Stratification du risque cardiovasculaire selon la fonction rénale

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Hypertension Update 2013

Cas clinique

- Homme de 60 ans, Hypertendu (160/100 mmHg) non contrôlé traité par antagoniste calcique
- BMI 28 Kg/m², périmètre abdominal 96 cm
- Biologie: Créatinine sérique 1.7 mg/dl, eGFR 44 ml/min
- Glycémie 105 mg/dl, Cholestérol Total 205 mg/dl, LDL cholestérol 130 mg/dl, Tg 180 mg/dl, HDL cholestérol 38 mg/dl
- Albuminurie A2 (µalbuminurie):100 mg/g créatininurie)
- Echocardiogramme: HVG débutante
- Echographie abdominale: Reins légèrement diminués de taille et athéromasie calcifiante de l'aorte abdominale
- **Quelle prise en charge chez ce patient avec S Métabolique et IR?**

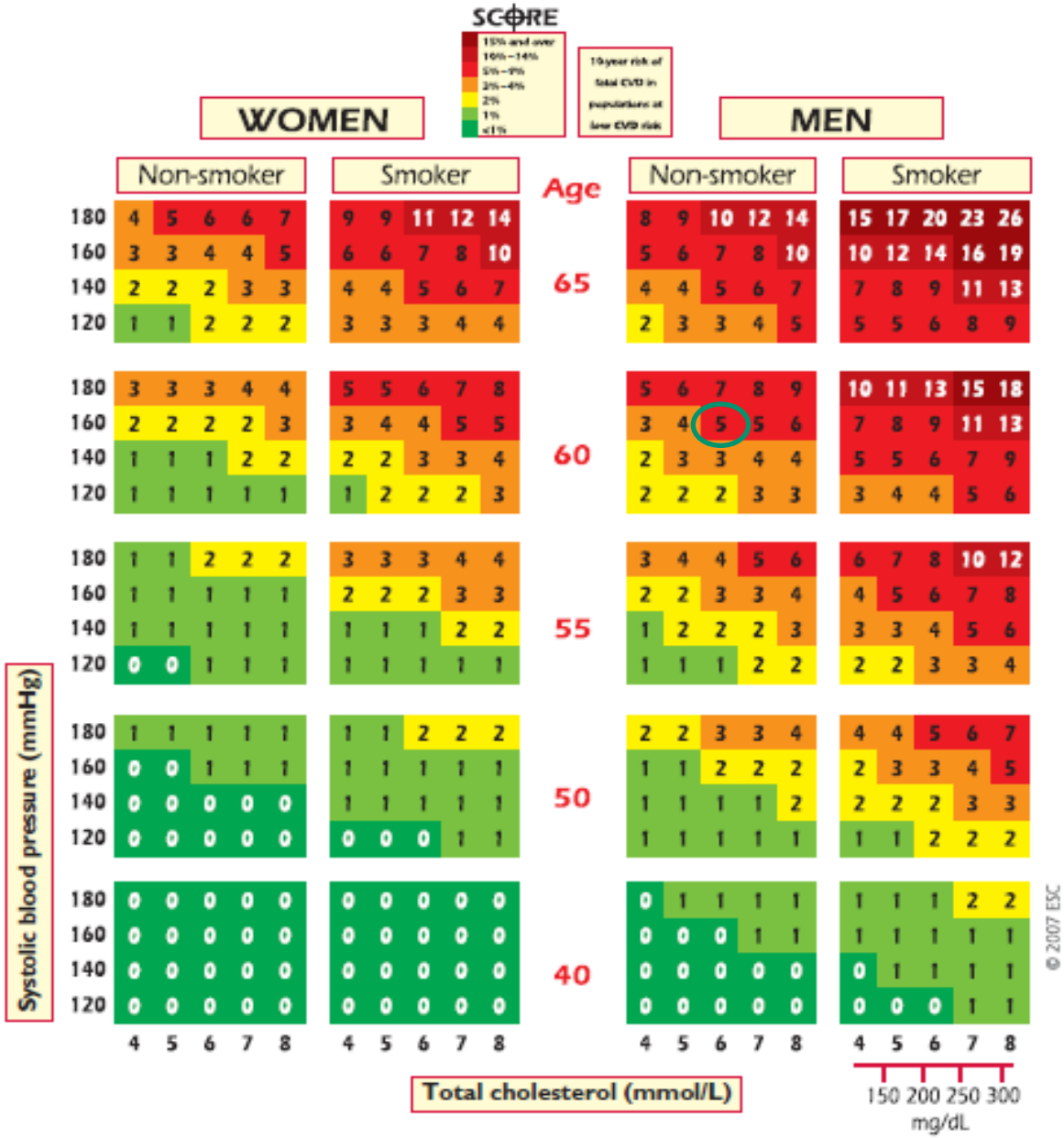


Figure 4 SCORE chart: 10-year risk of fatal cardiovascular disease (CVD) in countries at low CVD risk based on the following risk factors: age, sex, smoking, systolic blood pressure, and total cholesterol. Note that the risk of total (fatal + non-fatal) CVD events will be approximately three times higher than the figures given.

Confirmation de l'hypertension

- Mesure de la PA à domicile ou MAPA
- Chez notre patient, PA en automesure pendant 7 jours: 145/95 mmHg.

Home Blood Pressure Monitoring in CKD

Martin J. Andersen, DO, Wassim Khawandi, MD, and Rajiv Agarwal, MD

Conclusion: In patients with CKD, HBP is superior in reducing the misclassification of hypertension caused by the white-coat effect and masked hypertension commonly seen with CBPs. An average HBP of approximately 140/80 mm Hg appears to be the best correlate of hypertension defined by means of ABPM. *Am J Kidney Dis* 45:994-1001.

Intérêt de la MAPA chez l'IRC

Arch Intern Med. 2011;171(12):1090-1098

- Rôle de la PA de nuit dans la prédiction du risque CV et rénal chez l'IRC
- Etude sur 436 patients, 63 ans, GFR 43 ml/min
- Chez notre patient, HTA confirmée mais chute de 11% de la PA nocturne

Prognostic Role of Ambulatory Blood Pressure Measurement in Patients With Nondialysis Chronic Kidney Disease

Roberto Minutolo, MD, PhD; Rajiv Agarwal, MD; Silvio Borrelli, MD; Paolo Chiodini, MSc; Vincenzo Bellizzi, MD, PhD; Felice Nappi, MD; Bruno Cianciaruso, MD; Pasquale Zamboli, MD; Giuseppe Conte, MD; Francis B. Gabbai, MD; Luca De Nicola, MD, PhD

