### GESTIONE INTEGRATA DEL PAZIENTE A RISCHIO ALTO/MOLTO ALTO: LE RACCOMANDAZIONI DEL NEFROLOGO

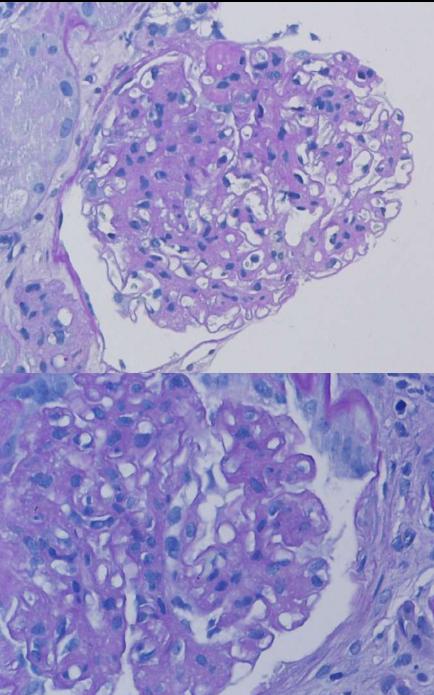




Sandro Feriozzi Nephrology and Dialysis, Viterbo, Italy

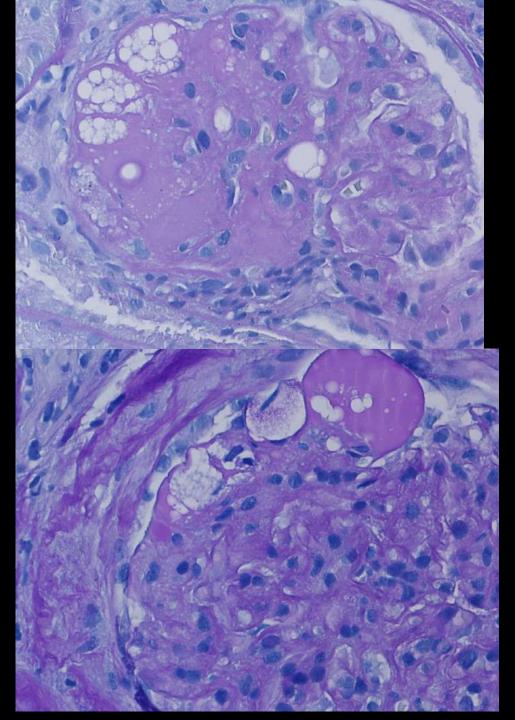


Professor Sandro Feriozzi has received travel assistance and honoraria for lecturing and participating in advisory boards from Sanofi, Takeda, Otsuka and Amicus



HISTOPATHOLOGY OF DIABETIC NEPHROPATHY

Nephropathology Lab, Viterbo



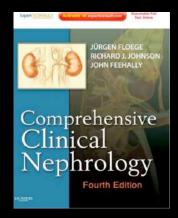
### DEFINITIONS

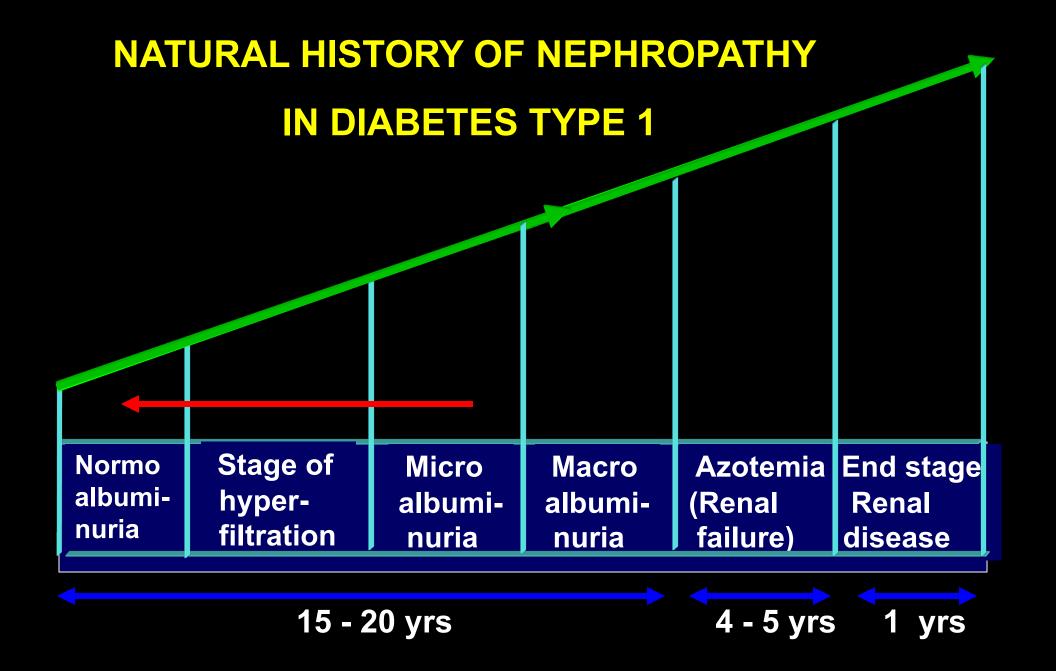
Diabetic nephropathy (DN) is the leading cause of end-stage renal disease (ESRD) in most Western societies. It can develop in the course of both type 1 and type 2 diabetes and as a consequence of other forms of diabetes mellitus (DM).

