

# **Valutazione della Progressione della Malattia Renale Cronica e Fattori di Rischio**

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# Malattia renale cronica

## DEFINIZIONE

Condizione in cui sia presente da almeno tre mesi una riduzione di GFR (Glomerular Filtration Rate) al di sotto di 60 mL/min/1.73 m<sup>2</sup>, oppure la persistente presenza di marcatori di danno renale (proteinuria e/o alterazioni del sedimento urinario, anomalie istologiche, storia di trapianto renale...).

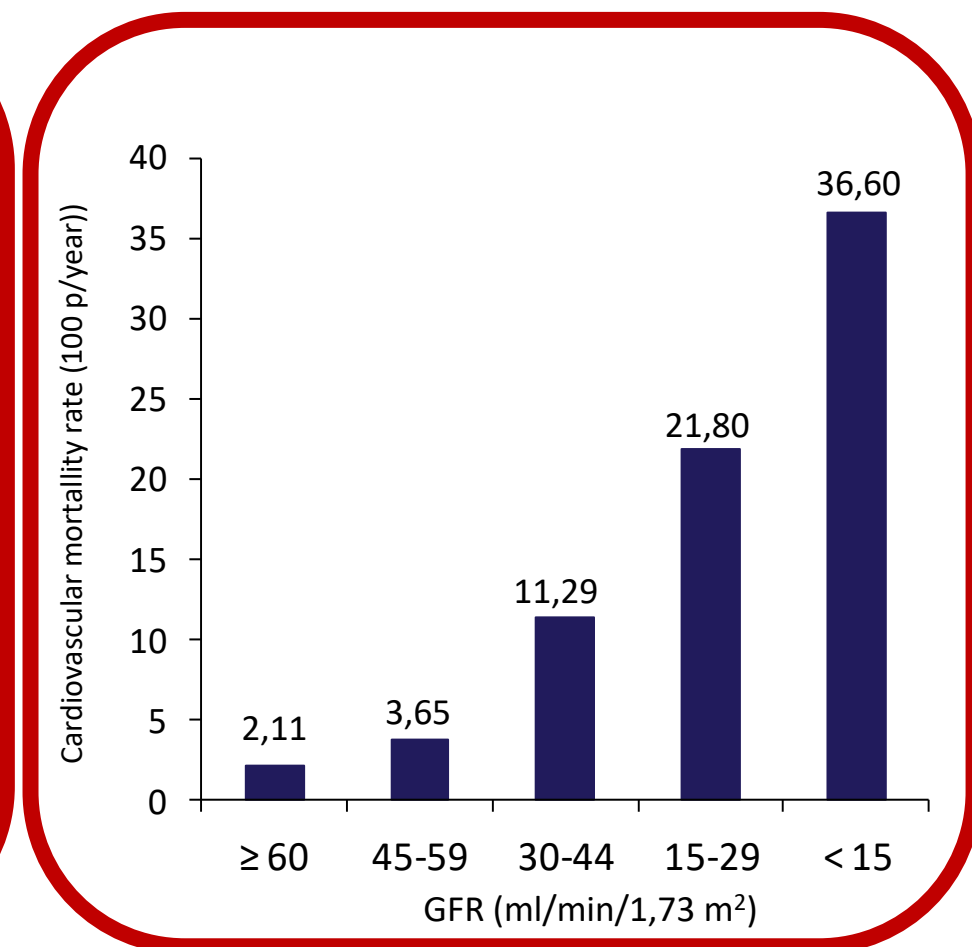
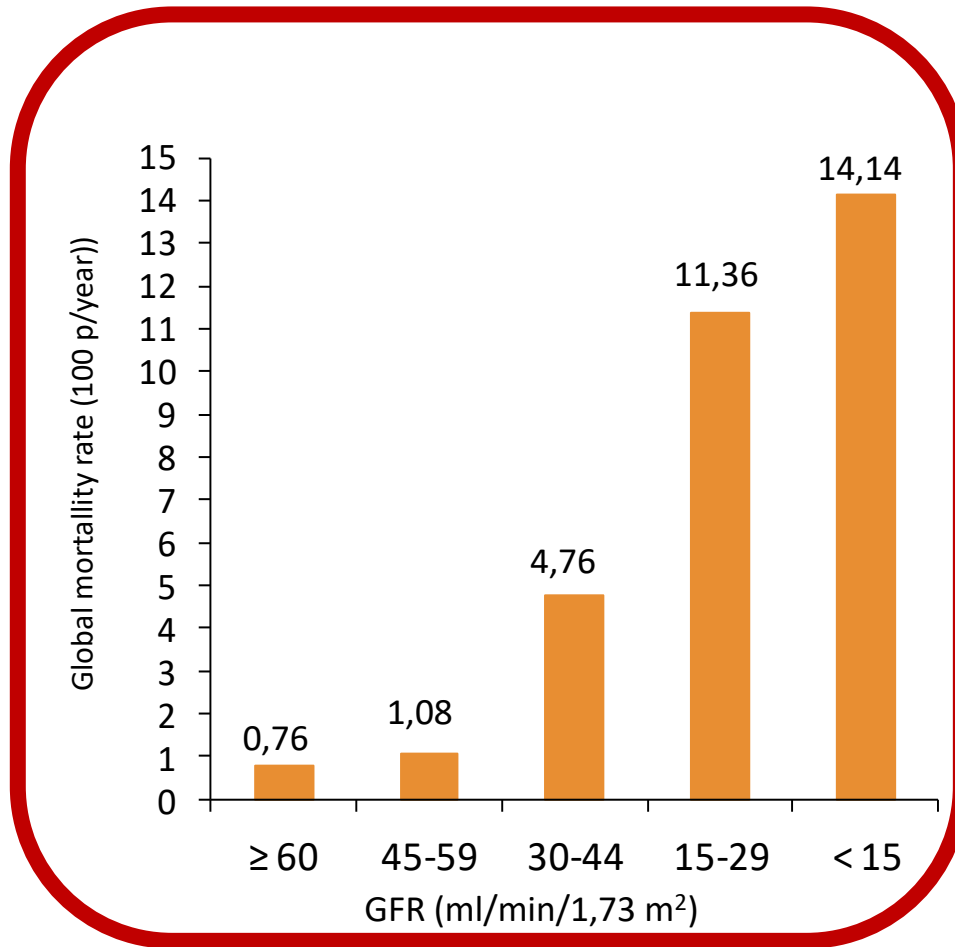
## PREVALENZA