Ann Int Med 2011

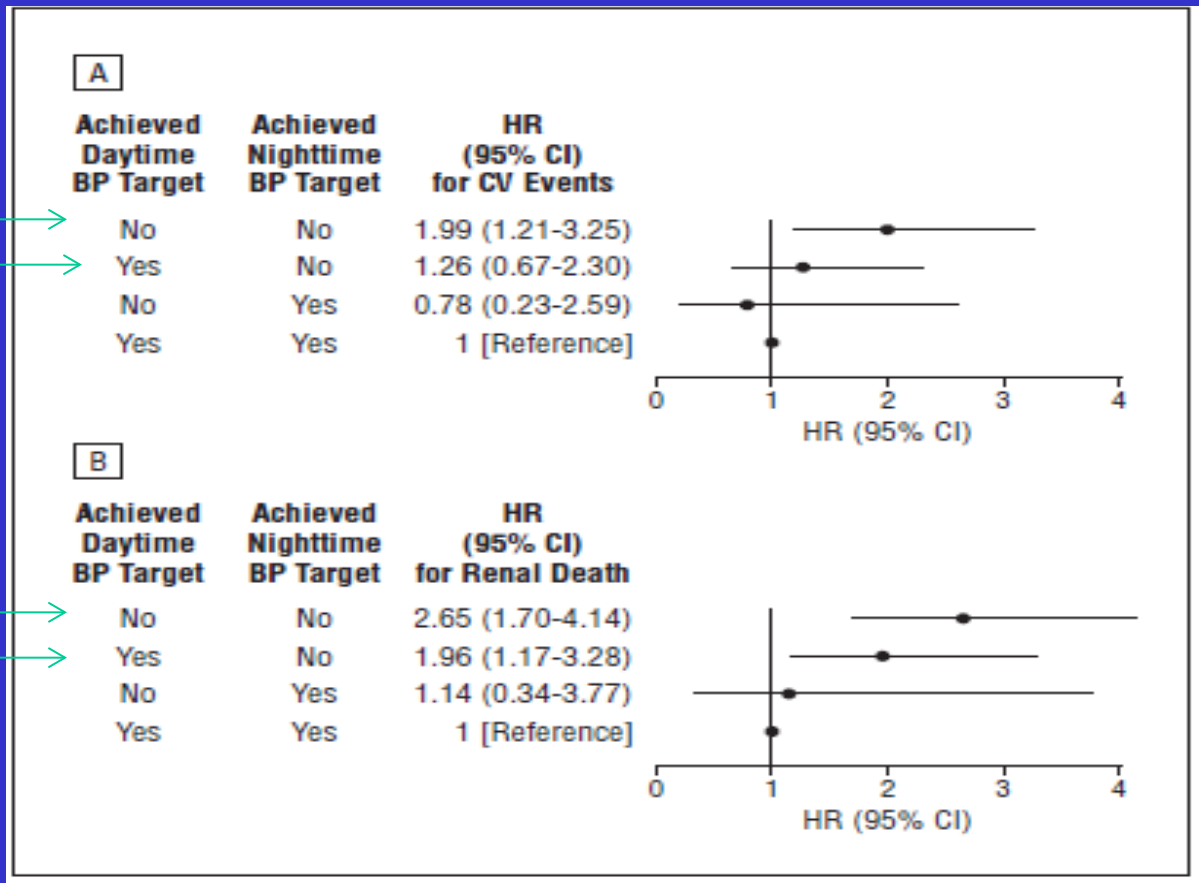


Figure 3. Risk of fatal and nonfatal cardiovascular (CV) events (A) and renal death (B) in patients stratified according to achievement of daytime blood pressure (BP) target (<135/85 mm Hg) and nighttime BP target (<120/70 mm Hg). CI indicates confidence interval; HR, hazard ratio.

Normes:
PA de jour <135/85
PA de nuit < 120/70

Intérêts d'une bonne mesure de GFR

- Détecter une IR le plus précocement possible
- Définition de l'IRC: atteinte rénale depuis > 3 mois. Surtout GFR < 60 ml/min
- Adapter la dose des médicaments à élimination rénale
- Faire la chasse aux néphrotoxiques
- Développer une stratégie de prévention de la progression et du **risque CV**

Table 1: Creatinine- (SCr; mg/dL) based equations for glomerular filtration rate (GFR) estimation.

4-variable MDRD Study equation

GFR (mL/min/1.73 m^2) = 175 × $SCr^{-1.154}$ × $Age^{-0.203}$ × 0.742 (if woman) × 1.21 (if black)

CKD-EPI Study equation (white subjects)

If woman:

if creatinine < 0.7 mg/dL:

GFR (mL/min/1.73 m^2) = 144 × $(SCr/0.7)^{-0.329}$ × 0.993^{age}

if creatinine > 0.7 mg/dL:

GFR (mL/min/1.73 m^2) = 144 × $(SCr/0.7)^{-1.209}$ × 0.993^{age}

If man:

if creatinine < 0.9 mg/dL:

GFR (mL/min/1.73 m^2) = 141 × $(SCr/0.9)^{-0.411}$ × 0.993^{age}

if creatinine > 0.9 mg/dL:

GFR (mL/min/1.73 m^2) = 141 × $(SCr/0.9)^{-1.209}$ × 0.993^{age}

Biologie 1 an avant : eGFR 50 ml/min
Donc IRC grade 3

KDIGO CLINICAL PRACTICE GUIDELINE FOR EVALUATION AND MANAGEMENT OF CKD

Kidney International Supplements (2013) **3,** 91–111

We recommend that all people with CKD be considered at increased risk for cardiovascular disease. (*1A*)

European Heart Journal (2012) **33**, 1635–1701
doi:10.1093/eurheartj/ehs092

European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

Key messages

- Atherosclerotic CVD, especially CHD, remains the leading cause of premature death worldwide.

health statement has been endorsed by a majority of the EU member states, defining the characteristics of people who tend to stay healthy as:

- No use of tobacco.
- Adequate physical activity: at least 30 min five times a week.
- Healthy eating habits.
- No overweight.
- Blood pressure below 140/90 mmHg.
- Blood cholesterol below 5 mmol/L (190 mg/dL).
- Normal glucose metabolism.
- Avoidance of excessive stress.

Risque CV élevé

2. High risk

Subjects with any of the following:

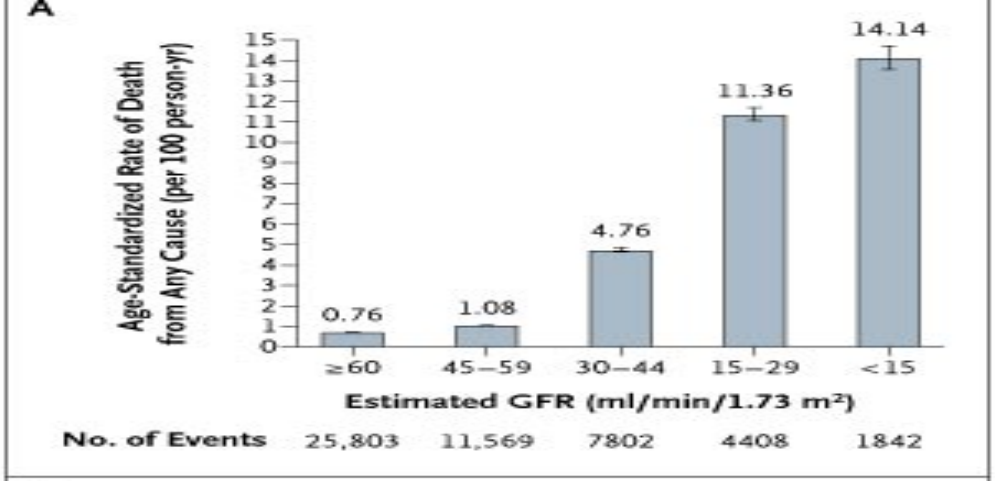
- Markedly elevated single risk factors such as familial dyslipidaemias and severe hypertension.
- Diabetes mellitus (type 1 or type 2) but without CV risk factors or target organ damage.
- Moderate chronic kidney disease (GFR 30–59 mL/min/1.73 m^2).
- A calculated SCORE of ≥5% and <10% for 10-year risk of fatal CVD.