resistance and insulin deficiency. The metabolic syndrome (insulin resistance, visceral obesity, hypertension, hyperuricemia, and dyslipidemia with high triglyceride levels and low amounts of highdensity lipoprotein [HDL]) is often followed by type 2 diabetes.

### EPIDEMIOLOGY

In most Western countries, DN has become the leading cause of ESRD. According to the U.S. Renal Data System (www.USRDS.org), in 2006, DN was the most frequent primary diagnosis with 159 per million population per year. The proportion of diabetics among patients with ESRD varies considerably between countries but had consistently been on the rise in all countries until recently, when the incidence figures have stabilized. In patients admitted for renal embeddement thereas



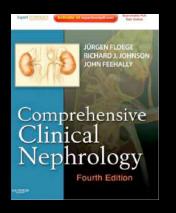


# DIABETIC NEPHROPATHY NOT ONLY KIMMESTIEL-

# **WILSON**

Since the original description of diabetic nephropathy, it has become clear that there are various forms of kidney disease attributable to diabetes, including nonclassical glomerular lesions and tubulointerstitial disease .

**Diabetic kidney disease**" is a clinical diagnosis based upon the presence of albuminuria, decreased estimated glomerular filtration **rate** (eGFR), or both, in patients with diabetes".

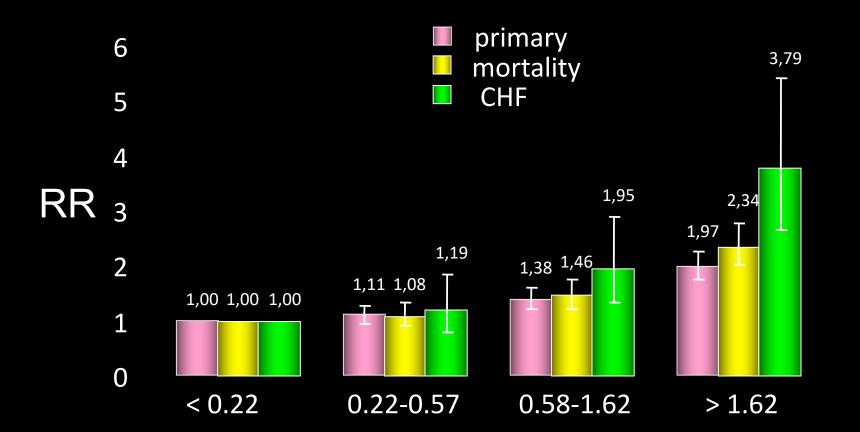


Notably, diabetic kidney disease (DKD) does not indicate the specific pathological phenotype of kidney damage due to diabetes.

Rather, the designation DKD (or "CKD in diabetes") is used to clarify that the underlying pathologic phenotype is unknown in most cases.

The likelihood that diabetic glomerulopathy is the underlying pathology of DKD varies widely depending upon the clinical circumstances.