7-10%, in aumento

# CLASSIFICAZIONE DELLA MALATTIA RENALE CRONICA E STRATIFICAZIONE DEL RISCHIO

				Grado di Albuminuria persistente			Rischio aumentato → → → → →
				A1	A2	A3	
				Normale o lievemente aumentata	Moderatamente aumentata	Gravemente aumentata	
				<30 mg/g	30-300 mg/g	>300 mg/g	
Stadio del danno renale	G1	Normale	VFG mL/min >90				
	G2	compromissione lieve	89-60				
	G3a	compromissione da lieve a moderata	59-45				
	G3b	compromissione moderata	44-30				
	G4	compromissione grave	29-15				
	G5	Insufficienza renale severa in fase di predialisi	<15				
						Rischio aumentato → → → → →	

# La Malattia Renale Cronica si associa ad aumento significativo del rischio di mortalità, in particolare per cause cardiovascolari



*n* = 1.120.295; follow-up: 2,84 years

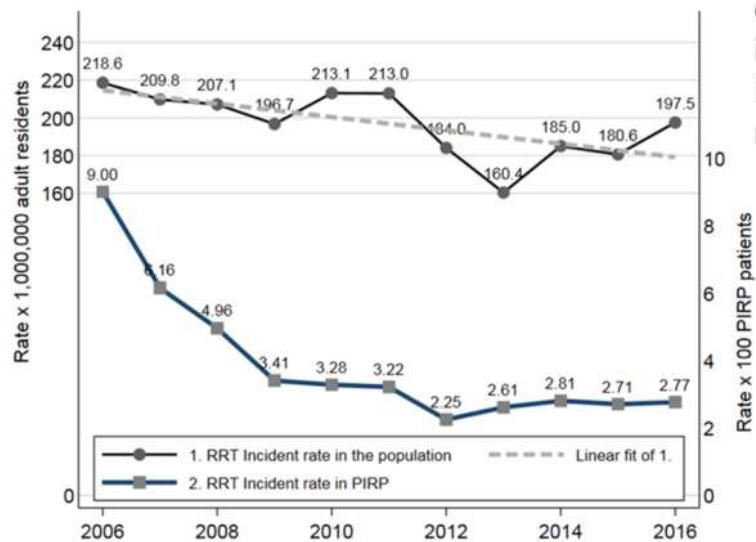
Go AS, et al. N Engl J Med 2004;351(13).

# The principles guiding referral include additional input from a nephrologist into management of CKD and preparation for RRT.

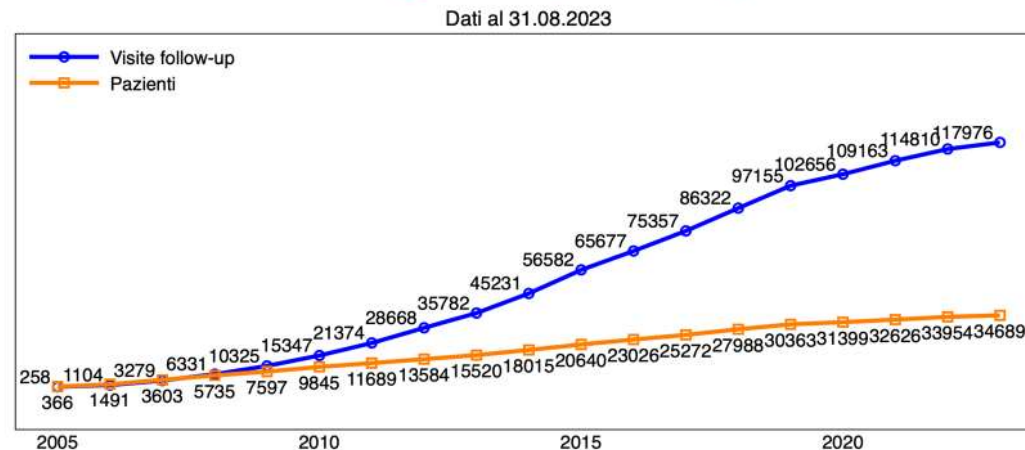
## PROGETTO PIRP

The PIRP (Prevenzione Insufficienza Renale Progressiva) project is endorsed and funded by the Emilia-Romagna Regional Health Board and involves all the Nephrology Units of the EmiliaRomagna Region (Italy). The project has a predominantly clinical purpose and is expected to bring about a continuous quality improvement in the treatment of patients with CKD.