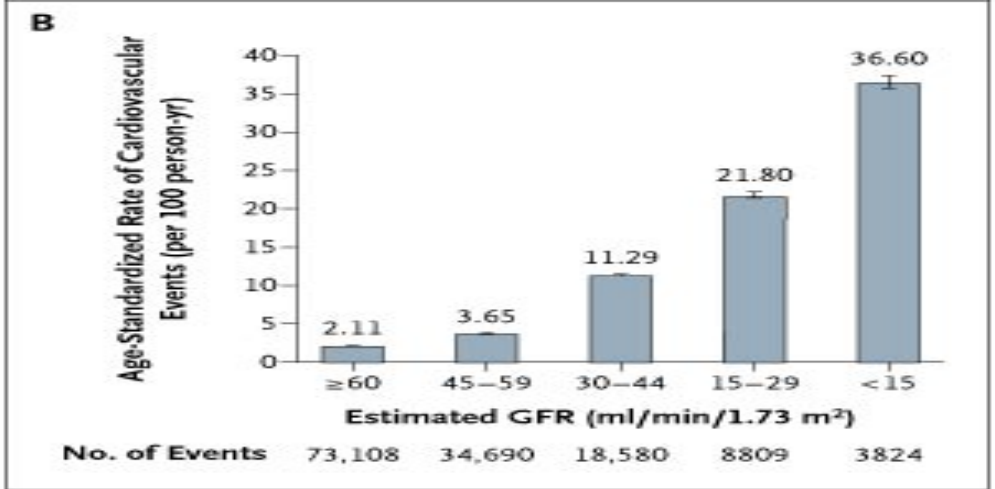
Age-Standardized Rates According to the Estimated GFR (MDRD) among 1,120,295 Adults

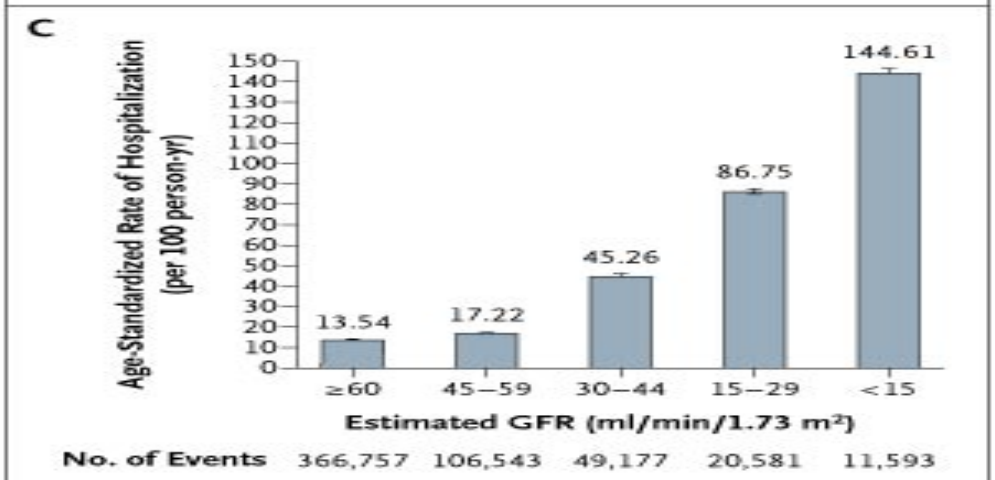
Death from Any Cause (Panel A),

Cardiovascular Events (Panel B),

Hospitalization (Panel C)

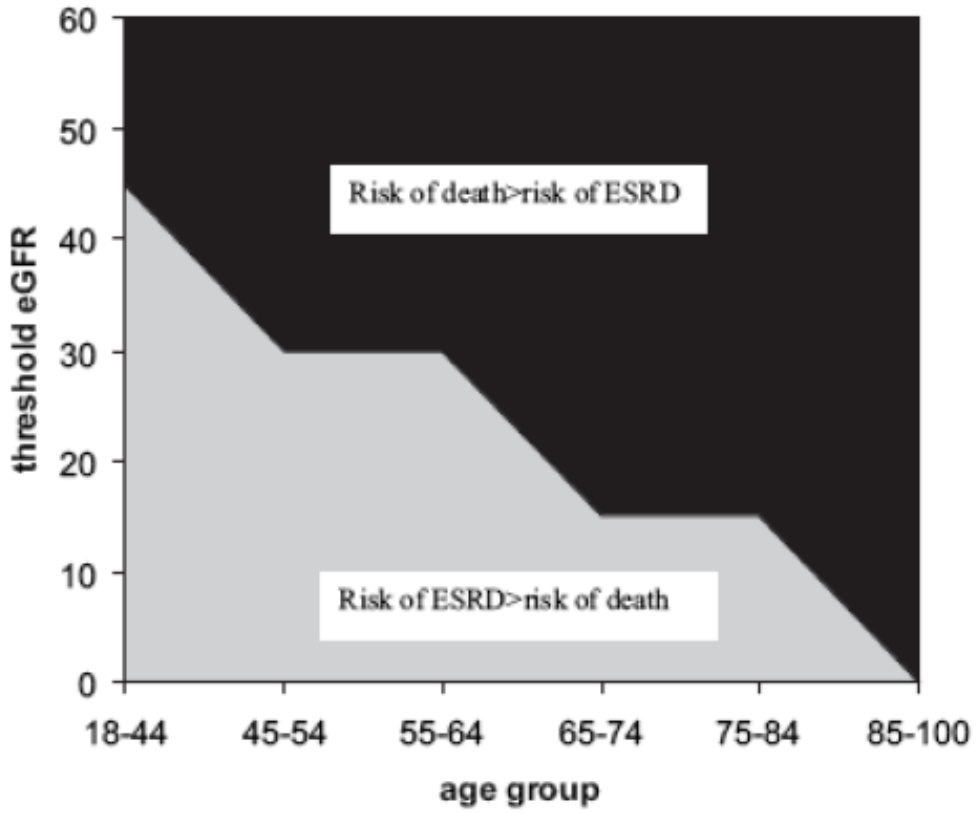






Go, A. S. et al. N Engl J Med 2004

Âge et Progression de la Maladie Rénale Chronique



RISQUE IRCT > DÉCÈS

- de 18 à 44 ans:

  DFG seuil 45 ml/min

- de 65 à 84 ans

  DFG seuil 15 ml/min

(O'Hare AM, JASN 18(2007):2758-65)

Appréciation du niveau de fonction rénale et risque de mortalité CV (KDIGO 2013)

Table 5 | GFR categories in CKD

GFR category	GFR (ml/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Kidney International Supplements (2013) **3**, 19–62

