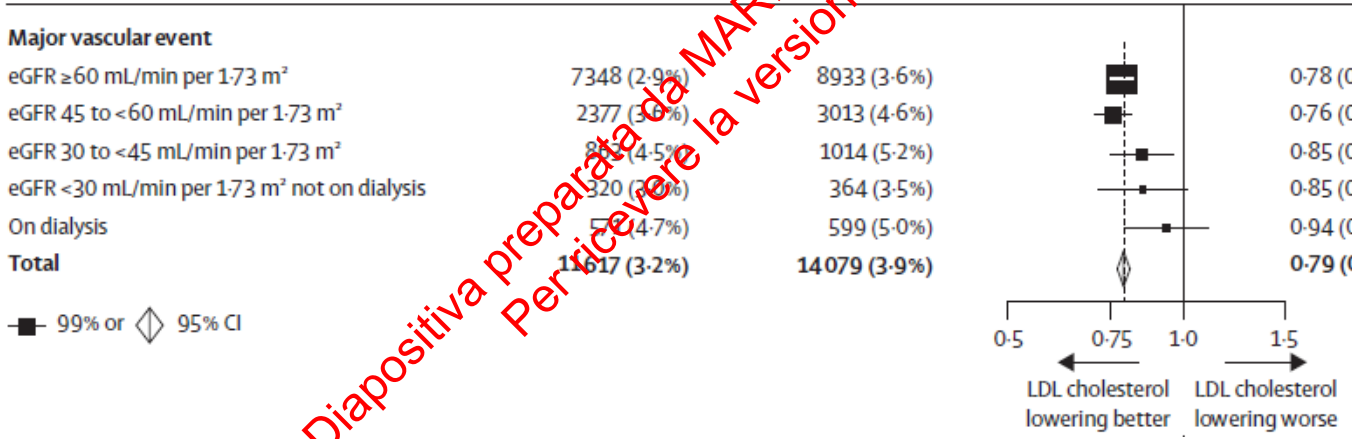
## Efficacy of cholesterol-lowering therapy in 18 686 people with diabetes in 14 randomised trials of statins: a meta-analysis

*Cholesterol Treatment Trialists' (CTT) Collaborators**

| Groups | Events (%) Treatment | Control | RR (CI) | Test for heterogenity or trend |
|---|---|---|---|---|
| **Estimated GFR (mL/min/1·73m²):** | | | | |
| <60 | 415 (20·6%) | 477 (24·0%) | 0·83 (0·71–0·97) | |
| ≥60–<90 | 816 (15·5%) | 961 (18·4%) | 0·81 (0·72–0·91) | $\chi^2_1$=2·9; p=0·09 |
| ≥90 | 194 (12·5%) | 286 (18·4%) | 0·65 (0·50–0·84) | |

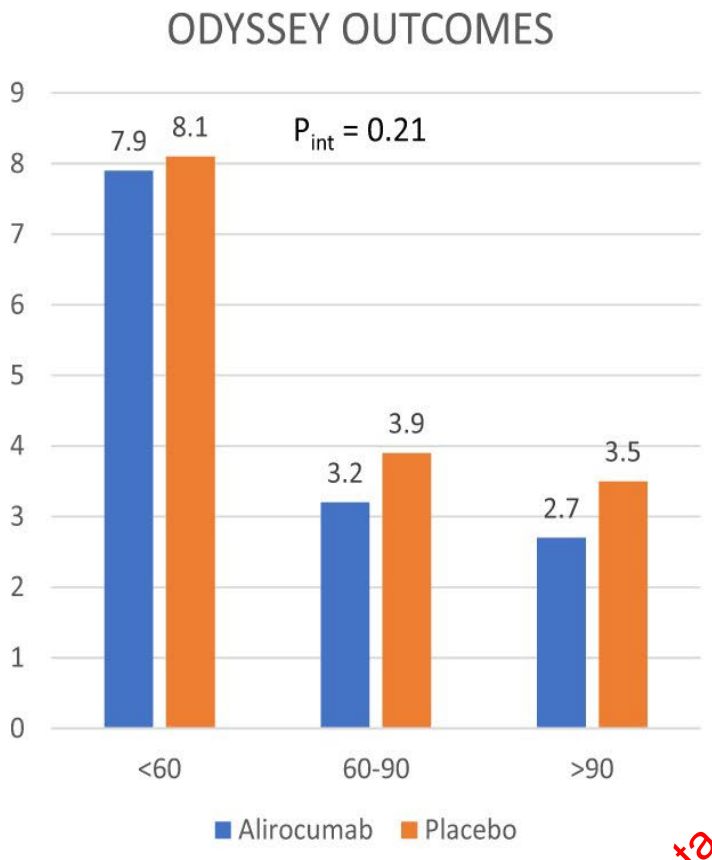

***CTT Collaboration Lancet Diab Endo 2010***

| | Number of events (% per annum) Statin or more intensive regimen | Control or less intensive regimen | RR (CI) per 1·0 mmol/L reduction in LDL cholesterol | p for trend |
|---|---|---|---|---|
| **Major vascular event** | | | | |
| eGFR ≥60 mL/min per 1·73 m² | 7348 (2·9%) | 8933 (3·6%) | 0·78 (0·75–0·82) | 0·008 |
| eGFR 45 to <60 mL/min per 1·73 m² | 2377 (3·6%) | 3013 (4·6%) | 0·76 (0·70–0·81) | |
| eGFR 30 to <45 mL/min per 1·73 m² | 853 (4·5%) | 1014 (5·2%) | 0·85 (0·75–0·96) | |
| eGFR <30 mL/min per 1·73 m² not on dialysis | 320 (3·0%) | 364 (3·5%) | 0·85 (0·71–1·02) | |
| On dialysis | 519 (4·7%) | 599 (5·0%) | 0·94 (0·79–1·11) | |
| **Total** | **11 617 (3·2%)** | **14 079 (3·9%)** | **0·79 (0·77–0·81)** | |