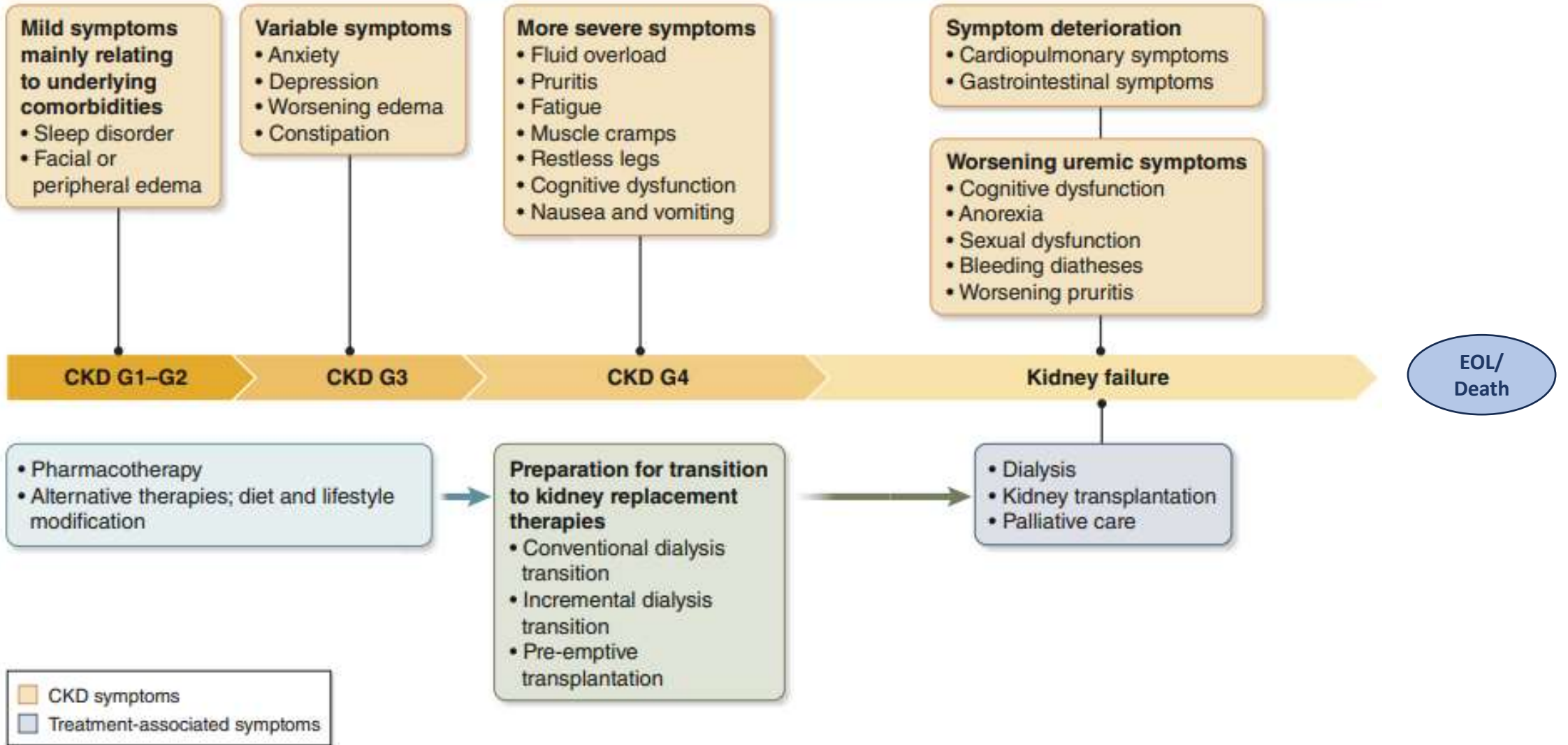
The effects of a closer and joint monitoring of CKD patients by GPs and nephrologists can be quantified by the reduction of the mean annual GFR decline (average annual CKD-EPI change:  $-0.34$  ml/min), and by the decrease in the overall incidence of patients who annually started dialysis in the Emilia-Romagna Region, that dropped from 218.6 ( $\times$  million) in 2006 to 197.5 ( $\times$  million) in 2016, corresponding to about 100 cases.



Attività del registro PIRP, cumulata negli anni



Increasing burden of uremic symptoms



 Kidney-preserving therapies and effective symptom management may delay dialysis and transplantation

Kidney failure management

# Progressione

Riduzione di eGFR  $> 5$  mL/min/1.73 m<sup>2</sup> in un anno,  
oppure  $> 10$  mL/min/1.73 m<sup>2</sup> in 5 anni

\* Considerare l'importanza clinica del declino di funzione, tenendo conto di **età e aspettativa di vita**

BECAUSE OF PHYSIOLOGICAL AGE-DECLINE "REDUCED GFR" HAVE COMPLETELY DIFFERENT INTERPRETATION IN CKD DISEASE vs AGEING

## Iohexol Clearance

Table 4. Predicted percentiles of GFR (ml/min per 1.73 m<sup>2</sup>) for healthy women and men according to age group

Age Group (yr)	Women			Men				
	Number of GFR Measurements	Median	2.5th Percentile	97.5th Percentile	Number of GFR Measurements	Median	2.5th Percentile	97.5th Percentile
50-54	226	93.4	73.7	113.1	217	93.0	73.1	113.0
55-59	405	88.8	69.2	108.3	423	89.4	69.6	109.3
60-64	566	84.2	64.7	103.6	521	85.8	66.1	105.5
65-69	296	79.6	60.3	98.9	293	82.2	62.7	101.8
70-74	129	75.0	55.8	94.1	102	78.6	59.2	98.0
75-79	253	70.4	51.4	89.4	225	75.0	55.7	94.3
80-84	164	65.8	46.9	84.7	188	71.4	52.2	90.6
85-89	68	61.2	42.4	79.9	79	67.8	48.8	86.8
≥90	20	56.6	38.0	75.2	34	64.2	45.3	83.1

Estimates corresponding to Figure 3.

Dopo i 30-40 anni di età si perde circa 1 ml/min/anno di GFR (invecchiamento fisiologico)

# Come valutare la progressione

- In soggetti in cui sia stata appena individuata una riduzione di eGFR, **ripeterne la determinazione entro 2 settimane**, al fine di escludere cause di deterioramento acuto di GFR
- Disporre di un minimo di 3 eGFR in un periodo non inferiore a 90 giorni
- Integrare la valutazione di eGFR con ACR o PCR