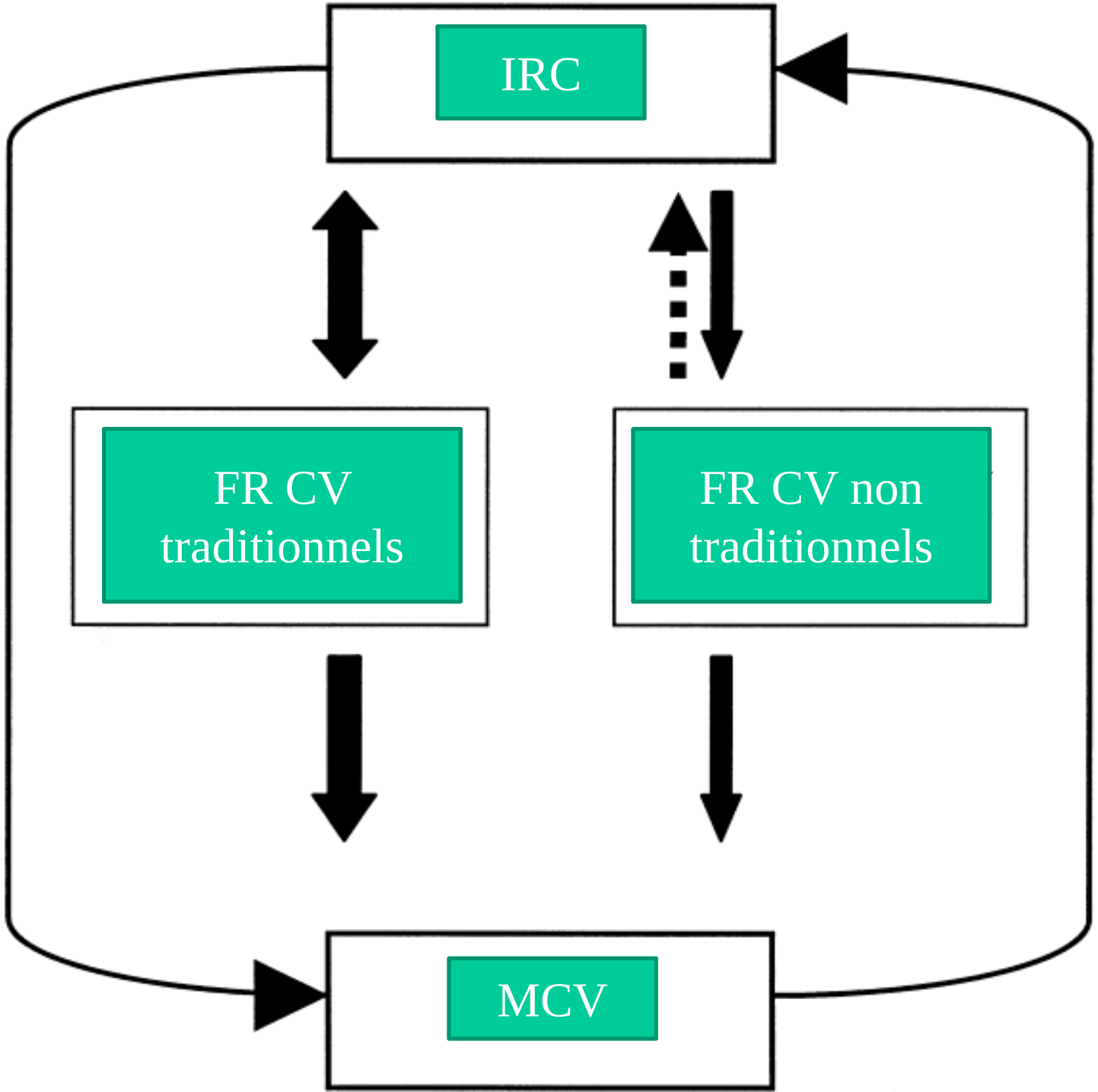
Table 6 | Albuminuria categories in CKD

Category	AER (mg/24 hours)	ACR (approximate equivalent) (mg/mmol)	ACR (approximate equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol]).

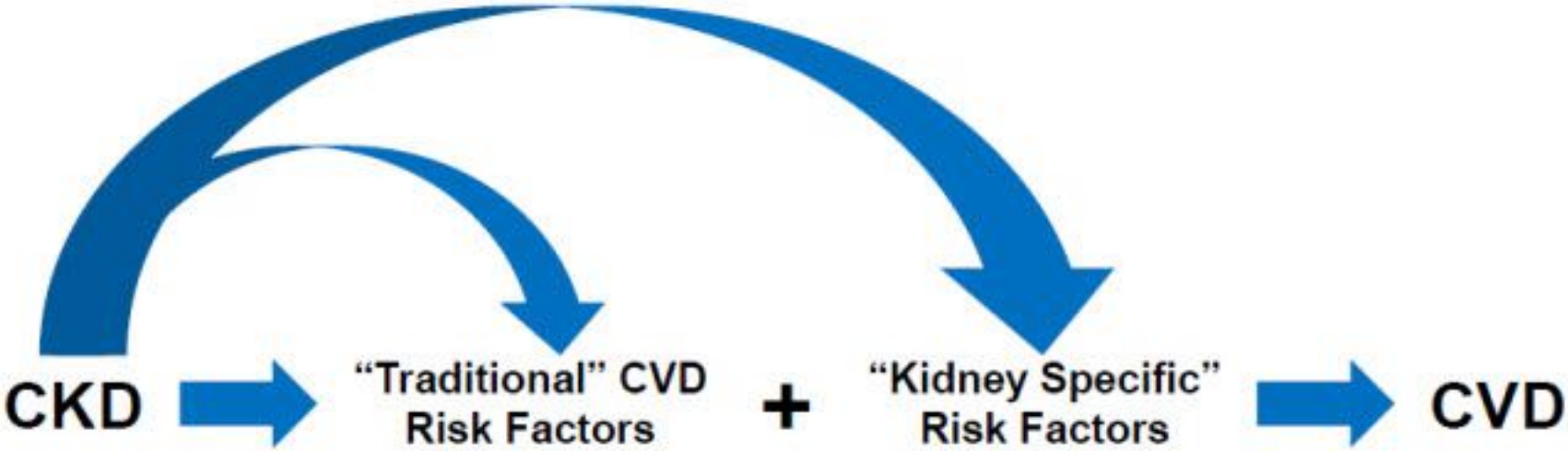
Cardiovascular mortality

	ACR <10	ACR 10–29	ACR 30–299	ACR ≥300
eGFR ≥105	0.9	1.3	2.3	2.1
eGFR 90–105	Ref	1.5	1.7	3.7
eGFR 75–90	1.0	1.3	1.6	3.7
eGFR 60–75	1.1	1.4	2.0	4.1
eGFR 45–60	1.5	2.2	2.8	4.3
eGFR 30–45	2.2	2.7	3.4	5.2
eGFR 15–30	14	7.9	4.8	8.1



IRC: insuffisance rénale chronique
FR CV: facteur de risque cardiovasculaire

MCV: Maladie cardiovasculaire



- Age
- Male gender
- Hypertension
- Dyslipidemia
- Diabetes
- Smoking
- Physical inactivity
- Family history of CVD
- LV hypertrophy

- Anemia
- Proteinuria
- Elevated Ca.P product
- Oxidative stress
- Inflammation

Table 27 | Prevalence of CKD complications by GFR category* derived from CKD cohorts

Complication	GFR category (ml/min/1.73 m^2)					Reference
	≥90	60-89	45-59	30-44	<30	
Anemia[1]	4.0%	4.7%	12.3%	22.7%	51.5%	
Hypertension[2]	18.3%	41.0%	71.8%	78.3%	82.1%	
25(OH) Vit D deficiency[3]	14.1%	9.1%	10.7%		27.2%	
Acidosis[4]	11.2%	8.4%	9.4%	18.1%	31.5%	
Hyperphosphatemia[5]	7.2%	7.4%	9.2%	9.3%	23.0%	
Hypoalbuminemia[6]	1.0%	1.3%	2.8%	9.0%	7.5%	
Hyperparathyroidism[7]	5.5%	9.4%	23.0%	44.0%	72.5%	

Kidney International Supplements (2013) **3**, 73–90

Prise en charge de l'hypertension chez l'insuffisant rénal (KI 2012)

Lifestyle Modification

2.3: Encourage lifestyle modification in people with CKD ND to lower BP and improve long-term cardiovascular and other outcomes:

2.3.1: We recommend achieving or maintaining a healthy weight (BMI 20 to 25). *(1D)*

2.3.2: We recommend lowering salt intake to <100 mmol (<2.4 g) per day of sodium (corresponding to 6 g of sodium chloride), unless contraindicated. *(1C)*

2.3.3: We recommend undertaking an exercise program compatible with cardiovascular health and tolerance, aiming for at least 30 minutes 5 times per week. *(1D)*