### HOPE: RELATIVE RISK ACCORDING TO QUARTILE OF ALBUMINURIA (N = 9,043)



P for trend \*< 0.0001 or \*\*<0.05 after controlling for: a) age, sex, SBP, DBP, WHR, DM, ramipril b) age, sex, SBP, DBP, WHR, DM, ramipril after removing MA participants

Gerstein et al, JAMA 2001;

#### care.diabetesjournals.org

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Risk of Rapid Kidney Function Decline, All-Cause Mortality, and Major Cardiovascular Events in Nonalbuminuric Chronic Kidney Disease in Type 2 Diabetes Diabetes Care 2020;43:122-129 | https://doi.org/10.2337/6c19.1438

Events Person-years Rate (95% CI) Hazard ratios (95% CI)\*\* ESKD\* 3.11 (2.07, 4.70) eGFR (≥120) 23 7362 1.20 (0.74, 1.94) No CKD eGFR (90-120) 65 24918 2.60 (2.04, 3.32) 1.0 (Reference) eGFR (60-90) 2.43 (1.92, 3.08) 1.00 (0.71, 1.43) 68 27919 Albuminuric non-CKD 125 5.06 (4.25, 6.03) 1.72 (1.27, 2.34) 24678 13.37 (9.64, 18.54) 4.52 (2.91, 7.01) Albuminuric CKD 36 2690 Non-albuminuric CKD 7 3864 1.81 (0.86, 3.79) 0.76 (0.34, 1.70) All-cause mortality eGFR (≥120) 113 7538 14.99 (12.46, 18.02) 1.20 (0.97, 1.49) No CKD eGFR (90-120) 319 25353 12.58 (11.27, 14.04) 1.0 (Reference) eGFR (60-90) 485 28285 17.14 (15.68, 18.74) 1.04 (0.90, 1.20) 30.68 (28.59, 32.91) 1.82 (1.59, 2.08) Albuminuric non-CKD 776 25292 48.31 (40.86, 57.12) 2.38 (1.92, 2.90) Albuminuric CKD 137 2835 Non-albuminuric CKD 110 3908 28.14 (23.34, 33.92) 1.42 (1.14, 1.78) MACE eGFR (≥120) 15.55 (12.78, 18.92) 100 24136 1.14 (0.91, 1.43) No CKD eGFR (90-120) 21903 307 14.01 (12.53, 15.67) 1.0 (Reference) eGFR (60-90) 500 24136 20.71 (18.97, 22.61) 1.31 (1.13, 1.51) Albuminuric non-CKD 702 20766 33.80 (31.13, 36.40) 1.88 (1.63, 2.16) Albuminuric CKD 2267 50.28 (41.85, 60.41) 2.37 (1.89, 2.97) 114 89 3330 26.72 (21.71, 32.89) 1.44 (1.13, 1.84) Non-albuminuric CKD 0 2 5

Decreased

risk

Increased

risk

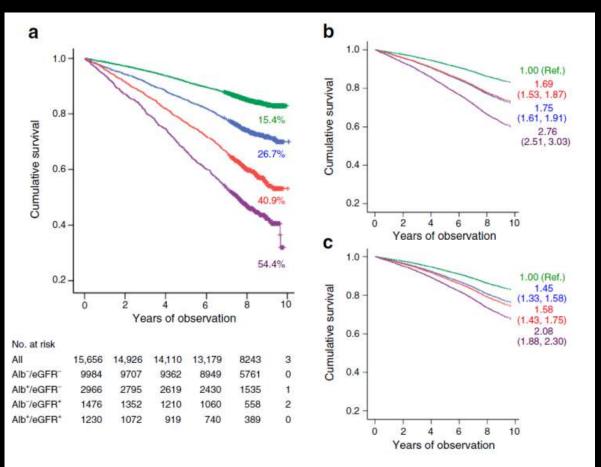
"Those with nonalbuminuric CKD showed a slower rate of decline in eGFR than did any other group; however, these individuals still carry a greater risk for death and MACE than do those with no CKD."

Daberologia https://doi.org/10.1007/s00125-018-4691-2 ARTICLE

Cross Mark

Non-albuminuric renal impairment is a strong predictor of mortality in individuals with type 2 diabetes: the Renal Insufficiency And Cardiovascular Events (RIACE) Italian multicentre study

Gisseppe Penno<sup>1</sup> - Ama Solini<sup>2</sup> - Emanuela Orsi<sup>1</sup> - Enzo Bonora<sup>4</sup> - Cacilla Fondelli<sup>5</sup> - Roberto Trevican<sup>4</sup> -Monica Vedovato<sup>2</sup> - Franco Cavalot<sup>4</sup> - Ofiga Lamacchia<sup>6</sup> - Marco Scardapane<sup>10</sup> - Antonio Nicolucci<sup>10</sup> -Giuseope Puglee<sup>10</sup> - of orthe Renal Insufficiency And Cardiovacular Events (IRACE) Study Group