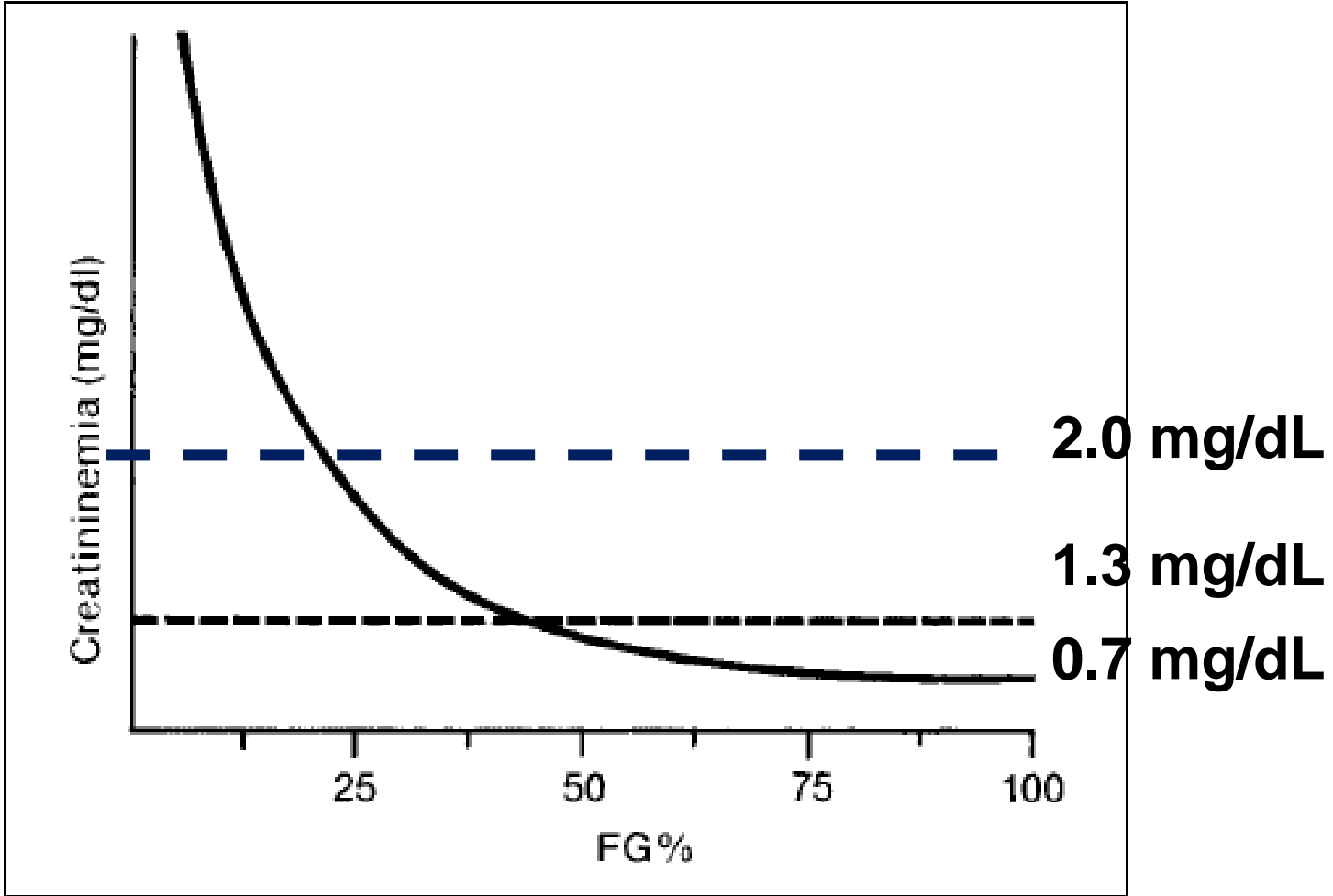


# Come valutare la progressione

- **Small fluctuations in GFR are common and are not necessarily indicative of progression.**

Many factors can cause a small change in GFR including **medications, volume status, measurement error, and biological variability.**

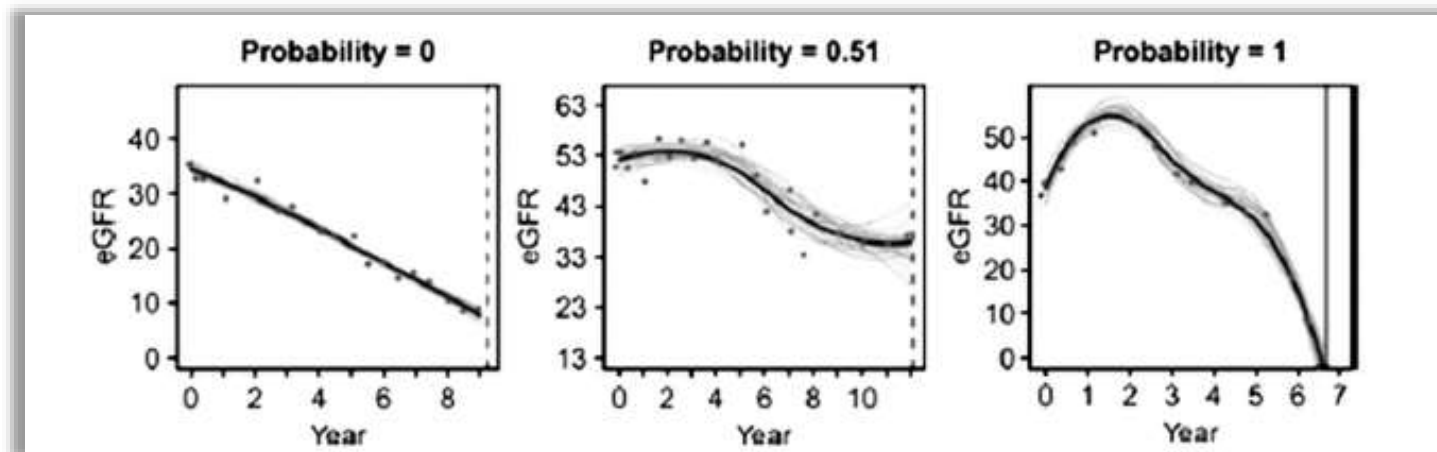
- **The confidence in assessing progression is increased with increasing number of serum creatinine measurements and duration of follow-up**



# Come valutare la progressione

CKD progression, contextualized for the individual circumstance, does not always require referral.