Prise en charge médicamenteuse de l'IRC

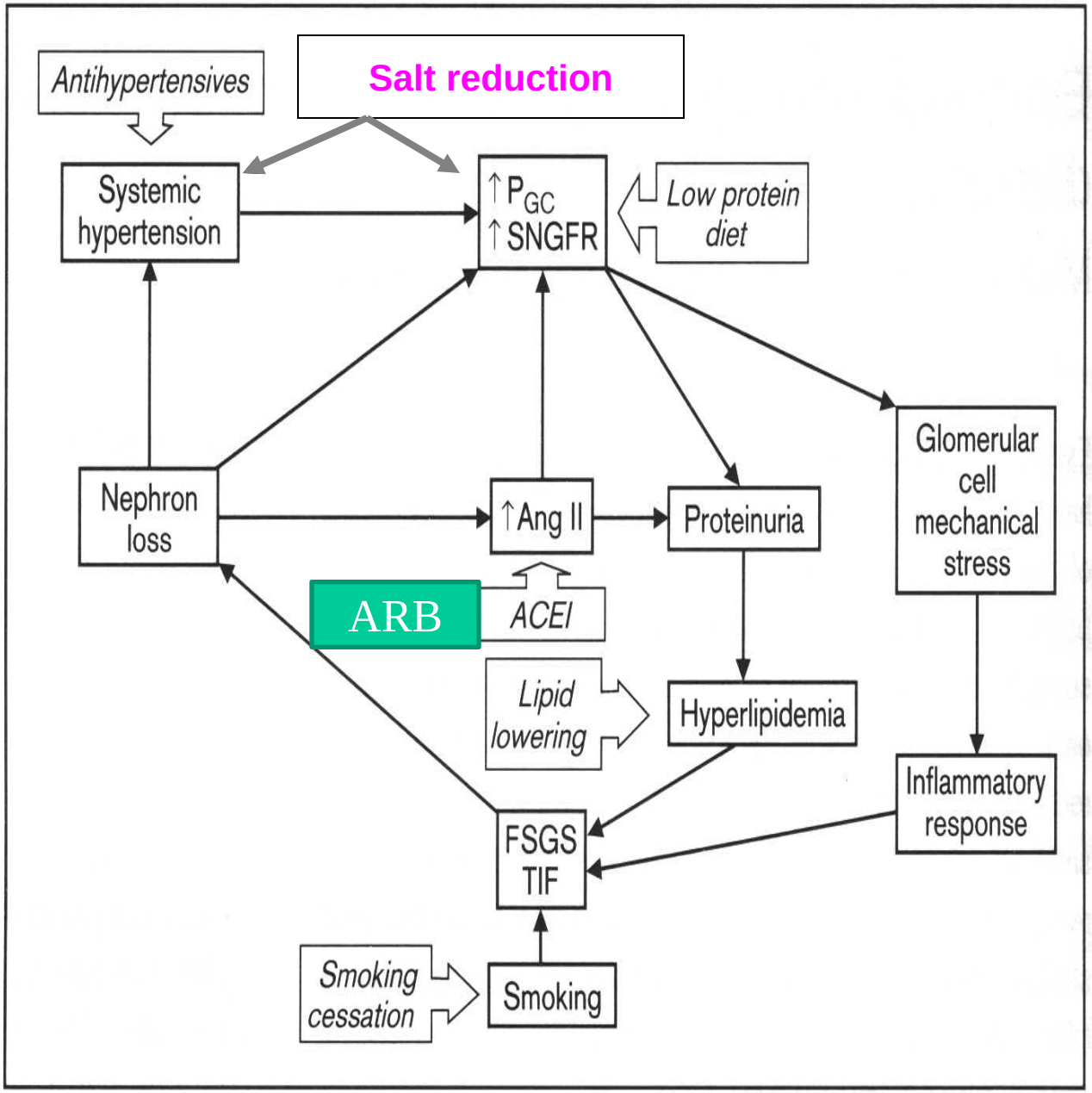
- Hypertension: antiHTA, ISRA
- Hyperlipidémie: statines
- Risque thrombotique: AAS
- Anémie: recours au Fer et EPO
- Métabolisme P-Ca: régime pauvre en PO4 et vit D

- Action sur le déclin de la GFR ***et*** sur le risque cardiovasculaire
- ISRA et statines abaissent en plus la protéinurie
- Corriger l'anémie réduit le risque de syndrome réno-cardiaque
- Réduire le risque de calcifications vasculaires

Figure 1. Proposed mechanisms resulting in a common pathway of progressive nephron loss in chronic renal disease

The actions of different interventions in interrupting this pathway are shown in italics. ACEI, angiotensin-converting enzyme inhibitor; Ang II, angiotensin II; FSGS, focal and segmental glomerulosclerosis; P_{GC}, glomerular capillary hydraulic pressure; SNGFR, single-nephron glomerular filtration rate; TIF, tubulointerstitial fibrosis.

Multifactorial approach



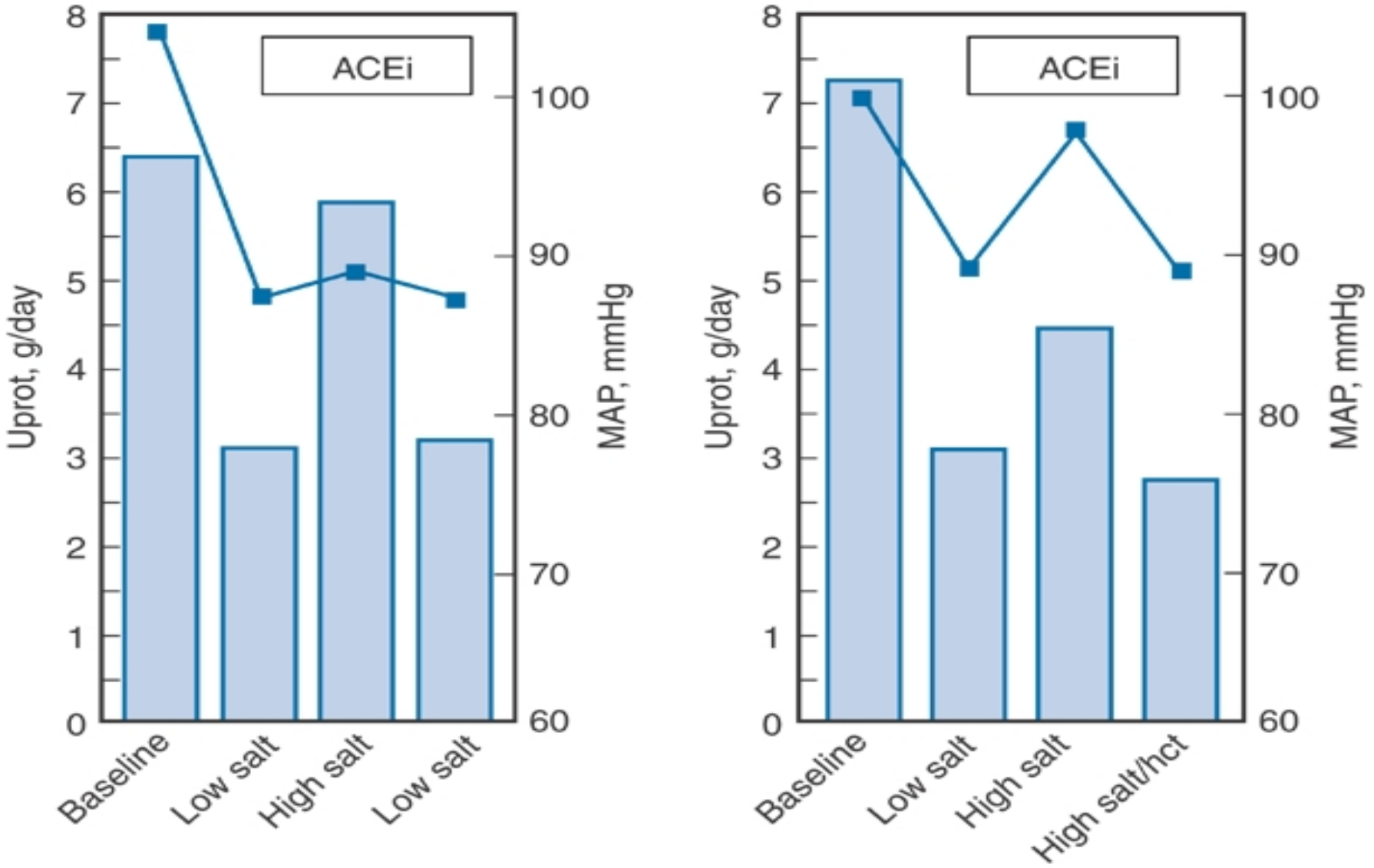
Cible tensionnelle chez l'HT IRC

KI 2013

Table 2 | Summary of recommendations for management of blood pressure in adult CKD patients with and without diabetes

Albuminuria (mg/day)[a]	BP Target mm Hg	Preferred agent
<30	⩽140/90 mm Hg	None
30–300	⩽130/80 mm Hg	ACE-I or ARB
>300	⩽130/80 mm Hg	ACE-I or ARB

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; CKD, chronic kidney disease.