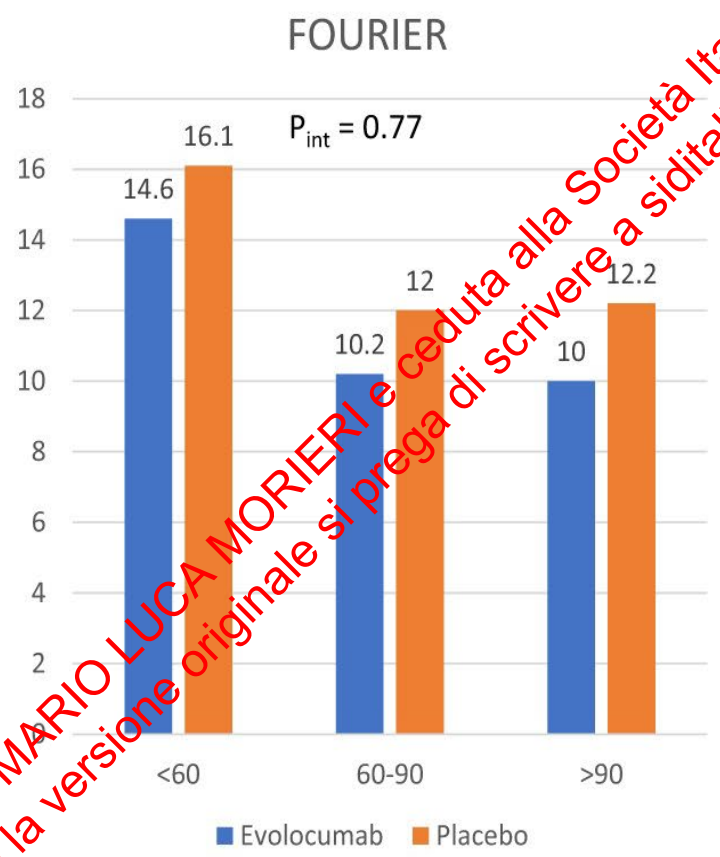



***CTT Collaboration Lancet Diab Endo 2016***

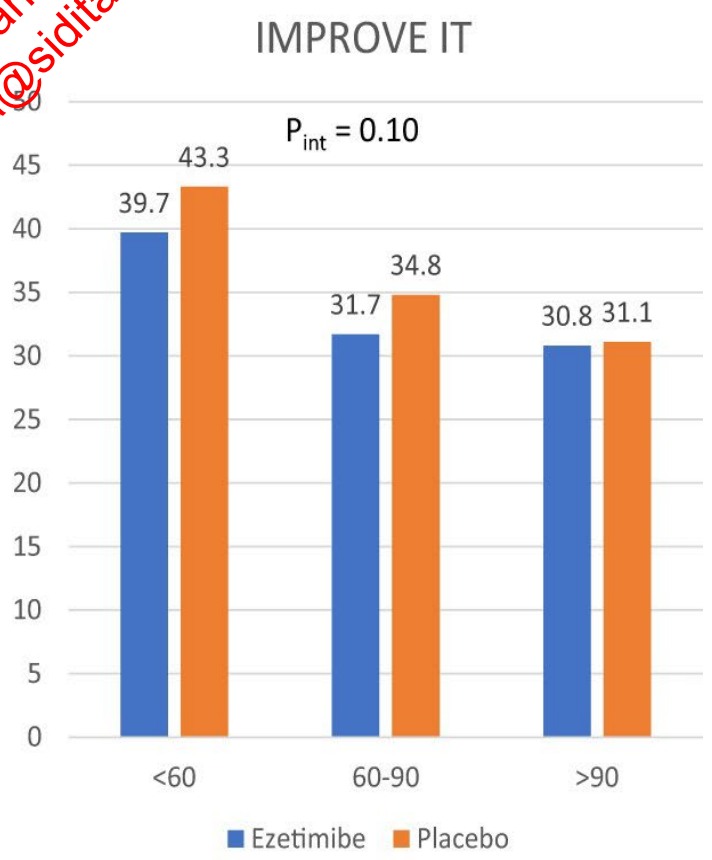
# Benefit of PCSK9i and Ezetimibe on CVD by eGFR (mixed populations)




CHD Death/MI/Stroke/UA




CV Death/MI/Stroke/UA/Revasc.




CV Death/MI/Stroke/UA/Revasc.



*Eur Heart J*, 2020 (41) 4124–4126, https://doi.org/10.1093/eurheartj/ehaa550

# Lack of benefit on prevention of DKD

**TABLE 3** Change in Kidney Function Over Time According to Treatment Group

| | Evolocumab (n = 13,782) | | Placebo (n = 13,772) | | Evolocumab vs. Placebo (n = 27,554) | | |
|---|---|---|---|---|---|---|---|
| | Events | KM (%) | Events | KM (%) | HR (95% CI) | p Value | p Interaction |
| Overall | | | | | | | |
| ≥30% decline in eGFR | 367 | 3.2 | 372 | 3.3 | 0.99 (0.86-1.14) | 0.90 | – |
| ≥40% decline in eGFR | 159 | 1.4 | 152 | 1.4 | 1.05 (0.84-1.31) | 0.66 | – |
| ≥50% decline in eGFR | 63 | 0.5 | 65 | 0.6 | 0.97 (0.69-1.37) | 0.86 | – |
| ≥50% decline in subgroups | | | | | | | |
| Diabetes | | | | | | | 0.15 |
| No diabetes (evolocumab n = 8,728, placebo n = 8,750) | 16 | 0.2 | 24 | 0.3 | 0.67 (0.36-1.27) | 0.22 | – |
| Diabetes (evolocumab n = 5,054, placebo n = 5,022) | 47 | 1.0 | 41 | 1.0 | 1.17 (0.77-1.78) | 0.46 | – |
| Baseline eGFR | | | | | | | 0.09 |
| Stage ≥ 3 CKD (evolocumab n = 2,302, placebo n = 2,141) | 24 | 1.1 | 26 | 1.2 | 0.87 (0.50-1.52) | 0.62 | – |
| Stage 2 CKD (evolocumab n = 7,456, placebo n = 7,578) | 32 | 0.5 | 23 | 0.4 | 1.39 (0.82-2.38) | 0.23 | – |
| Preserved kidney function (evolocumab n = 4,024, placebo n = 4,053) | 7 | 0.2 | 16 | 0.5 | 0.45 (0.19-1.10) | 0.07 | – |

Event rate for binary changes in eGFR overall (≥30%, 40%, or 50% decline in eGFR) or in subgroups defined by diabetes or baseline CKD stage. Calculations were based on Cox proportional hazards models adjusted for randomization strata (LDL-C ≥85 mg/dl and region).

eGFR = estimated glomerular filtration rate; other abbreviations as in Table 2.



**Fourier – renal outcomes**

# Effect of Icosapent Ethyl by CKD status

ORIGINAL RESEARCH ARTICLE

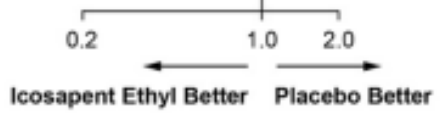
Benefits of Icosapent Ethyl Across the Range of Kidney Function in Patients With Established Cardiovascular Disease or Diabetes: REDUCE-IT RENAL

| End point/Subgroup | Icosapent Ethyl | Placebo | Icosapent Ethyl vs.Placebo | | Interaction P-value | NNT |
|---|---|---|---|---|---|---|
| | *n/N (%)* | *n/N (%)* | *HR (95%CI)* | | | |
| **Primary Composite End point** | | | | | | |
| **Overall Population** | 705/4089 (17.2) | 901/4090 (22.0) | | 0.75 (0.68, 0.83) | | |
| **Prespecified Baseline eGFR Group** | | | | | 0.41 | |
| <60 mL·min$^{-1}$·1.73 m$^{-2}$ | 197/905 (21.8) | 263/911 (28.9) | | 0.71 (0.59, 0.85) | | 14 |
| 60 to <90 mL·min$^{-1}$·1.73 m$^{-2}$ | 380/2217 (17.1) | 468/2238 (20.9) | | 0.80 (0.70, 0.92) | | 27 |
| ≥90 mL·min$^{-1}$·1.73 m$^{-2}$ | 128/963 (13.3) | 170/939 (18.1) | | 0.70 (0.56, 0.89) | | 21 |

**≈ 50% with Diabetes**

# Effect of Icosapent Ethyl by CKD status

| Endpoint/Subgroup | Icosapent Ethyl | Placebo | Icosapent Ethyl vs. Placebo | Interaction P-value |
|---|---|---|---|---|
| | *n/N (%)* | *n/N (%)* | *HR (95% CI)* | |
| **Primary Composite Endpoint** | | | | |
| **Overall Population** | 705/4089 (17.2) | 901/4090 (22.0) | 0.75 (0.68, 0.83) | |
| ***Post hoc* Baseline eGFR Group** | | | | 0.52 |
| ≥15 to <30 mL/min/1.73 m² | 7/29 (24.1) | 10/37 (27.0) | 0.59 (0.21, 1.68) | |
| ≥30 to <45 mL/min/1.73 m² | 63/219 (28.8) | 77/232 (33.2) | 0.83 (0.59, 1.16) | |
| ≥45 to <60 mL/min/1.73 m² | 127/657 (19.3) | 176/642 (27.4) | 0.66 (0.53, 0.84) | |
| ≥60 mL/min/1.73 m² | 508/3180 (16.0) | 638/3177 (20.1) | 0.77 (0.69, 0.87) | |
| **Key Secondary Composite Endpoint** | | | | |
| **Overall Population** | 459/4089 (11.2) | 606/4090 (14.8) | 0.74 (0.65, 0.83) | |
| ***Post hoc* Baseline eGFR Group** | | | | 0.97 |
| ≥15 to <30 mL/min/1.73 m² | 7/29 (24.1) | 9/37 (24.3) | 0.67 (0.23, 1.95) | |
| ≥30 to <45 mL/min/1.73 m² | 46/219 (21.0) | 64/232 (27.6) | 0.72 (0.49, 1.05) | |
| ≥45 to <60 mL/min/1.73 m² | 99/657 (15.1) | 132/642 (20.6) | 0.71 (0.55, 0.92) | |
| ≥60 mL/min/1.73 m² | 307/3180 (9.7) | 401/3177 (12.6) | 0.75 (0.64, 0.87) | |