Faster or unusual trajectories of progression should alert the patient and physician to **assess for potentially reversible causes of progression.**

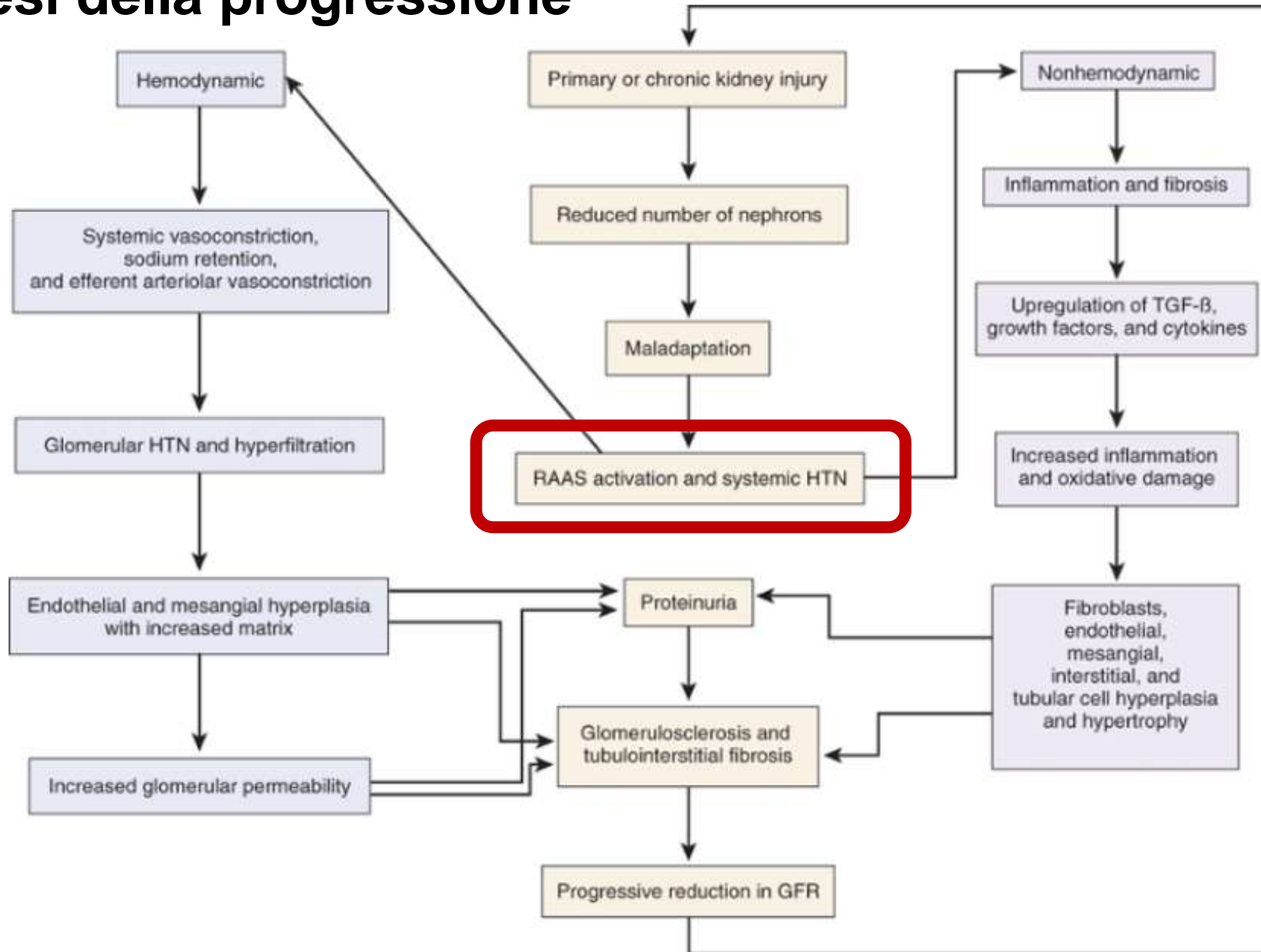




## The most common risk factors identified for acute decline in GFR for patients with established CKD include:

- **obstruction of the urinary tract;**
- **volume depletion;**
- **nonsteroidal anti-inflammatory drugs (NSAIDs), including COX 2 inhibitors;**
- **select antimicrobial agents such as aminoglycosides and amphotericin B;**
- **radiocontrast agents;**
- **angiotensin-converting enzyme inhibitors (ACE-Is) and angiotensin-receptor blockers (ARBs).**

# Patogenesi della progressione



# Fattori di rischio per la progressione della MRC

## Non modificabili

- Età
- Familiarità
- Fattori genetici
- Menopausa

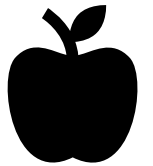
## Modificabili

- Iperattività RAAS
- Iperattività simpatico
- Diabete mellito
- Dislipidemia
- Ipertensione arteriosa
- Proteinuria
- Anemia
- Calcificazioni vascolari
- Stress ossidativo
- Infiammazione
- Malnutrizione
- Disfunzione endoteliale
- Sovraccarico di fluidi

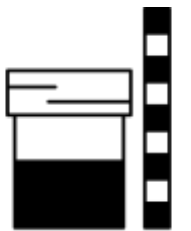
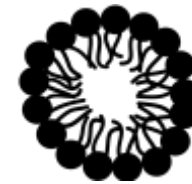
# Prevenzione della progressione della MRC

## FATTORI DI RISCHIO MODIFICABILI

- Provvedimenti non farmacologici



- Provvedimenti farmacologici





# Prevenzione della progressione



- ✓ **Lifestyle:** We recommend that people with CKD be encouraged to undertake **physical activity** compatible with cardiovascular health and tolerance (aiming for at least 30 minutes 5 times per week), achieve a **healthy weight** (BMI 20 to 25, according to country specific demographics), and **stop smoking**.
- ✓ **Additional dietary advice:** We recommend that individuals with CKD receive expert dietary advice and information in the context of an education program, tailored to severity of CKD and the need to intervene on **salt, phosphate, potassium, and protein intake** where indicated.





# Prevenzione della progressione



- ✓ **Salt intake:** We recommend lowering salt intake to  $<90$  mmol ( **$<2$  g**) per day of sodium (corresponding to **5 g of sodium chloride**) in adults, unless contraindicated.

In subjects with CKD, impaired excretion of sodium is often present. High sodium intake increases BP and proteinuria, induces glomerular hyperfiltration and blunts the response to RAAS blockade. Lowering salt intake not only reduces BP, but also lowers albuminuria.