KDIGO category	A1a	A1b	A2	A3
G1	1	0.94	1.31	2,19
	(Ref.)	(0.78, 1.12)	(1.08, 1.60)	(1.55, 3.11)
G2a	0.80	1.05	1.31	2.48
	(0.67, 0.96)	(0.89, 1.25)	(1.09, 1.58)	(1.82, 3.38)
G2b	1.10	1.06	1.39	1.71
	(0.83, 1.12)	(0.88, 1.27)	(1.15,1.68)	(1.23, 2.36)
G3a	1.32	1.39	1.48	2.26
	(1.07, 1.62)	(1.14, 1.69)	(1.22, 1.80)	(1.71, 3.00)
G3b	1.85	2.25	2.09	2.78
	(1.40, 2.44)	(1.79, 2.82)	(1.69, 2.59)	(2.14, 3.63)
G4-5	1.61	2.25	2.79	4.66
	(0.88, 2.97)	(1.49, 3.37)	(2.09, 3.70)	(3.59, 6.05)

« Non-albuminuric renal impairment is a strong predictor of mortality...»

### **CARDIORENAL SYNDROME**

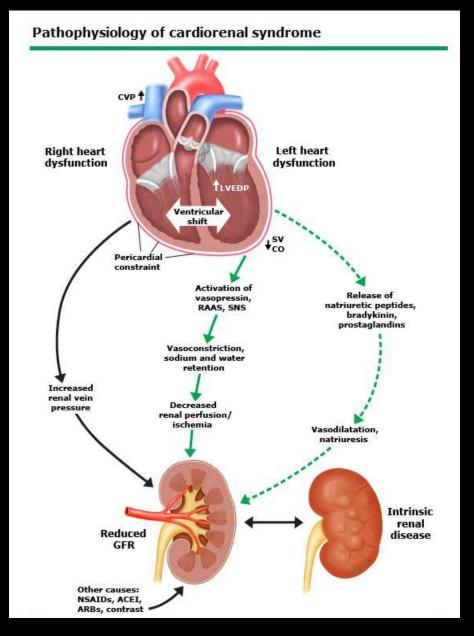
• *Type 1 (acute)* – Acute HF results in AKI

• *Type 2 – Chronic cardiac dysfunction*) causes chronic kidney disease (CKD)).

• *Type 3 – Abrupt and primary worsening of kidney function* Ex.renal ischemia or glomerulonephritis with acute cardiac dysfunction

• *Type 4 – Primary CKD with* contributes to cardiac dysfunction

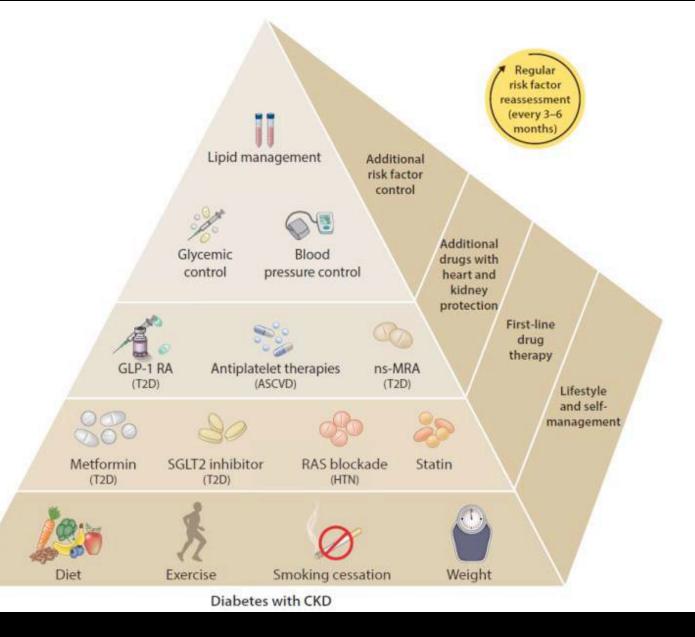
• *Type 5 (secondary) – Acute or chronic systemic disorders (*eg, sepsis or diabetes mellitus) that cause both cardiac and renal dysfunction.