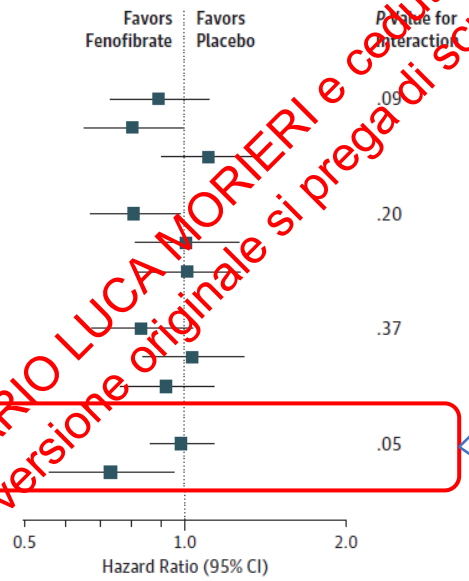

- ***No effect on eGFR decline***
- ***No evaluation of albuminuria***

# Effect of fenofibrate on CVD and DKD

**Fenofibrate (on top of statins) benefit is further confirmed after 9.7 years of follow-up in ACCORDION**
**→ extension follow-up of ACCORD clinical trial**

Figure 3. Hazard Ratios for the Primary Outcome in Prespecified Subgroups

| Characteristic | Statin + Fenofibrate Events/No. (%) | Statin + Placebo Events/No. (%) | Hazard Ratio (95% CI) | P Value for Interaction |
|---|---|---|---|---|
| LDL-C | | | | |
| <85 | 169/925 (18.27) | 175/885 (19.77) | 0.90 (0.73-1.11) | .09 |
| 85+111 | 155/928 (16.70) | 182/916 (19.87) | 0.80 (0.65-1.00) | |
| ≥112 | 182/871 (20.90) | 179/919 (19.48) | 1.11 (0.91-1.37) | |
| HDL | | | | |
| <35 | 197/956 (20.61) | 224/903 (24.81) | 0.81 (0.67-0.98) | .20 |
| 35-40 | 159/852 (18.66) | 157/858 (18.30) | 1.01 (0.81-1.26) | |
| ≥41 | 150/916 (16.38) | 155/959 (16.16) | 1.02 (0.81-1.27) | |
| Triglycerides | | | | |
| <129 | 146/879 (16.61) | 186/930 (20.00) | 0.83 (0.67-1.03) | .37 |
| 129-203 | 171/918 (18.63) | 160/908 (17.62) | 1.04 (0.84-1.29) | |
| ≥204 | 189/927 (20.39) | 190/882 (21.54) | 0.93 (0.76-1.13) | |
| Dyslipidemia | | | | |
| No | 407/2242 (18.15) | 415/2266 (18.31) | 0.99 (0.86-1.13) | .05 |
| Triglycerides >204 and HDL-C <34 | 99/482 (20.54) | 121/454 (26.65) | 0.73 (0.56-0.95) | |




**With atherogenic dyslipidemia**
**(TG>204 mg/dl AND HDL-c <34 mg/dl)**
**27 % risk reduction of MACE over 10 yrs**
**(95% C.I. 5-44%)**

**Without atherogenic dyslipidemia**
**(TG<204 mg/dl OR HDL-c >34 mg/dl)**
**no risk reduction of MACE over 10 yrs**

*Elam, JAMA Cardiology, 2019*

# Effects of fibrate on albuminura

Journal of the American College of Cardiology
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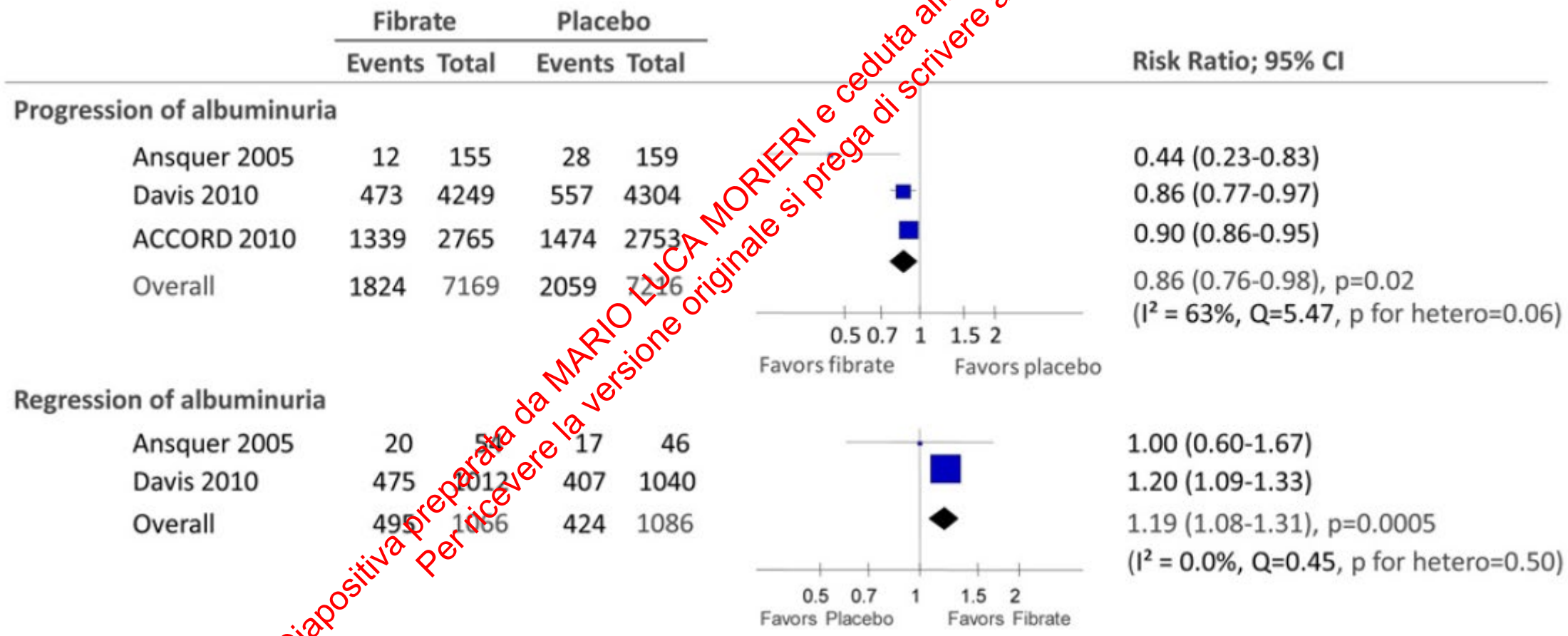
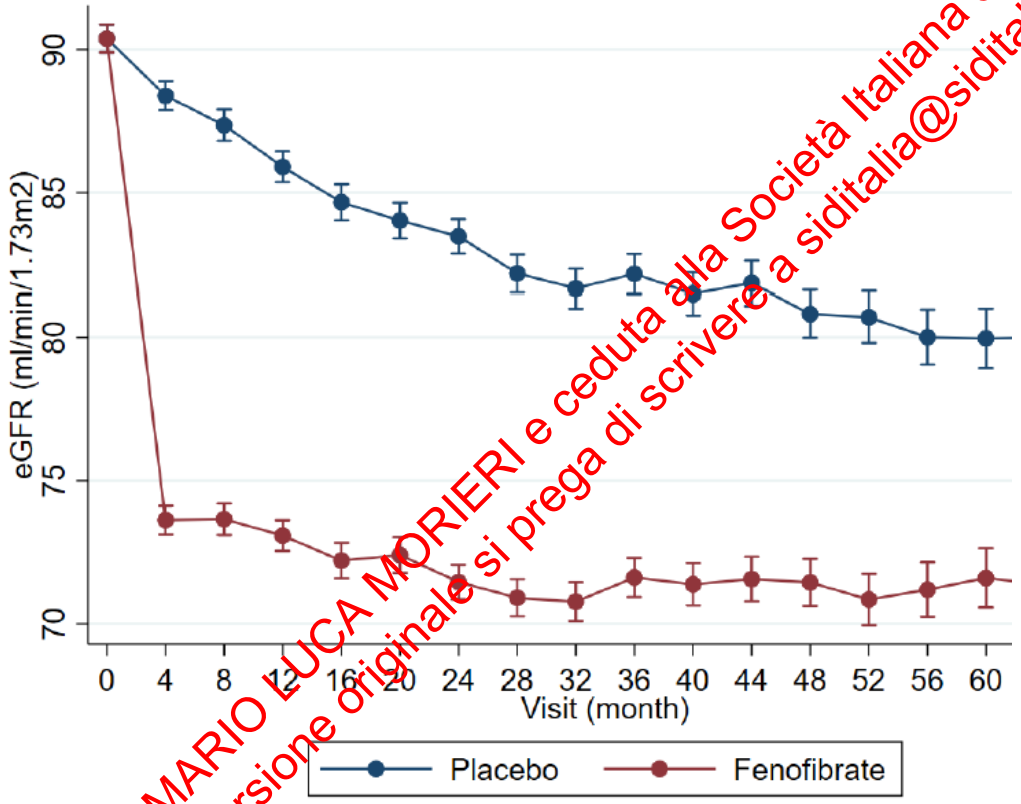
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.07.049