# **Terapia nutrizionale**

# Terapia Nutrizionale

## DEFINIZIONI

**Normal diet:** 0.8-1.0 g/Kg/day\* (RDA)

**High protein diet:** > 1.3 g/Kg/day

\*With 0.8 g/Kg/day nitrogen balance is maintained in normal subjects

**Low protein diet (LPD) or conventional LPD:**

0.6 g/Kg/day (animal proteins) or 0.7 g/Kg/day (vegan)

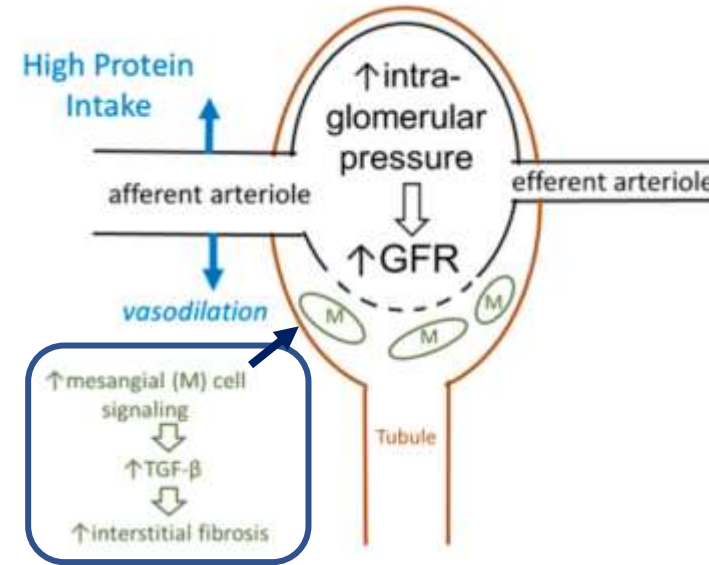
IN CKD

**Very low protein diet (VLPD):**

0.6 g/Kg/day (vegetarian diet (0.3-0.4 g/Kg) supplemented with KA/EAA to achieve the 0.6 g/Kg/day target)

## RAZIONALE

- Ridurre l'iperfiltrazione glomerulare e l'ipertensione glomerulare e quindi il danno renale



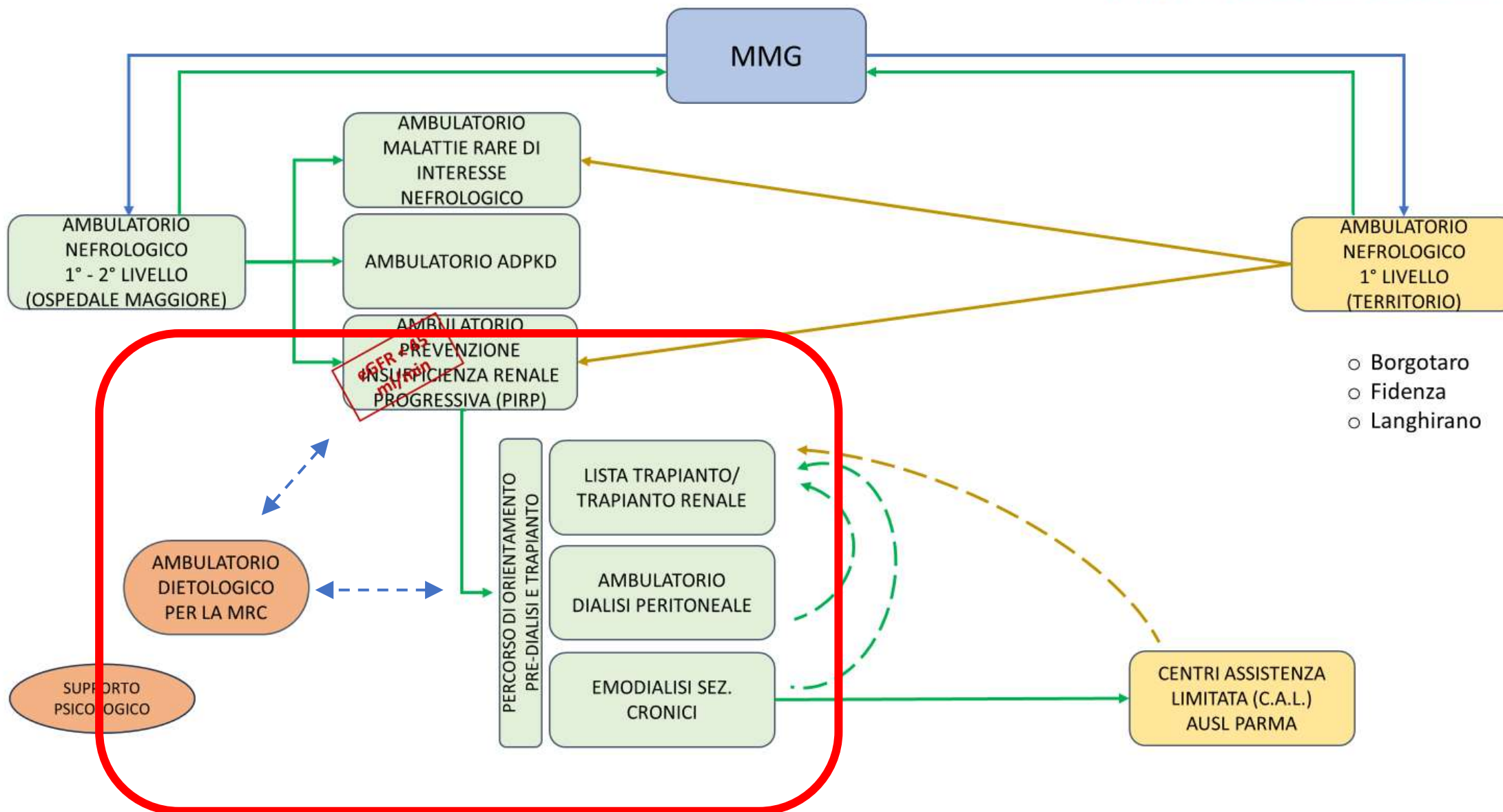
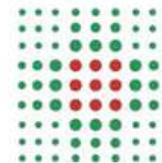
JASN 31: 1667–1679, 2020.

