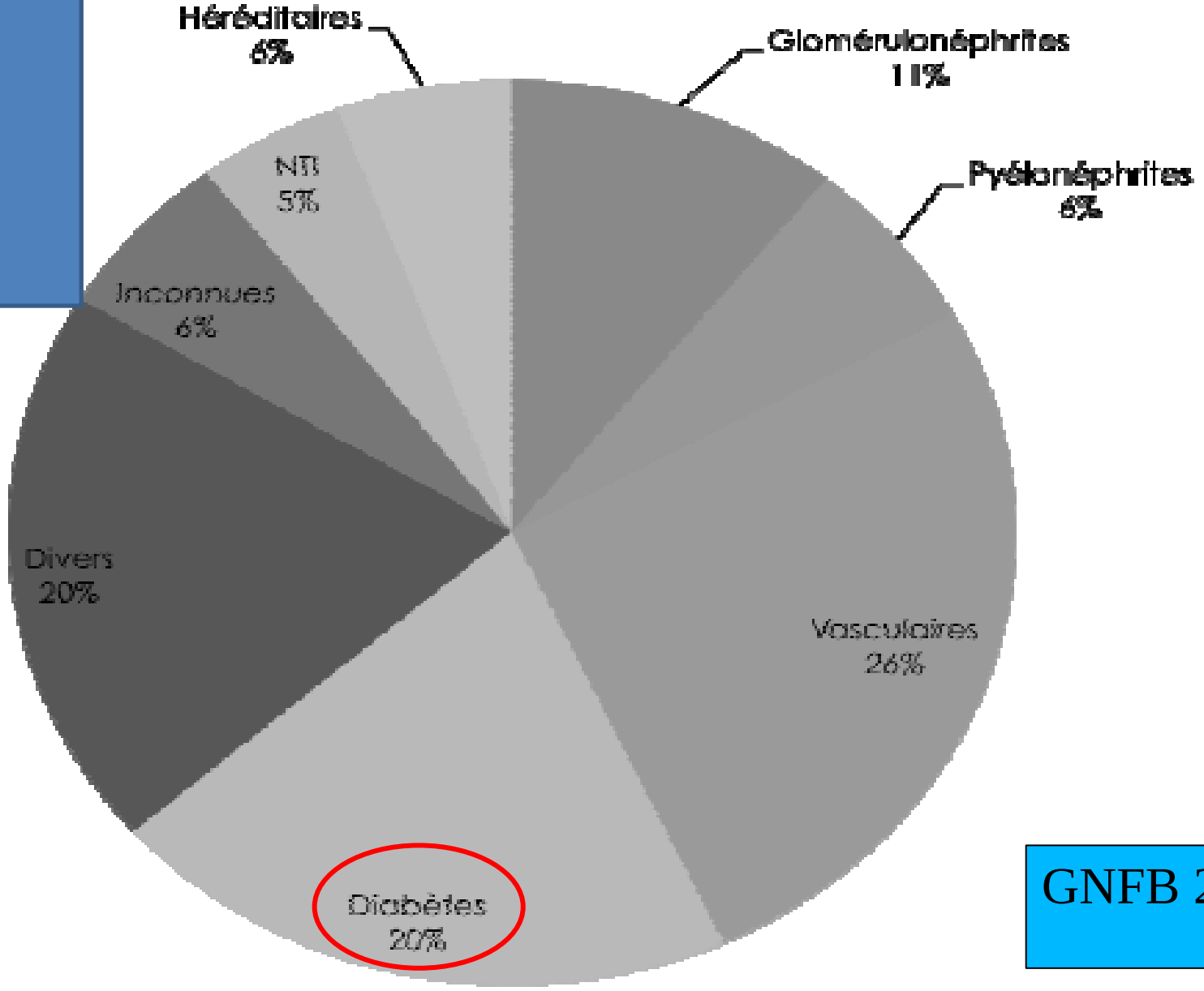
Maladies rénales et diabète
Rôle du Médecin Généraliste

JM Krzesinski
ULg-CHU Liège
Service de Néphrologie- Dialyse-Transplantation

Répartition des Néphropathies (Année 2011)