(Adapted from Heeg JE, de Jong PE, van der Hem GK, de Zeeuw D: Reduction of proteinuria by angiotensin converting enzyme inhibition. Kidney Int 32:78-83, 1987; and Buter H, Hemmelder MH, Navis GJ, et al: Blunting of the antiproteinuric efficacy of ACE inhibition by high sodium intake can be restored by hydrochlorothiazide. Nephrol Dial Transplant 13:1682-1685, 1998.)

European Heart Journal (2011) **32**, 1769–1818
doi:10.1093/eurheartj/ehr158

Recours aux statines
si IRC **non dialysé**

Table 28 Recommendations for lipid lowering drugs in patients with moderate to severe CKD (stages 2–4, GFR 15–89 mL/min/1.73 m^2)

Recommendations	Class[a]	Level[b]	Ref[c]
CKD is acknowledged as a CAD risk equivalent; in these patients LDL-C reduction is recommended as the primary target of therapy.	I	A	189, 190
LDL-C lowering reduces CVD risk in CKD subjects and should be considered.	IIa	B	111, 193
Statins should be considered to slow the rate of kidney function loss modestly and thus protect against the development of ESRD requiring dialysis.	IIa	C	-
Since statins have a beneficial effect on pathological proteinuria (>300 mg/day) they should be considered in patients with stage 2–4 CKD.	IIa	B	194
In moderate to severe CKD statins as monotherapy or in combination with other drugs should be considered to achieve LDL-C <1.8 mmol/L (less than ~70 mg/dL).	IIa	C	-

Benéfice des statines quand IRC (méta-analyse de Palmer et al Ann Int Med 24/8/2012)

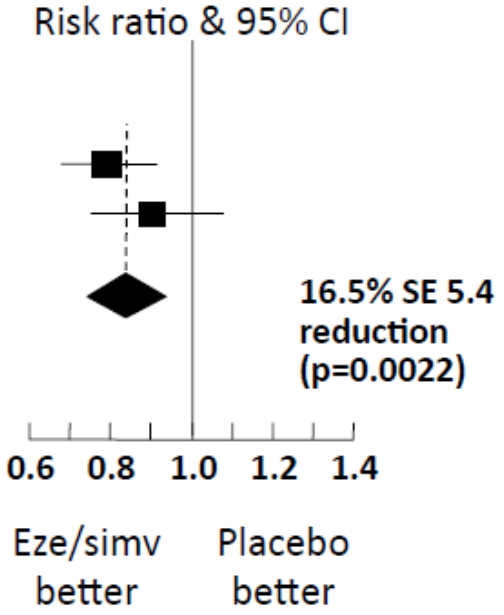
- Publication basée sur 81 études regroupant 51099 patients soit sous statine soit sous placebo.
- Sous statine, réduction significative de la mortalité totale (0.81), ou cardio-vasculaire (0.76) quand IRC non dialysée.
- Chez les dialysés, pas de bénéfice et chez les greffés rénaux résultats incertains.

SHARP: major atherosclerotic events by renal status at randomization

Study on Heart and renal protection

	Eze/simv (n=4650)	Placebo (n=4620)
Non-dialysis (n=6247)	296 (9.5%)	373 (11.9%)
Dialysis (n=3023)	230 (15.0%)	246 (16.5%)
Major atherosclerotic event	**526 (11.3%)**	**619 (13.4%)**

No significant heterogeneity between non-dialysis and dialysis patients (p=0.25)



Baigent C, et al. *The Lancet* 2011;377(9784):2181 - 2192

KDIGO CLINICAL PRACTICE GUIDELINE FOR LIPID MANAGEMENT IN CHRONIC KIDNEY DISEASE

- Coronary risk is sufficiently high to justify prescription of statins in people aged ≥50 and with CKD 1-5 ND, or with a kidney transplant

- Coronary risk in people aged <50 years and with CKD 1-5 ND is lower, but the presence of additional cardiovascular risk factors may increase risk to justify statin prescription. Given the evidence that treatment with statins improve vascular outcomes in this population, such treatment is suggested for patients aged <40 years with CKD 1-5 ND and other risk factors that increase the 10-year risk of coronary death or non-fatal myocardial infarction (as estimated using a validated risk calculator) to >10%.

- Patients with CKD 5D should not be initiated on statin or statin/ezetimibe treatment, given the lack of evidence that such treatment is beneficial. However, statin or statin/ezetimibe treatment should not necessarily be discontinued when dialysis treatment is initiated.
- Physicians should be alert to the possibility of toxicity resulting from substances that increase blood levels of statins (e.g., grapefruit juice, certain medications).

Public Review Draft
November 2012

Acide acétylsalicylique à faible dose chez l'IR?

Aspirin therapy produces greater absolute reduction in major cardiovascular events and mortality in hypertensive patients with CKD than with normal kidney function. An increased risk of major bleeding appears to be outweighed by the substantial benefits. (J Am Coll Cardiol 2010;56:956–65) © 2010 by the American College of