## Effects of Fibrates in Kidney Disease

A Systematic Review and Meta-Analysis



# Effects of fenofibrate on eGFR



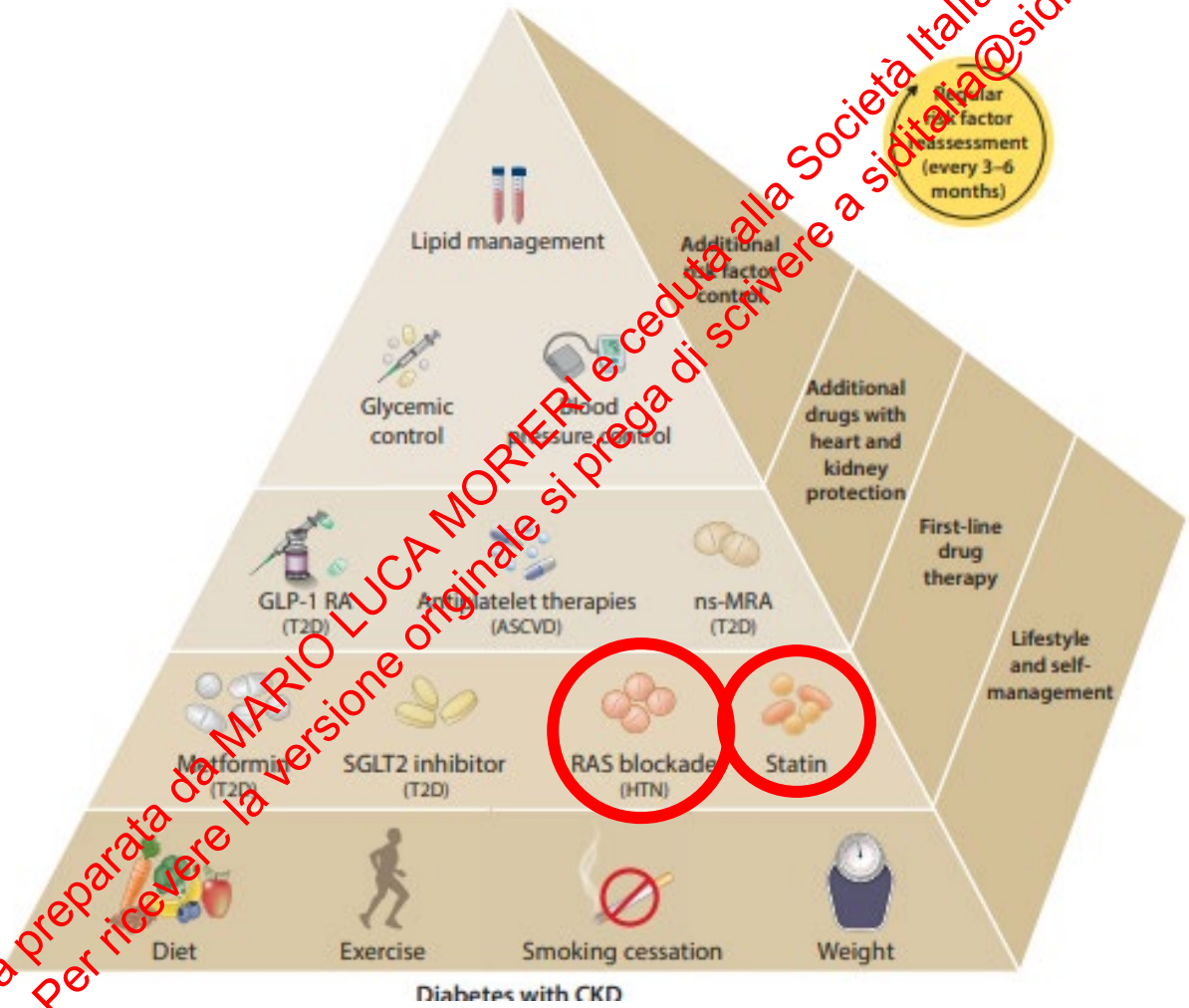

**slopes +1.4 (0.8 to 1.9) ml/min/1.73m2 per year in favor of fenofibrate**

- **Initial deep → reversible after discontinuation**
- **With slower log-term eGFR decline placebo**



*Ferreira et al Diabetes Care 2022*

# Diabete e CKD – non dimenticate la statina per il rischio cardiovascolare!




**Kidney–heart risk factor management**

*KDIGO guidelines 2023*

# Target pressione arteriosa

### 3.4. Blood pressure control

**Recommendation 3.4.1: We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, when tolerated, using standardized office BP measurement (2B).**

*KDIGO guidelines 2023*

**Practice Point 3.4.1: Consider less intensive BP-lowering therapy in people with frailty, high risk of falls, very limited life expectancy, or symptomatic postural hypotension.**

| Recommendations and statements | CoR | LoE |
|---|---|---|
| **Patients 65 to 79 years old** | | |
| The recommended office threshold for initiation of drug treatment is 140/90 mmHg. | I | A |
| The primary goal of treatment is to lower BP to <140/80mmHg. | I | A |
| However, lowering BP to below 130/80mmHg can be considered if treatment is well tolerated. | I | B |
| Drug treatment strategies in patients with type 2 diabetes should be the same as for patients without diabetes and the primary aim is to lower BP below <130/80 mmHg. | I | A |

*ESH 2023*

# Target pressione arteriosa

## Treatment strategies in patients with kidney disease

| Recommendations and statements | CoR | LoE |
|---|---|---|
| BP should be monitored at all stages of CKD, because hypertension is the most important risk factor for end-stage kidney disease (ESKD). | I | A |
| In all patients with CKD the primary goal is to lower office BP to <140 mmHg systolic and <90 mmHg diastolic. | I | A |
| In most CKD patients (young patients, patients with an albumin/creatinine ratio ≥ 300 mg/g, high CV risk patients) office BP may be lowered to <130/80 mmHg if tolerated. | II | B |
| An ACEi or an ARB, titrated to the maximum tolerated doses is recommended for patients with CKD and moderate (UACR 30 to 300 mg/g) or severe (UACR > 300 mg/g) albuminuria. | I | A |
| In patients with CKD, a BP target of less than 120/70 mmHg is not recommended. | III | C |