UpToDate 2023

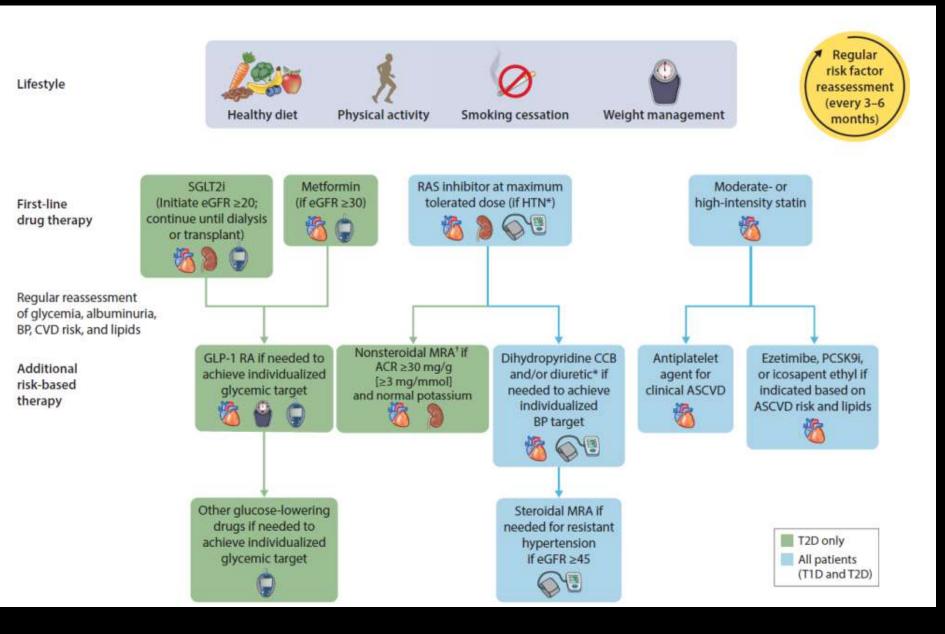


### Kidney-heart risk factor management



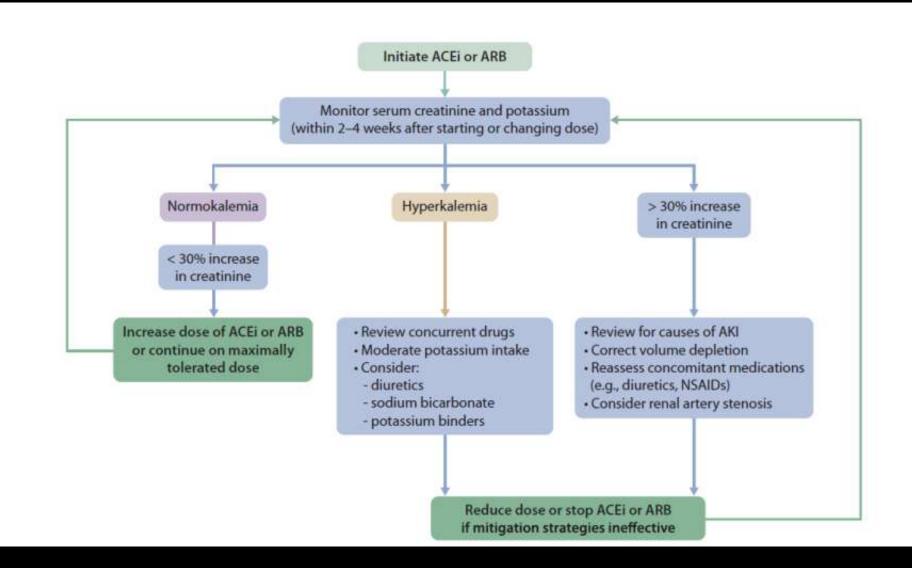


Holistic approach for improving outcomes in patients with diabetes and chronic kidney disease





Monitoring of serum creatinine and potassium during angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) treatment—dose adjustment and monitoring of side effects.

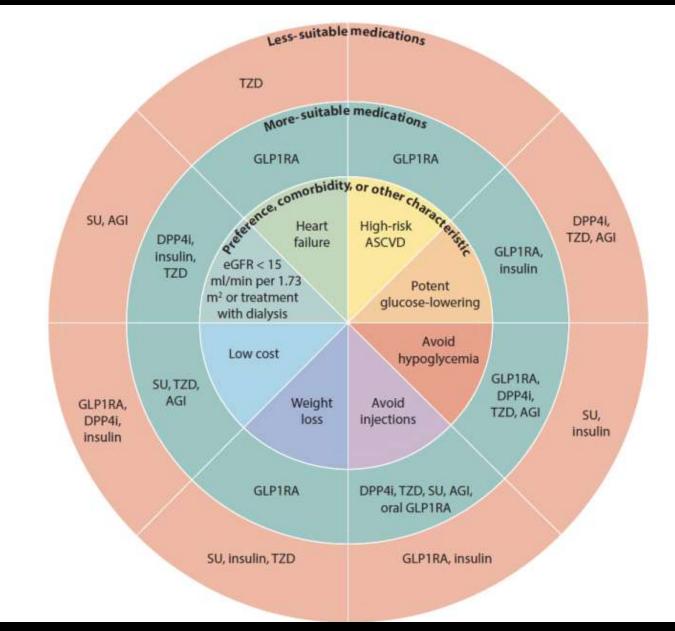




(CKD).