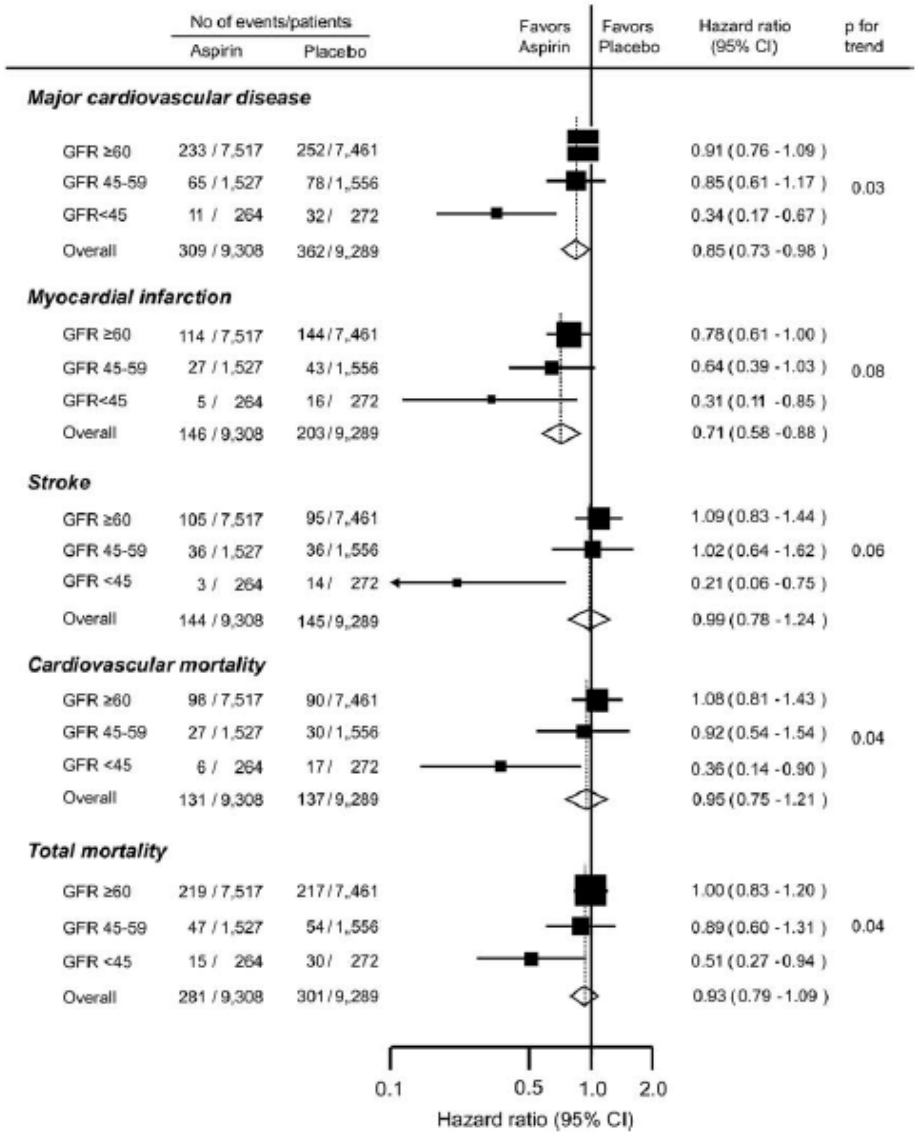


Figure 2 Effect of Aspirin According to eGFR Category

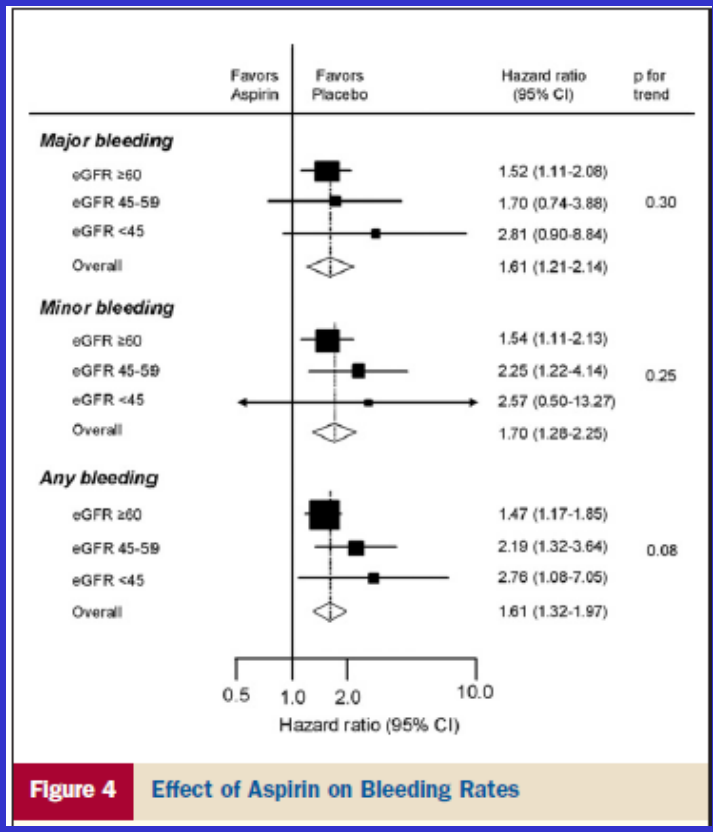


Figure 4 Effect of Aspirin on Bleeding Rates

Vitamin D levels and patient outcome in chronic kidney disease

Pietro Ravani[1,2], Fabio Malberti[3], Giovanni Tripepi[4], Paola Pecchini[3], Sebastiano Cutrupi[4], Patrizia Pizzini[4], Francesca Mallamaci[4] and Carmine Zoccali[4]

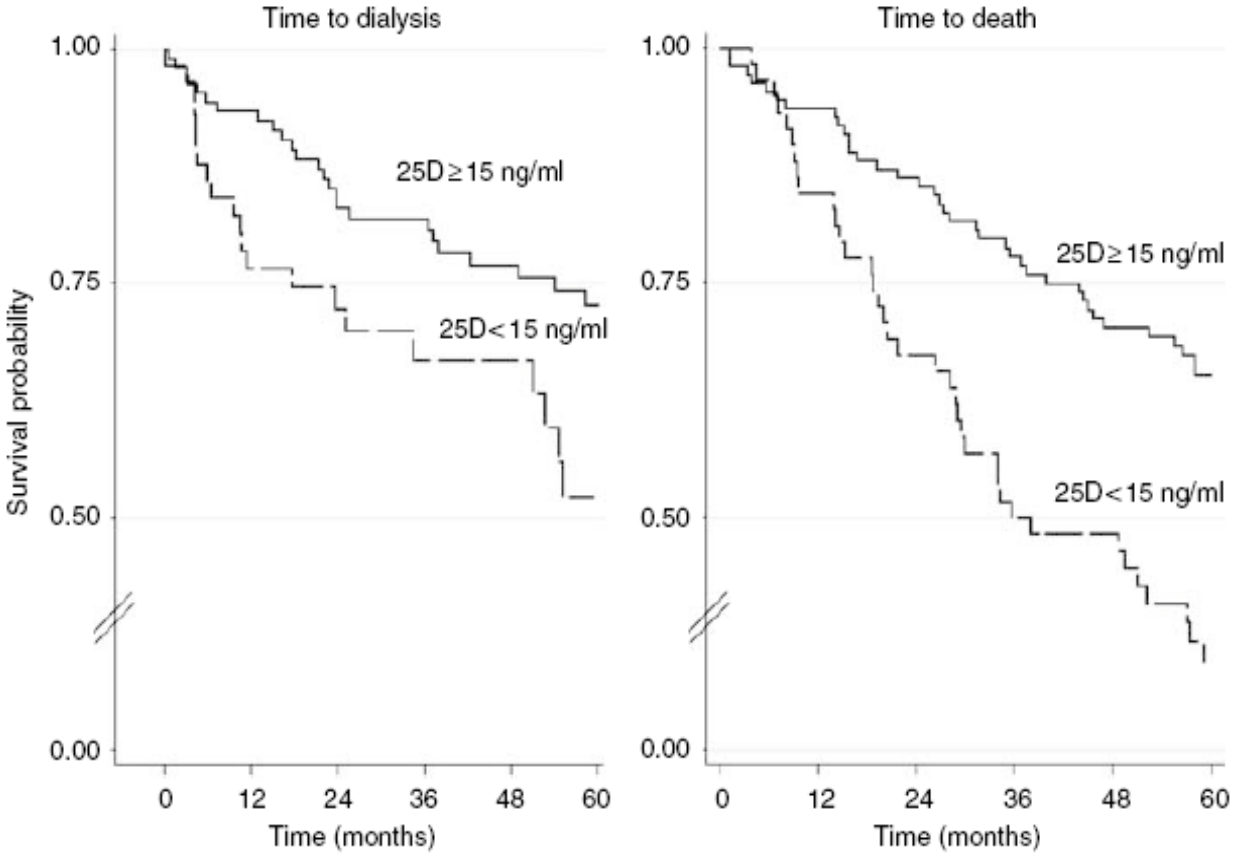


Figure 3 | Crude renal and patient survival curves by presence of 25D deficiency (levels of 25D <15 vs 15 ng/ml or greater).