*ESH 2023*

# Target pressione arteriosa

**Recommendation Table 10 — Recommendations for blood pressure management in patients with diabetes**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| **Screening for hypertension** | | |
| Regular BP measurements[c] are recommended in all patients with diabetes to detect and treat hypertension to reduce CV risk.[193,232,233] | I | A |
| **Treatment targets** | | |
| Anti-hypertensive drug treatment is recommended for people with diabetes when office BP is ≥140/90 mmHg.[196,202,234,235] | I | A |
| It is recommended to treat hypertension in patients with diabetes in an individualized manner. The BP goal is to target SBP to 130 mmHg and <130 mmHg if tolerated, but not <120 mmHg. In older people (age >65 years), it is recommended to target SBP to 130–139 mmHg.[196,236–238] | I | A |
| An on-treatment SBP target of <130 mmHg may be considered in patients with diabetes at particularly high risk of a cerebrovascular event to further reduce their risk of stroke.[194–198,239,240] | IIb | B |
| **Treatment and evaluation** | | |
| Lifestyle changes (weight loss if overweight, physical activity, alcohol restriction, sodium restriction, increased consumption of vegetables, using low-fat dairy products) are recommended in patients with diabetes and hypertension.[205–207,210] | I | A |
| It is recommended to initiate treatment with a combination of a RAS inhibitor and a CCB or thiazide/thiazide-like diuretic.[196,213–216,218,241] | I | A |
| Home BP self-monitoring should be considered in patients with diabetes on anti-hypertensive treatments to check that BP is appropriately controlled.[242] | IIa | B |
| 24 h ambulatory blood pressure monitoring should be considered to assess abnormal 24 h BP patterns, including nocturnal hypertension and reduced or reversed nocturnal BP dipping, and to adjust anti-hypertensive treatment.[243] | IIa | B |

# Claudio – fine visita

***Conclusione: Diabete tipo 2 in paziente con IRC stadio 3b con microalbuminuria, sovrappeso, ipertensione arteriosa in prevenzione cardiovascolare primaria ma a rischio cardiovascolare molto elevato***

***→ Seguire indicazioni dietetiche (+ visita dietistica);***
***→ Attività fisica → cercare di raggiungere i 150 min sett.***
***- Empagliflozin 10 mg 1 cp la mattina***
***- Metformina RP 1000 mg 1 cp la sera***
***- Atorvastatina 20 mg + ezetimibe 10 mg (target LDL <55 mg/dl)***
***- Incremento ramipril a 10 mg/die e monitoraggio PAal domicilio (target PAS < 130 mmHg)***

***Tra 4-6 mesi invio esami via email per eventuale aggiunta GLP1 agonista per prevenzione cardiovascolare e target HbA1c (<6,5%).***
***(Esenzione) Fundus oculi, visita cardiologica con ECG, eco-addome, doppler TSA, test cardiovascolari per neuropatia autonomica.***
***Visita di controllo a 9-12 mesi.***

# Che altri accertamenti/valutazioni servirebbero per inquadrare meglio il paziente?

**Non altri esami recenti disponibili:**
**ma esami di un anno prima con creatinina simile (VFG 49 ml/min)**
**non c'è UACR**

**Ecoaddome (steatosi epatica? - fibroscan per fibrosi?)**

**Fundus oculi,**
**valutazione neuropatia (test cardiovascolari per neuropatia autonomica)**
**Valutazione/descrizione del piede**

**Riclassificazione del rischio CV:**
**Visita cardiologica con ECG**
**Doppler TSA**
**Lp(a)**

# SGLT2i effects by KDIGO stages on eGFR



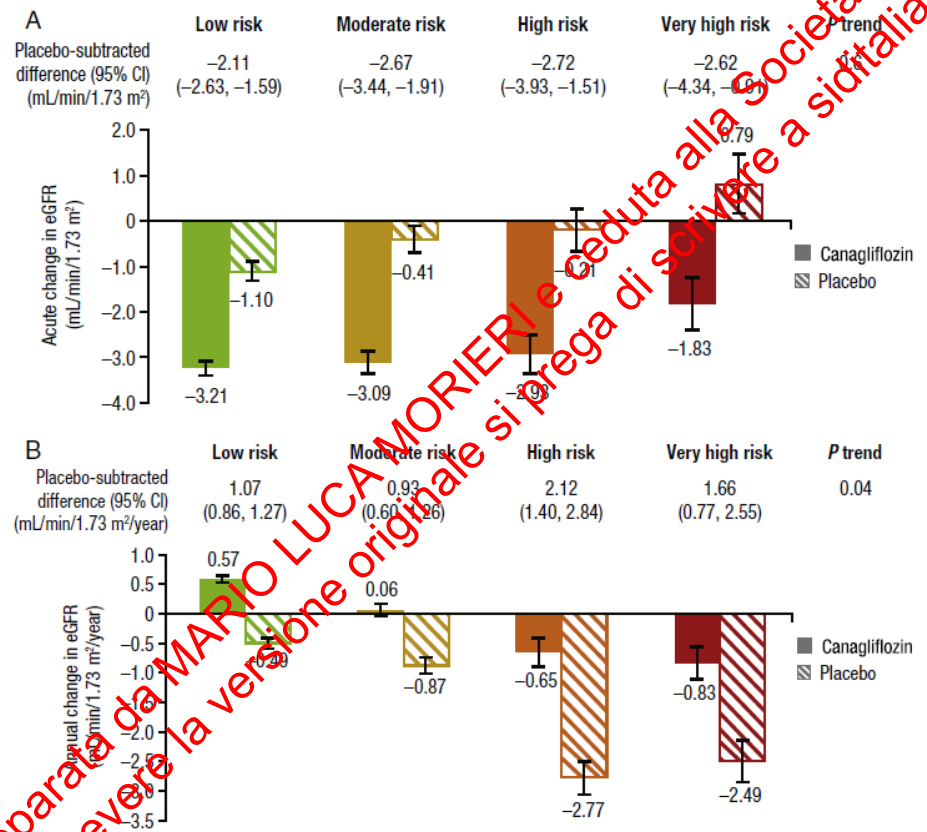
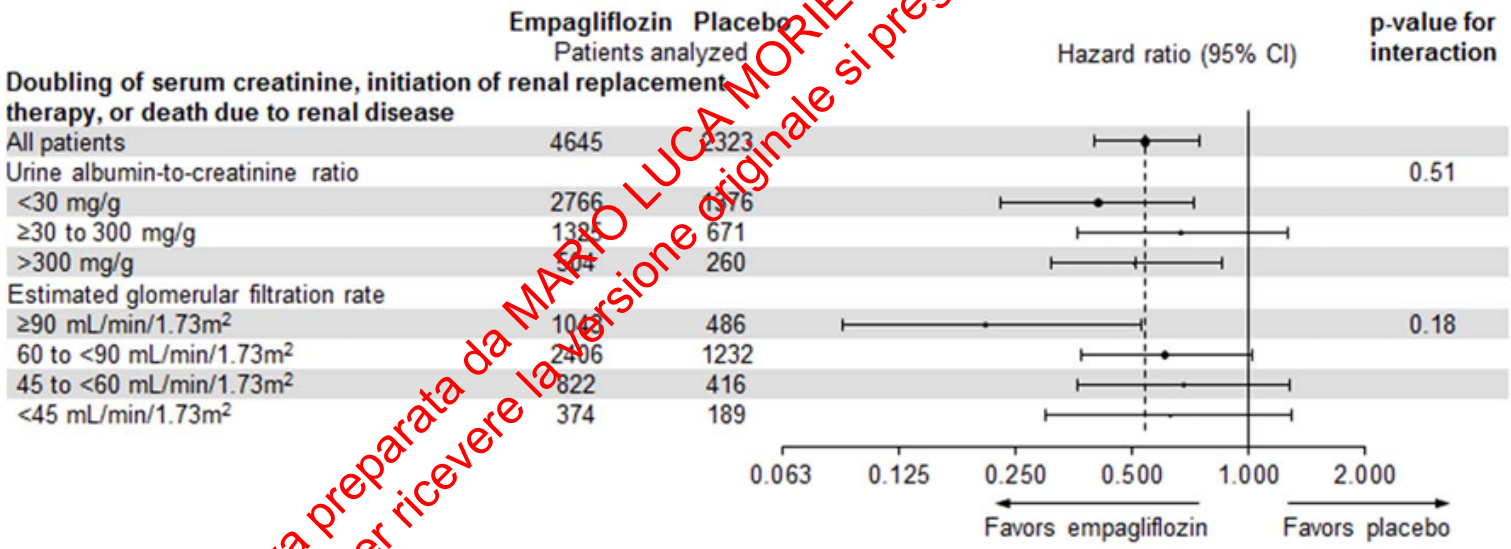