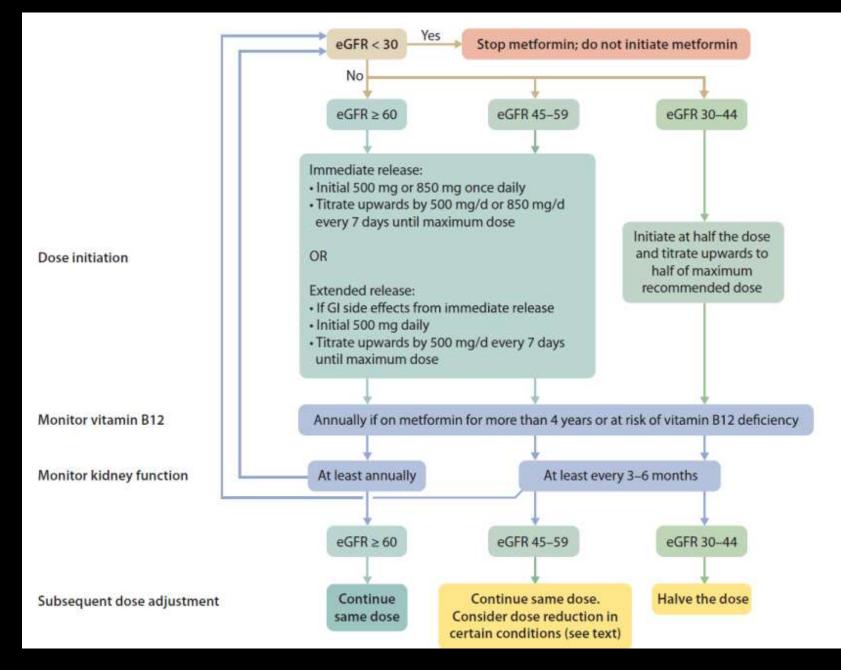
Patient factors influencing the selection of glucose-lowering drugs other than sodium–glucose cotransporter-2 inhibitor (SGLT2i) and metformin in type 2 diabetes (T2D) and chronic kidney disease

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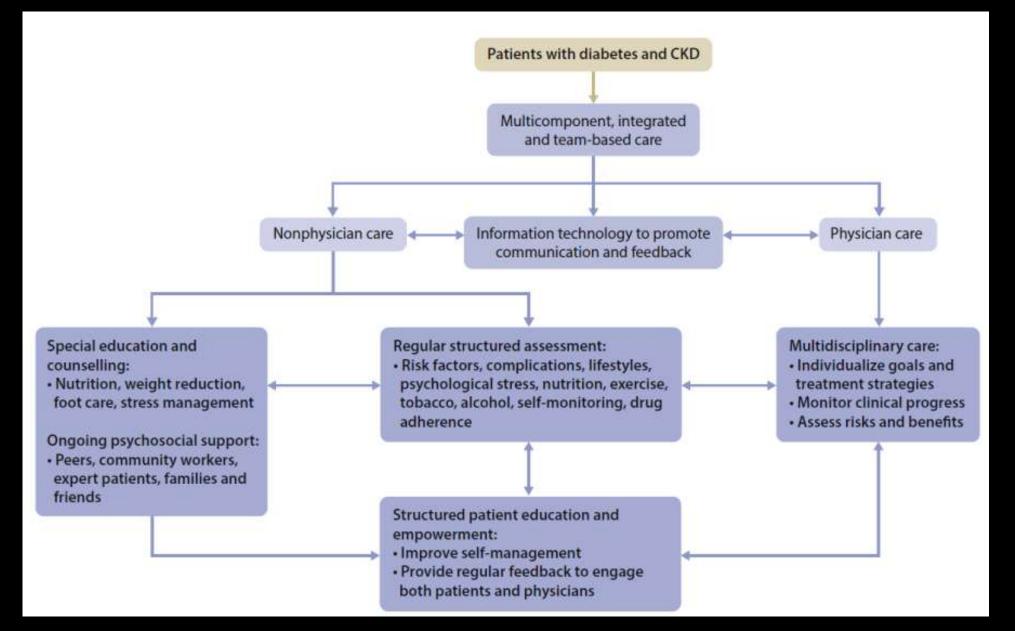