- Ridurre la produzione di prodotti di scarto (“tossine uremiche”,  $H^+$ , P...)

- Nitrogen products
- $H^+$
- Phenols
- Oxalates
- Phosphorus
- Uric acid



Uremic  
Syndrome



# LPD

- Quantità e qualità delle proteine
- Adeguate apporto calorico (20-35 kcal/kg iBW/die)



**PREVENIRE  
PEW**

## Protein-free food composition

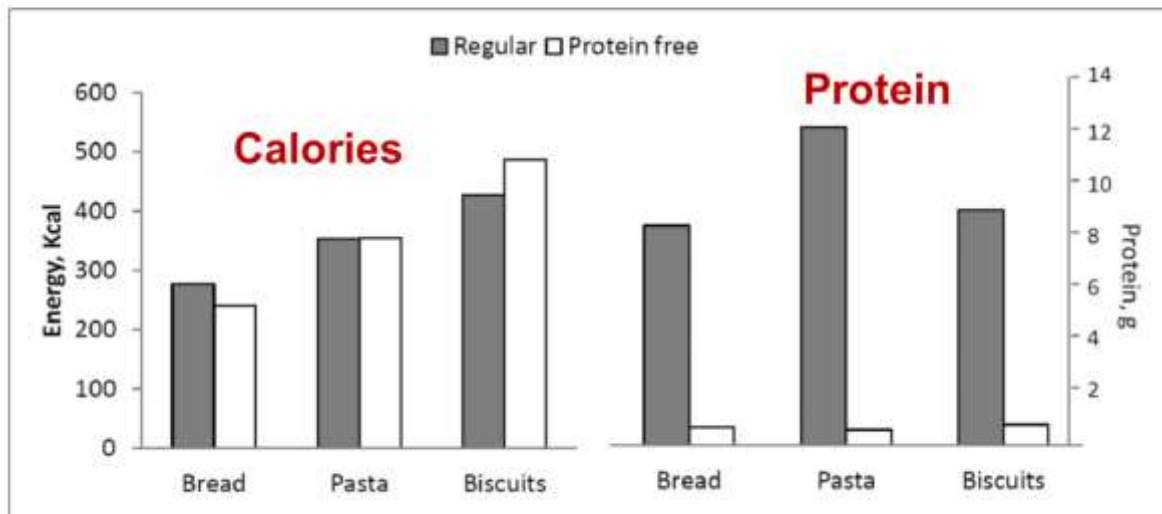


Figure 1.—Energy and protein content of regular (full columns) or protein-free (empty columns) products, expressed as average per 100 g of food.

# Vantaggi della LPD nella MRC

- Riduce iperfiltrazione glomerulare e quindi la proteinuria
- Riduce il declino della GFR (rallenta la progressione della MRC)
- Riduce la resistenza insulinica e lo stress ossidativo
- Riduce la fosforemia
- Migliora la sintomatologia uremica
- Ritarda l'ingresso in dialisi

# Altri vantaggi di una dieta corretta



Acidosi

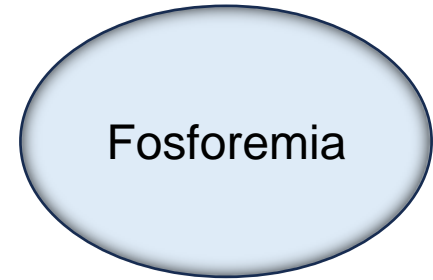
**La dieta vegetariana  
è alcalinizzante,  
come il bicarbonato**

Dietary acid reduction with fruits and vegetables or bicarbonate attenuates kidney injury in patients with a moderately reduced glomerular filtration rate due to hypertensive nephropathy

Nimrit Goraya<sup>1,2</sup>, Jan Simoni<sup>3</sup>, Chanhee Jo<sup>4</sup> and Donald E. Wesson<sup>1,4</sup>

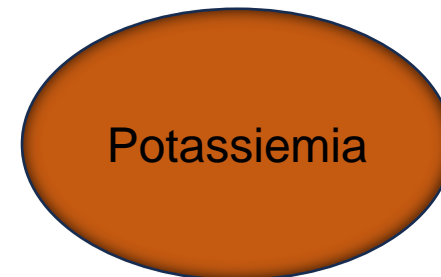
**Bicarbonate Supplementation Slows Progression of CKD and Improves Nutritional Status**

Ione de Brito-Ashurst, Mira Varaganam, Martin J. Raftery, and Muhammad M. Yaqoob



Fosforemia

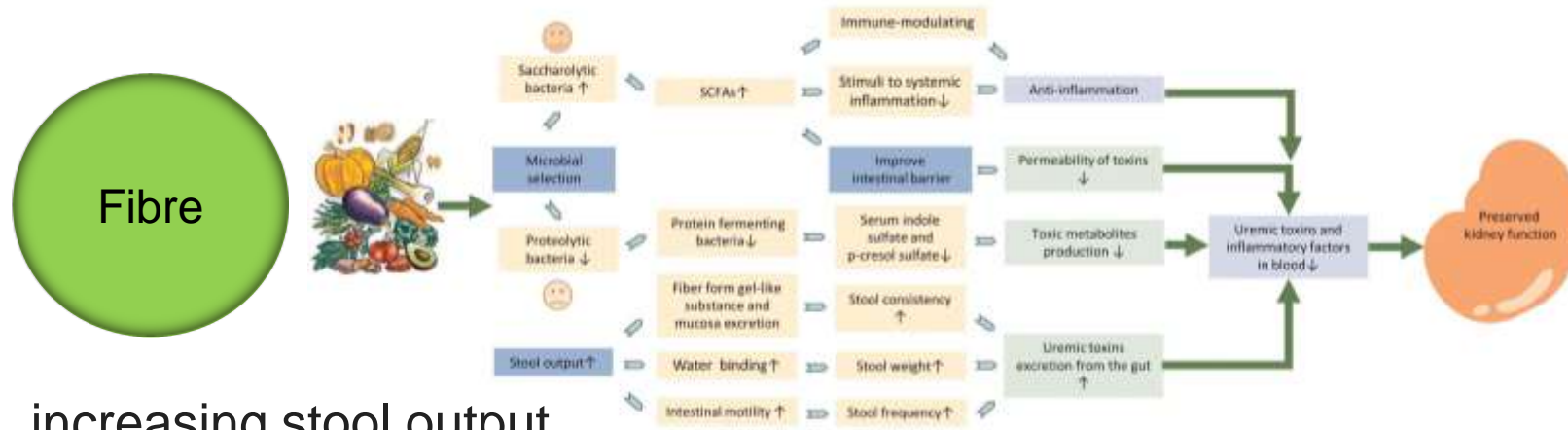
Source:	Plant	Animal	Inorganic Additives
Common Foods:	Grains Legumes Nuts	Meat Cheese Fish	Soda Prepared Foods Canned Foods
Bioavailability:	30-50%	60-90%	90-100%