**Figure 3.** Absolute effect of canagliflozin versus placebo on (A) acute change in estimated glomerular filtration rate (eGFR) and (B) chronic eGFR slope (data are reported for week 6 in CANagliflozin cardioVascular Assessment Study (CANVAS) and week 13 in CANVAS-R) in participant subgroups defined by baseline KDIGO (Kidney Disease: Improving Global Outcomes) risk categories (eGFR values shown are mean ± standard error).

# Empa-reg Kidney – by eGFR and UACR

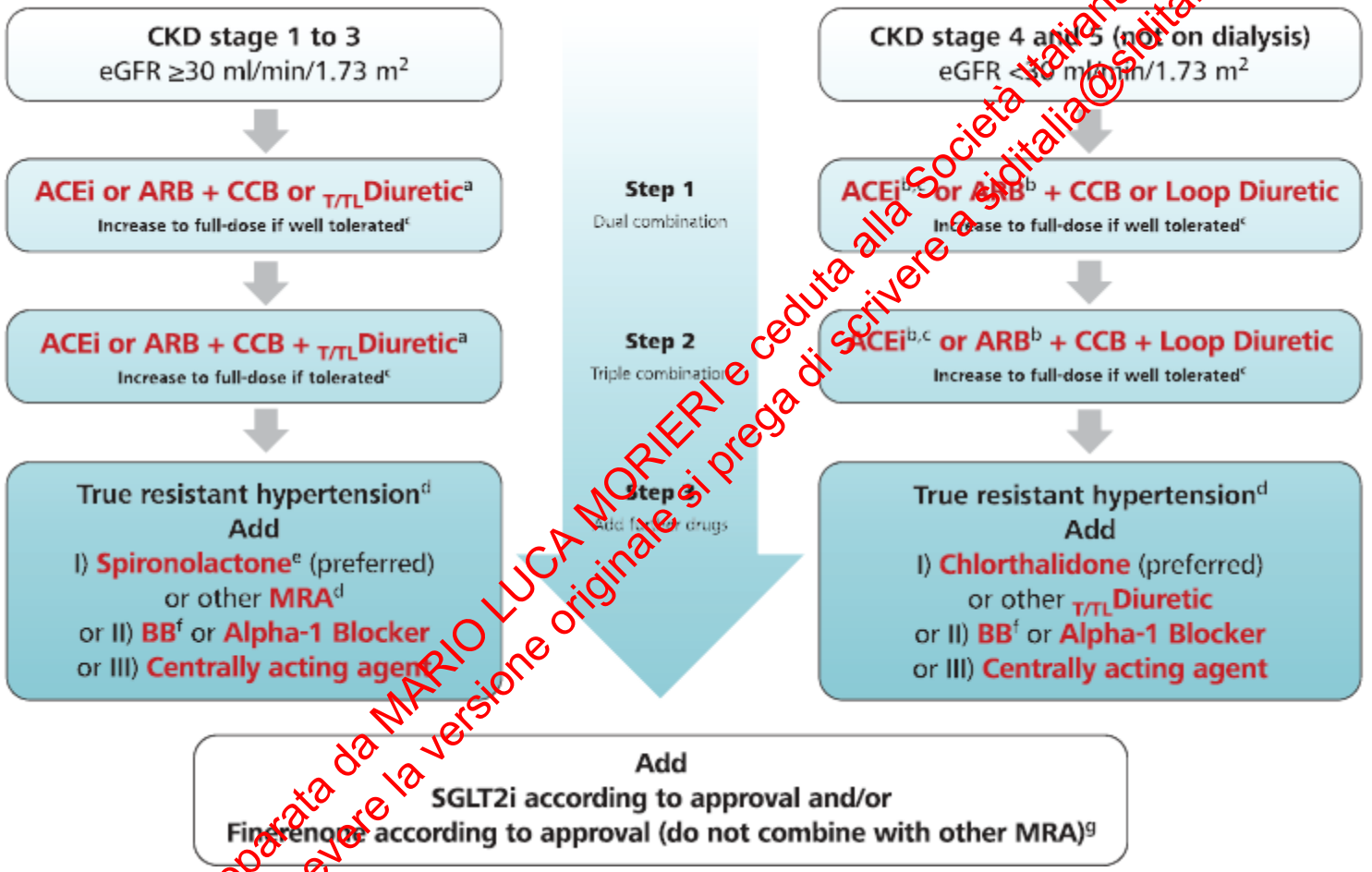
**Figure S6. *Post-hoc* subgroup analyses of doubling of serum creatinine, initiation of renal replacement therapy, or death due to renal disease.**

Cox regression analyses in patients treated with ≥1 dose of study drug. p-value is for test of homogeneity of treatment group difference among subgroups (test for treatment group by covariate interaction) with no adjustment for multiple testing.




*NEJM 2016*

# HTN





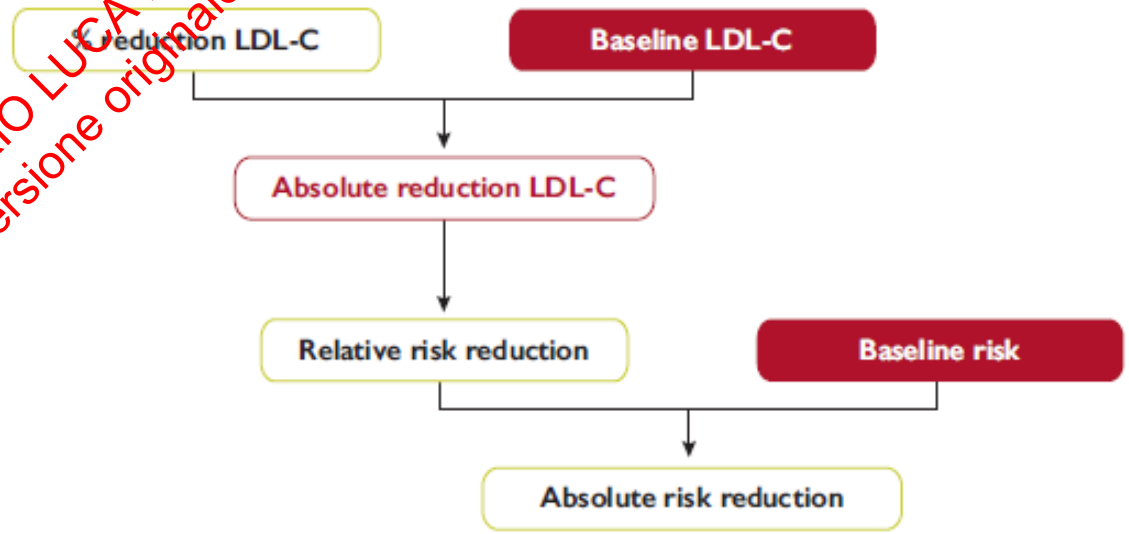

*ESH 2023*

# Effective treatments options to lower LDL-cholesterol

**Intensity of lipid lowering treatment**

| Treatment | Average LDL-C reduction |
|---|---|
| Moderate intensity statin | = 30% |
| High intensity statin | = 50% |
| High intensity statin plus ezetimibe | = 65% |
| PCSK9 inhibitor | = 60% |
| PCSK9 inhibitor plus high intensity statin | = 75% |
| PCSK9 inhibitor plus high intensity statin plus ezetimibe | = 85% |