### Suggested approach in dosing metformin based on the level of kidney function



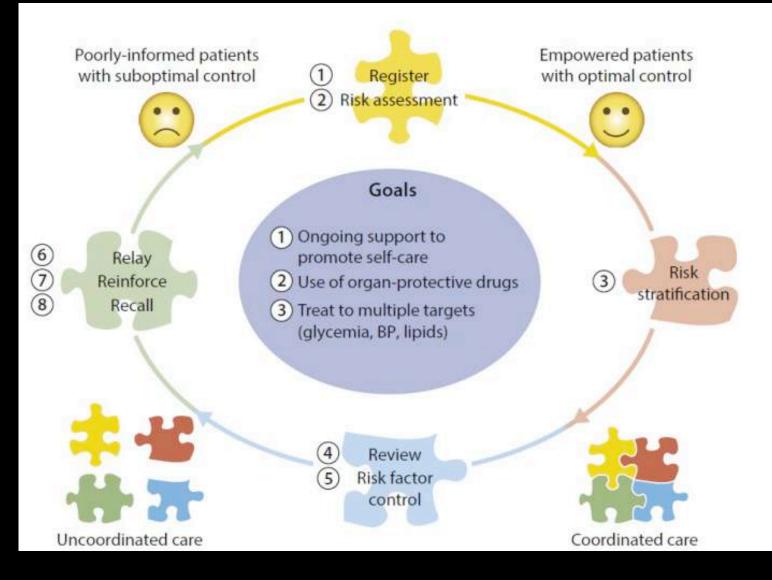


Integrated care approach to improve outcomes, self-management, and patient–provider communication in patients with diabetes and chronic kidney disease (CKD).429-





Team-based integrated care delivered by physicians and nonphysician personnel supported by decision-makers.



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## **CARDIOVASCULAR MANAGEMENT**

**Diuretics** 

**RAS-RAAS** 

ARNI

**SGLT2** inhibitors

Vasodilators

**Inotropic drugs** 

Ultrafiltration

Vasopressin receptor antagonists

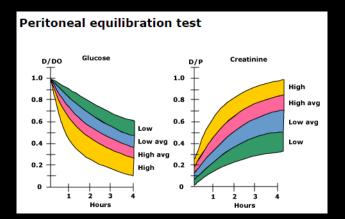
### TREATMENT

### **GENERAL MANAGEMENT** interference with ESA; glycated albumin

**PATIENTS NOT ON DIALYSIS** doubts on AC1 values and outcome; insulin dose empiric

### **PATIENTS ON HEMODIALYSIS** long acting insulin (?)

### PATIENTS ON PERITONEAL DIALYSIS



# TROUBLESHOOTING

**Hyperglycemia:** microvascular disease can cause erratic absorption of insulin from the subcutaneous tissue

**Severe hyperglycemia and ketoacidosis (dialysis):** hypovolemia and marked hypernatremia do not occur, since glucosuria is absent in anuric individuals. The net effect is minimal symptoms, even among those with extreme hyperglycemia marked hyperkalemia due to potassium efflux from cells

**Hypoglycemia** severe underdialysis, with poor calorie intake, or occult disease, such as infection or malignancy. Drugs that interfering with the counter regulatory response to hypoglycemia (BB, long-acting insulin and oral agents)

**Alternating hypoglycemia and hyperglycemia:** gastroparesis, timing of insulin injections, poor compliance, erratic eating habits, and poor timing of CAPD)