Potassiemia



# Altri vantaggi di una dieta corretta



- increasing stool output
- promoting the growth of beneficial microbiota
- improving the gut barrier
- decreasing inflammation
- decreasing uremic toxin production

Controllo glicemico

Peso corporeo

Controllo pressorio

# Limitazioni

- Scarsa palatabilità
- Difficoltà nella preparazione dei cibi
- Costi elevati
- Monotonia

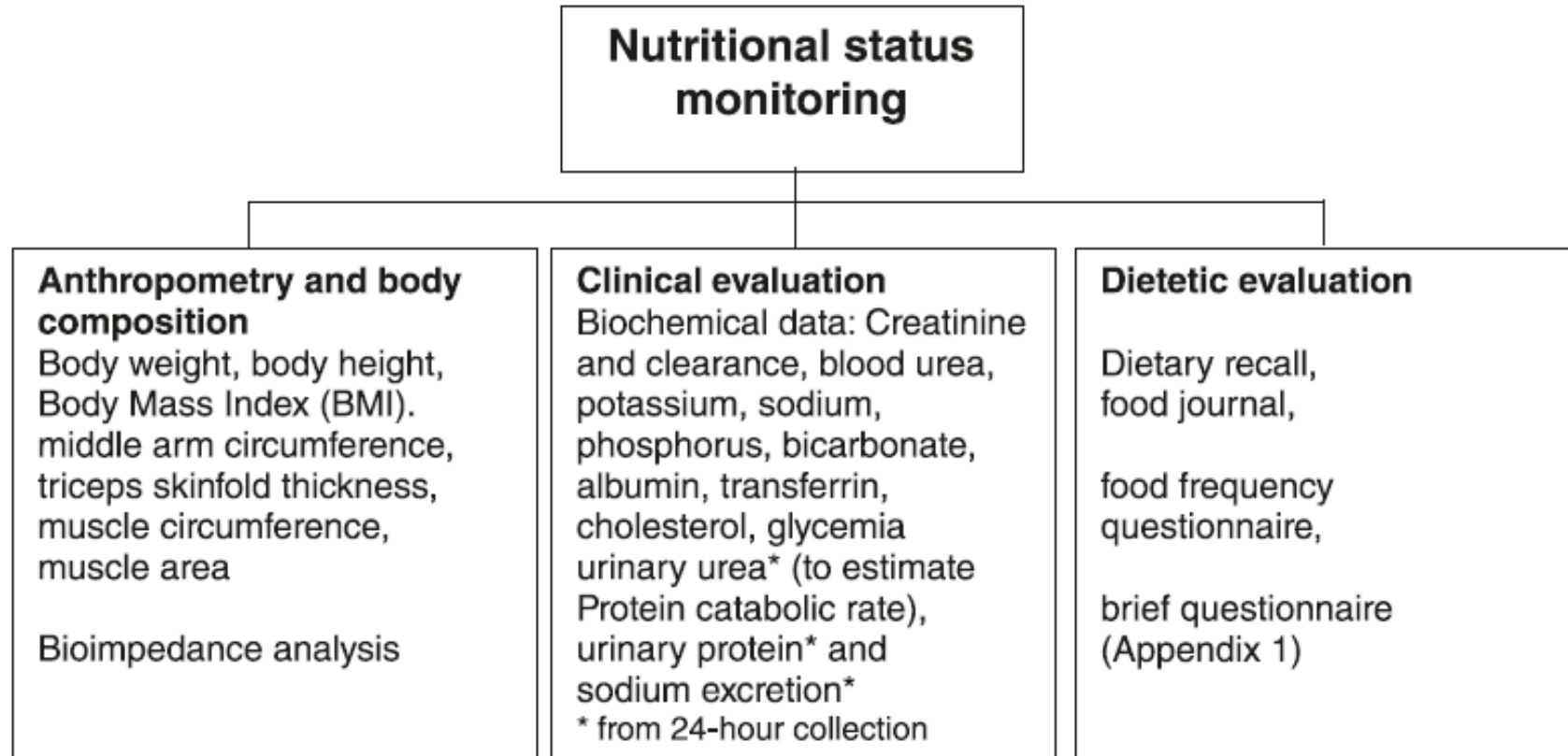
# Rischi

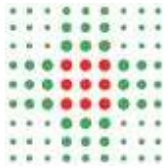
- Inadeguato apporto calorico
- Perdita massa magra e ipercatabolismo
- Infiammazione
- Peggioramento dell'acidosi
- Malnutrizione

**Protein  
Energy  
Wasting**

**Worse clinical  
outcomes**

# Strumenti per monitorare lo stato nutrizionale (e la compliance)





SERVIZIO SANITARIO REGIONALE  
EMILIA-ROMAGNA  
Azienda Ospedaliero-Universitaria di Parma



**\*Specialista On-call (Nefrologo)**

**dalle 10 alle 12 dei giorni feriali  
per prenotazione visite nefrologiche  
urgenti/urgenze differibili e/o per  
consulti telefonici:**

**0521-703450 (SOLO PER IL MEDICO  
RICHIEDENTE)**

**0521-703998 PDA (8.30-13.30 LUN-VEN)**

**0521-702126**

**0521-702388**



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