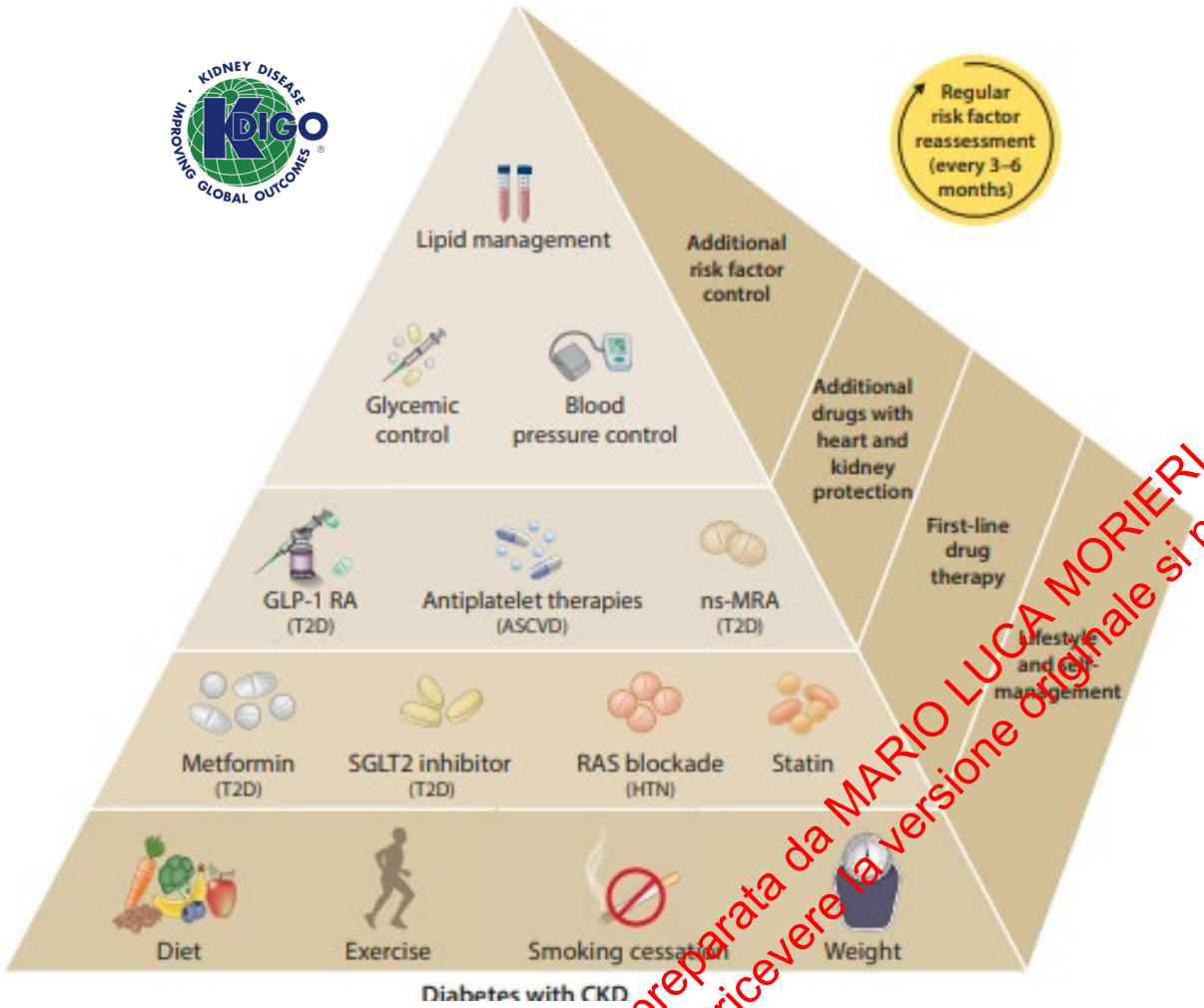
| | |
|---|---|
| **Bempedoic** | **22%** |
| **Eze+Bempedoic** | **42%** |
| **+ bempedoic** | **42%** |
| **+ bempedoic** | **59%** |
| **+ bempedoic** | **71%** |
| **+ bempedoic** | **69%** |
| **+ bempedoic** | **79%** |
| **+ bempedoic** | **88%** |