### **VITERBO: CARTELLA CONDIVISA NEFRO-DIABETOLOGIA**

						00/02/2025	Mostra altri
Anamnesi	Insufficienza Renale cronica	Classificazioni			Modifica	Aggiungi	-LDL
	Insufficienza Renale cronica Insufficienza Renale cronica Ateromasia vasi epiaortici	Diagnosi (classificazione)	Dal	Attivo	Ricovero	04/04/2023	LDL - / 103,2
-	Ateromasia vasi epiaortici Malattia epatica cronica e cirr	Insufficienza Renale cronica	17/04/2023	Non Attivo	No	13/01/2023	- / 94,6
Occhio						Aggiungi	Mostra altri
0	1	Storico Diagnosi Descrizione	Dai	AI	Ricovero	<b>e</b> Creatinina /	eGFR EPI-CDK
					-	28/04/2023	1,77 / -
	Insufficienza Renale cronica Insufficienza Renale cronica	Insufficienza Renale cronica	23/02/2021	Ċ	No	21/04/2023	1,91 / -
0	Insufficienza Renale cronica	(A) Insufficienza Renale cronica	25/11/2020	Ū	No	Aggiungi	Mostra altri
	Insufficienza Renale cronica	(A) Insufficienza Renale cronica	18/06/2020	Ð	No	Эликона (1996)	ibA1c
	Ipertensione Arteriosa (riscontro per 3-6 mesi di valori	(A) Insufficienza Renale cronica	22/01/2020	Ø	No	21/04/2023	41 / -
	PAO > 130/86 mmHg) Ipertensione Arteriosa (riscon	Insufficienza Renale cronica	24/04/2019		No	04/04/2023	37 / 5,5
	Non Arteriopatia arti inferiori			30.00		Aggiungi	Mostra altri
periferici	Non Arteriopatia arti inferiori			Visu	sualizza tutte le complicanze		S / PAD
	ECOCOLORDOPPLER ARTERIOSO ARTI INFERIORI	Prestazioni 🖾			Aggiungi	13/04/2023	120 / 60
Nervi	Polineuropatia sensitivo	Questionario ipercolesterolemia				08/02/2023	120 / <mark>6</mark> 0
periferici	motoria simmetrica distale Polineuropatia distale,	Questionano ipercolesterolenna				Aggiungi	Mostra altri
	simmetrica.	Nota			Modifica	🕑 Sco	core Q
Piede		Giunge a prima visita la figlia portando in visione esami ematici della madre che mostrano quadro di IRC con e-GFR 12 ml/min.				07/05/2021	25/40
5	1	In APR: -DIABETE MELLITO TIPO 2 DA CIRCA 15 ANNI IN INSULINO-TERAPIA				2020	30/40
		-IPERTENSIONE ARTERIOSA				Stile	e di vita
A CONTRACTOR OF A	Ateromasia vasi epiaortici	CIRROSI EPATICA (EZIOLOGIA NON RIFERITA, ULTIMO CONTROLLO ECOGRAFICO CON MDC ASSENTE PATOLOGIA NEOPLASTICA) IPOTIROIDISMO				Fumatore	No
45	Ateromasia vasi epiaortici - Con stenosi <60%	-BRONCHITE CRONICA ASMATICA -PORTATRICE PROTESI GINOCCHIO SN				Sigarette	
1	Ateromasia vasi epiaortici - C	- DA DICEMBRE 2022 DOLORE LOMBO-SACRALE (SEGUITA DALLA TERAPIA DEL DOLORE)					
Altro		<ul> <li>-IRC (VALORI PRECEDENTI AD ULTIMI ESAMI NON VISIONABILI))</li> <li>Ad esami ematici K 5.9 si rilasciano indicazioni per dieta ipokaliemica, inizia terapia con lokelma 1 bustina/die. (si rilascia piano terapeut</li> </ul>	utico).				
8	6	Il 24/04/2023 ripete prelievo potassemia. Esame urine ndr, urinocoltura negativa, prodidogramma nella norma, proteinuria assente.					
~	4	Si consiglia sospendere Bivis, inizia Norvasc 10 mg ore 8.00, se la pressione è maggiore di 140/80 mmHg aggiunge Cardura 4 mg (ore 2	/ 20.00)				
Dieta		Proseguirà follow-up in ambulatorio dedicato alle complicanze del diabete mellito. prossimo controllo tra 2 mesi con esami richiesti.					

## CONCLUSIONIS

Diabetic patient with advanced renal disease is a complex clinical feature.

The variables involved are many; patient, drugs, cardiopathy, impaired GFR etc.)

It needs to create a close interaction among all players, including all specialists ( multidisciplinary approach).

# The aim is to improve the patient's quality of life



KDIGO 2022 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE

Key objectives are to:
Improve diabetes-related knowledge, beliefs, and skills
Improve self-management and self-motivation
Encourage adoption and maintenance of healthy lifestyles
Improve vascular risk factors
Increase engagement with medication, glucose monitoring, and complication screening programs
Reduce risk to prevent (or better manage) diabetes-related complications
Improve emotional and mental well-being, treatment satisfaction, and quality of life