Vit D, a new hope for CKD prevention (with RAS inhibitors)

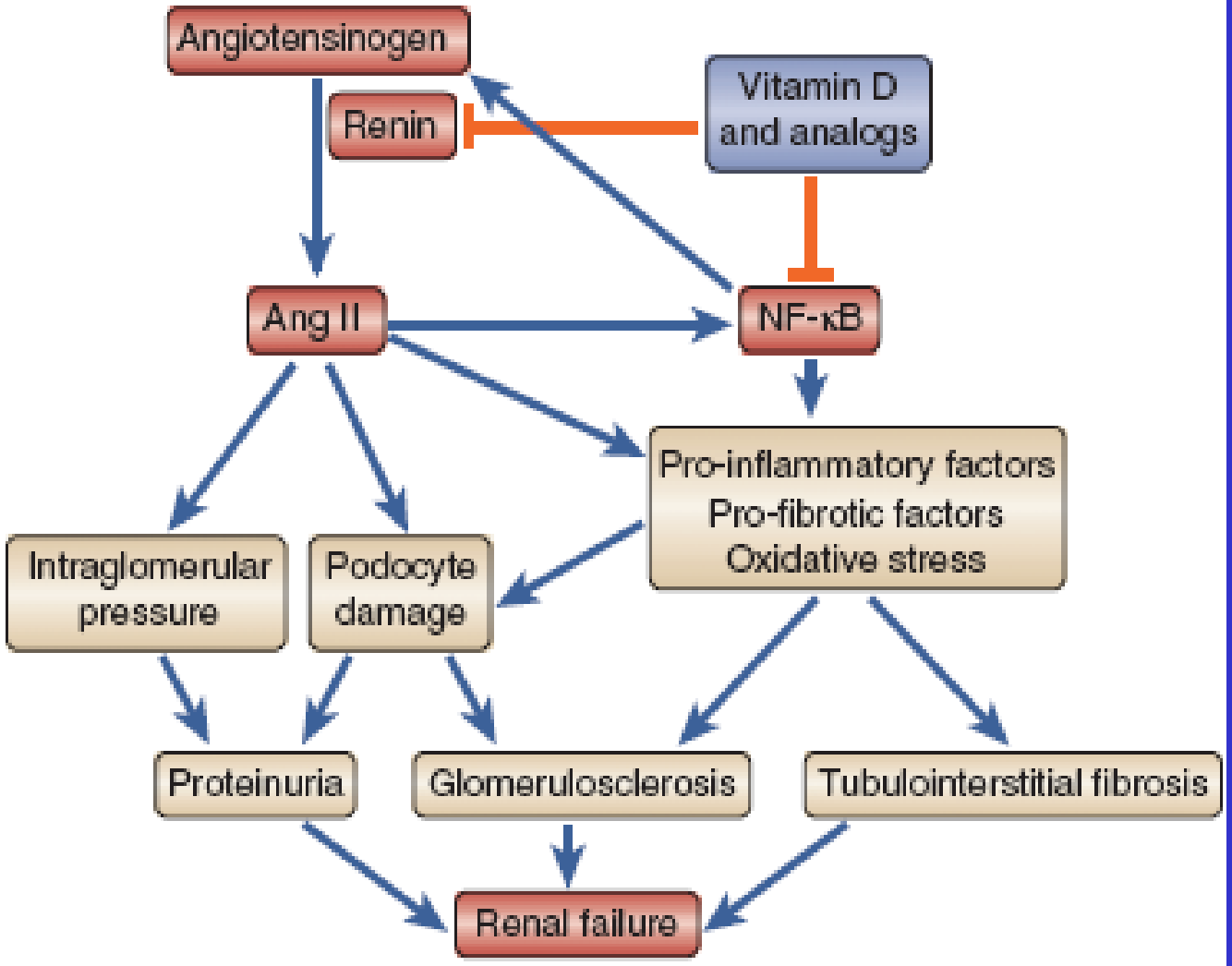


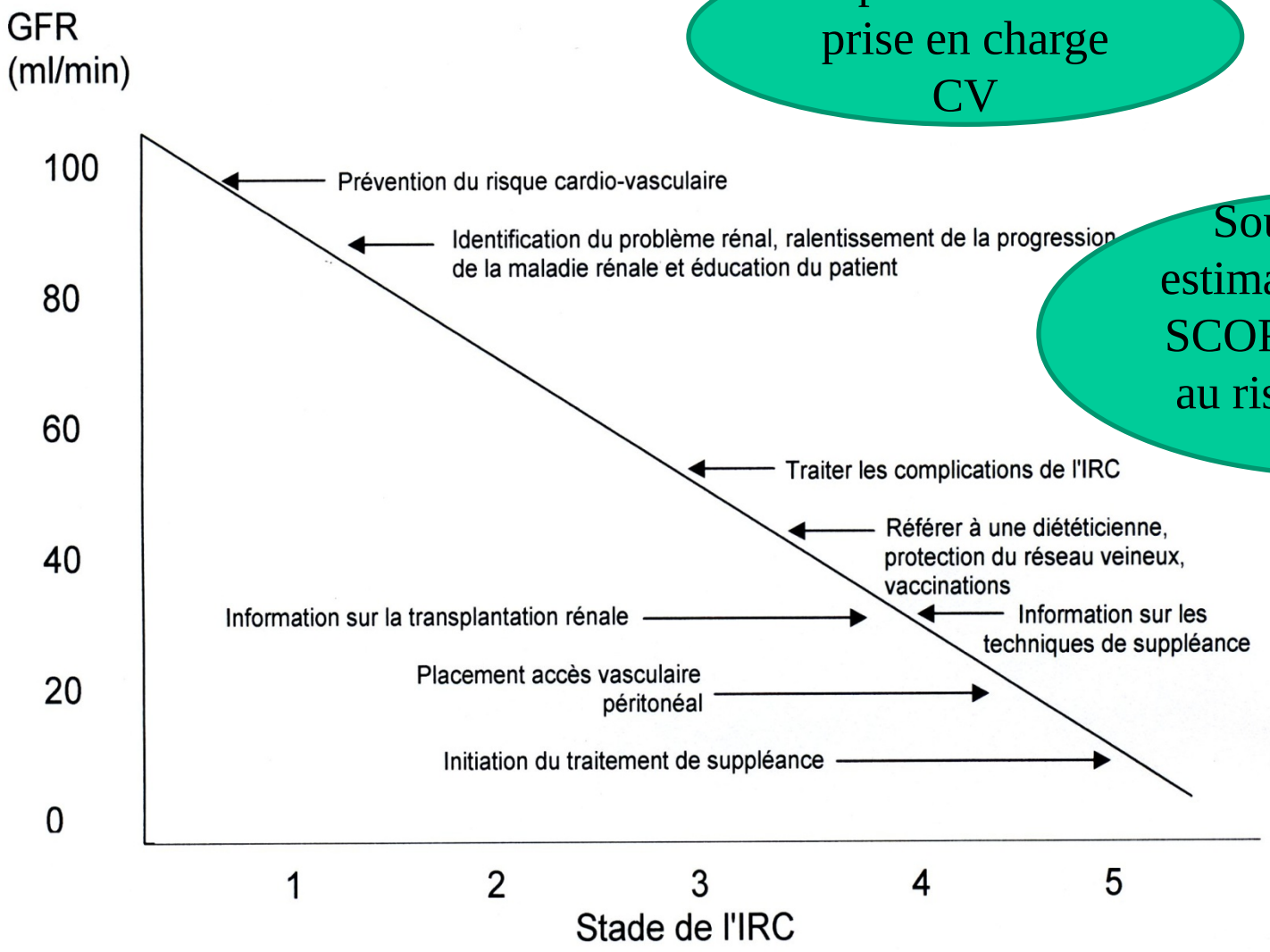
Figure 2 | Mechanism of renoprotection by vitamin D and its analogs. The renin–angiotensin system and the NF-κB activation

Kidney International (2010) **78,** 134

Cas clinique à haut risque CV surtout (un peu moins rénal)

- Régime hypocalorique hyposodé, diminué en graisses animales, avec moins de Protéines et de Phosphates.
- HTA traitée par IEC (ou losartan) avec cible tensionnelle 130/80 mmHg (donc association antiHTA nécessaire, poursuite AC et SN diurétique)
- Statine avec cible en LDL chol <100 mg/dl
- Prise d'AAS 100 mg/j
- Suivi de la GFR/3 mois et de l'albuminurie!
- Suivi du taux d'Hb et de 25OH vitD : SN introduction de Fer, d'EPO et de vit D3 (cible Hb 11 g/dl et 25OHvitD >30 ng/ml)

Figure 1 : Prise en charge du patient souffrant de maladie rénale chronique



Importance de la prise en charge CV

Souvent, sous-estimation du risque SCORE par rapport au risque réel chez l'IRC

Krzesinski J-M, Crismer A, *Rev Med Liège*, 2006 .