*EAS-ESC guidelines for dyslipidemia 2019*

# Diabetes and CKD

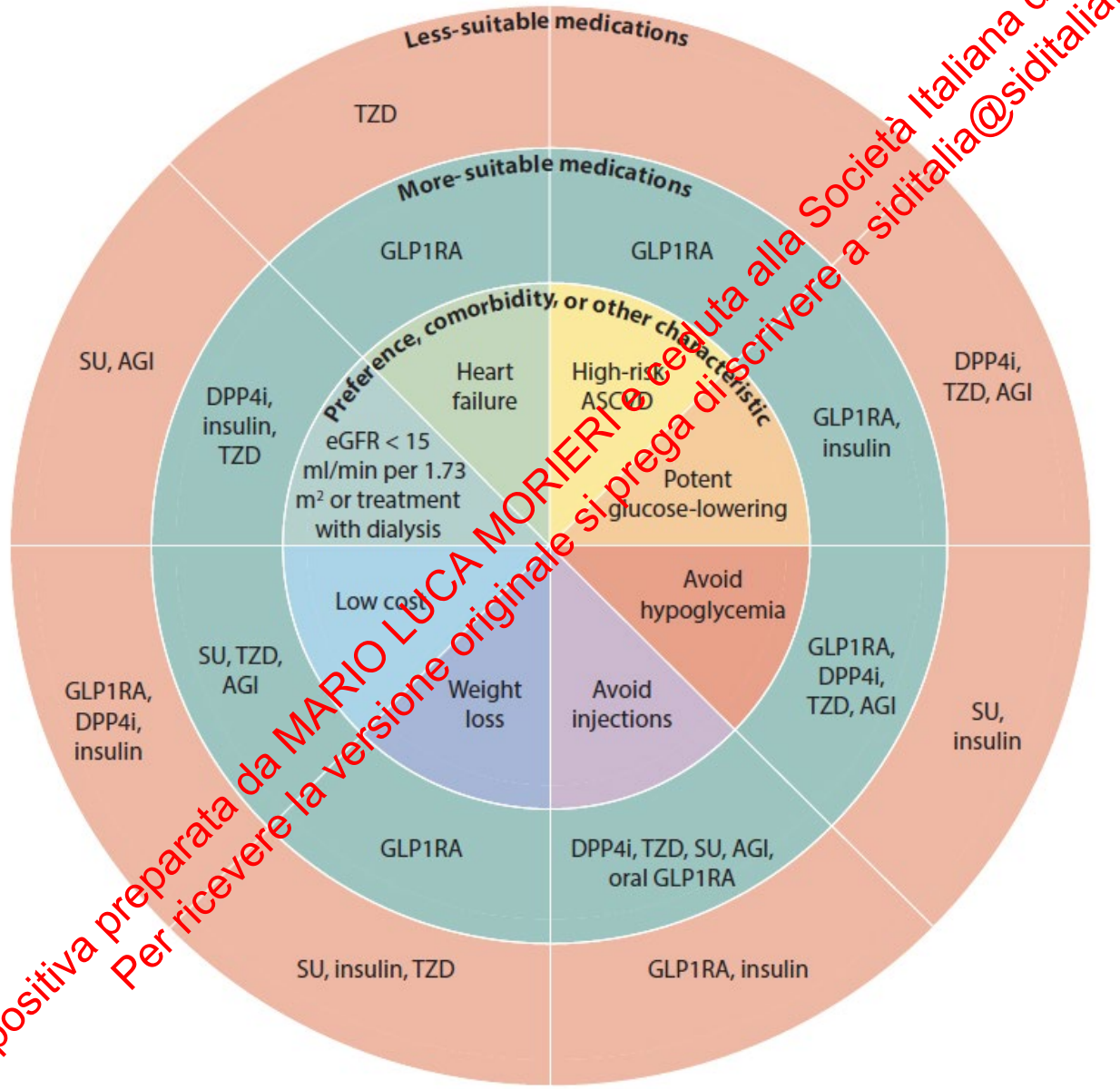



**Kidney–heart risk factor management**

**Recommendations for lipid management in patients with moderate-to-severe chronic kidney disease (Kidney Disease Outcomes Quality Initiative stages 3–5).**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| The use of statins or statin/ezetimibe combination is recommended in patients with non-dialysis-dependent, stage 3–5 CKD.[525,544,545] | I | A |
| In patients already on statins, ezetimibe, or a statin/ezetimibe combination at the time of dialysis initiation, continuation of these drugs should be considered, particularly in patients with ASCVD. | IIa | C |
| In patients with dialysis-dependent CKD who are free of ASCVD, commencing statin therapy is not recommended.[546,547] | III | A |

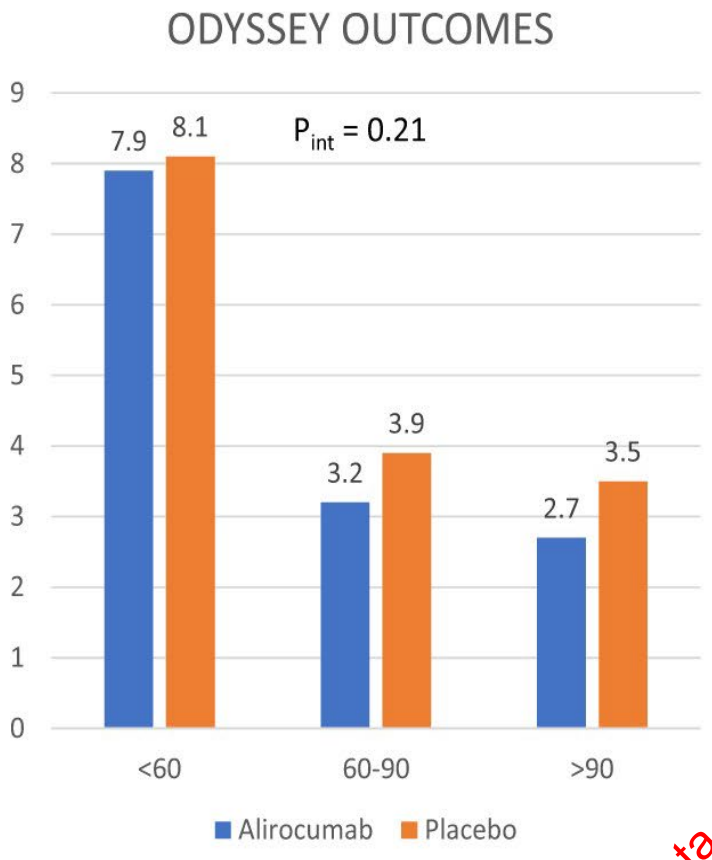
# Personalized approach



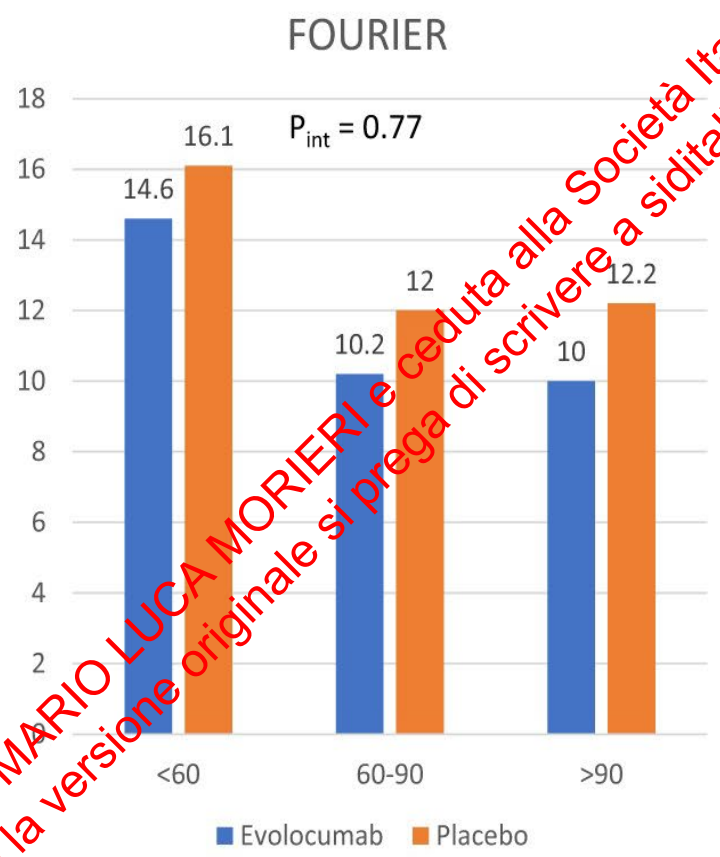



*KDIGO guidelines 2023*

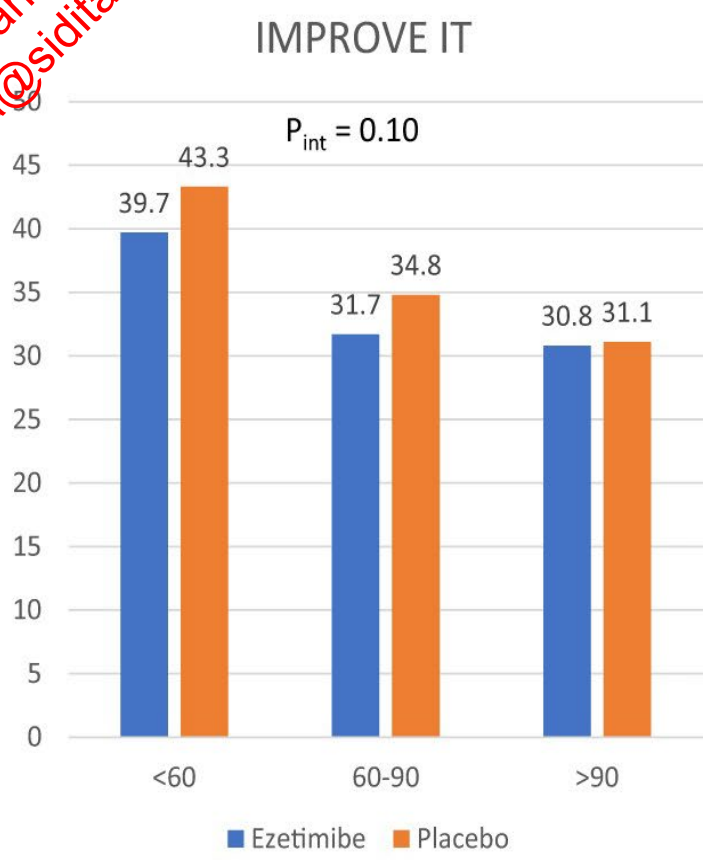
# Benefit of PCSK9i and Ezetimibe on CVD by eGFR (mixed populations)




CHD Death/MI/Stroke/UA




CV Death/MI/Stroke/UA/Revasc.




CV Death/MI/Stroke/UA/Revasc.



*Eur Heart J*, 2020 (41) 4124–4126, https://doi.org/10.1093/eurheartj/ehaa550