USA: 30%
Asie: 50%

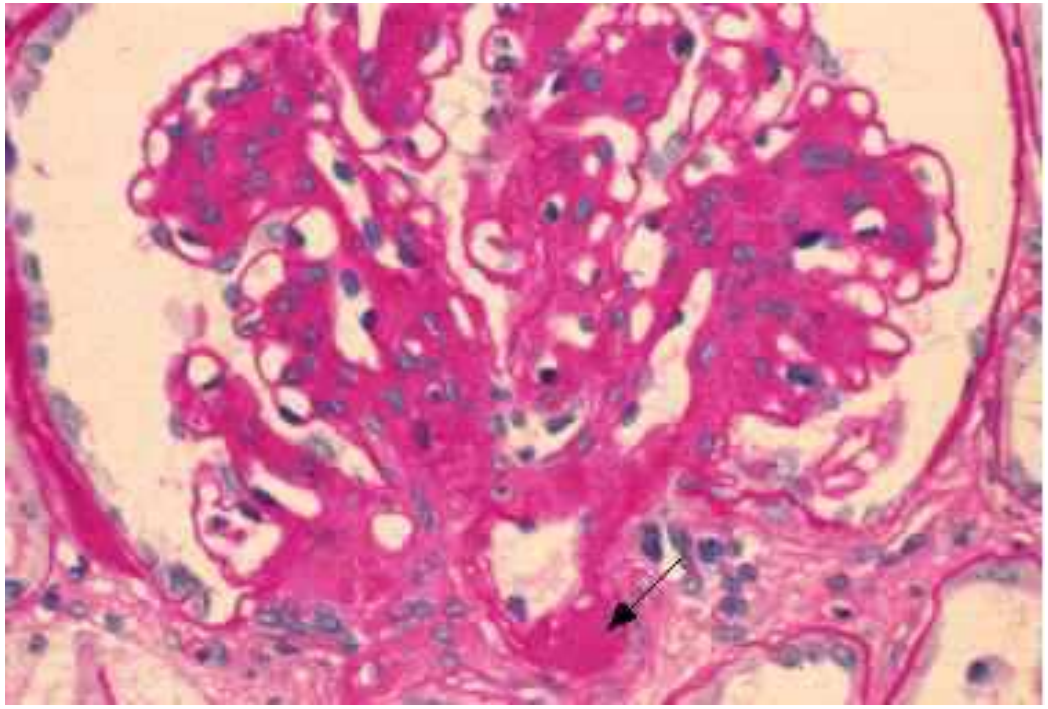


GNFB 2012

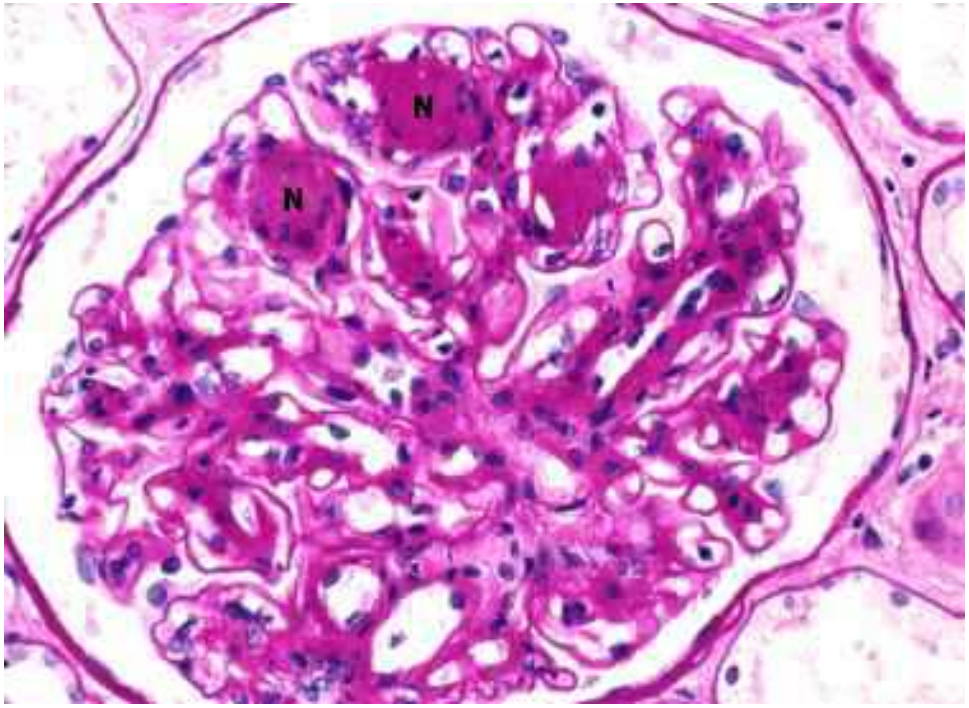
Pathologies rénales et diabète

- Néphropathie diabétique typique (glomérulosclérose diabétique, surtout type 1)
- Néphropathie vasculaire (SAR, athéromasie aorte, néphroangiosclérose)
- Néphropathie tubulo-interstitielle (infection urinaire, médicaments, hyperuricémie)

Histologie ND

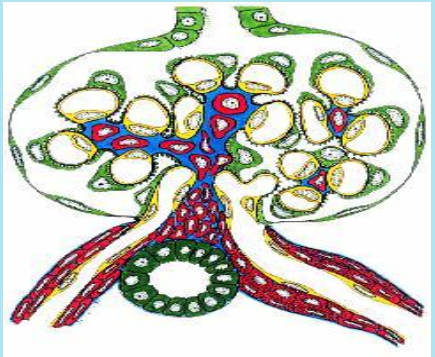


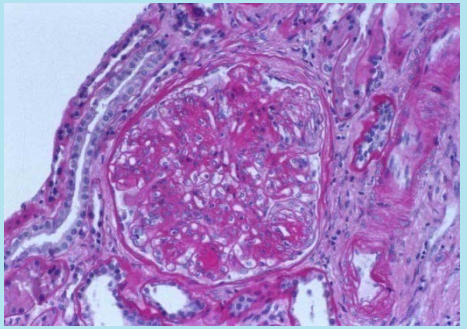
Forme diffuse



Forme nodulaire décrite par Kimmelstiel et Wilson

Diabetic Nephropathy





Nephropathy in Patients with Type 2 Diabetes Mellitus

Eberhard Ritz, M.D., and Stephan Reinhold Orth, M.D.

The New England Journal of Medicine

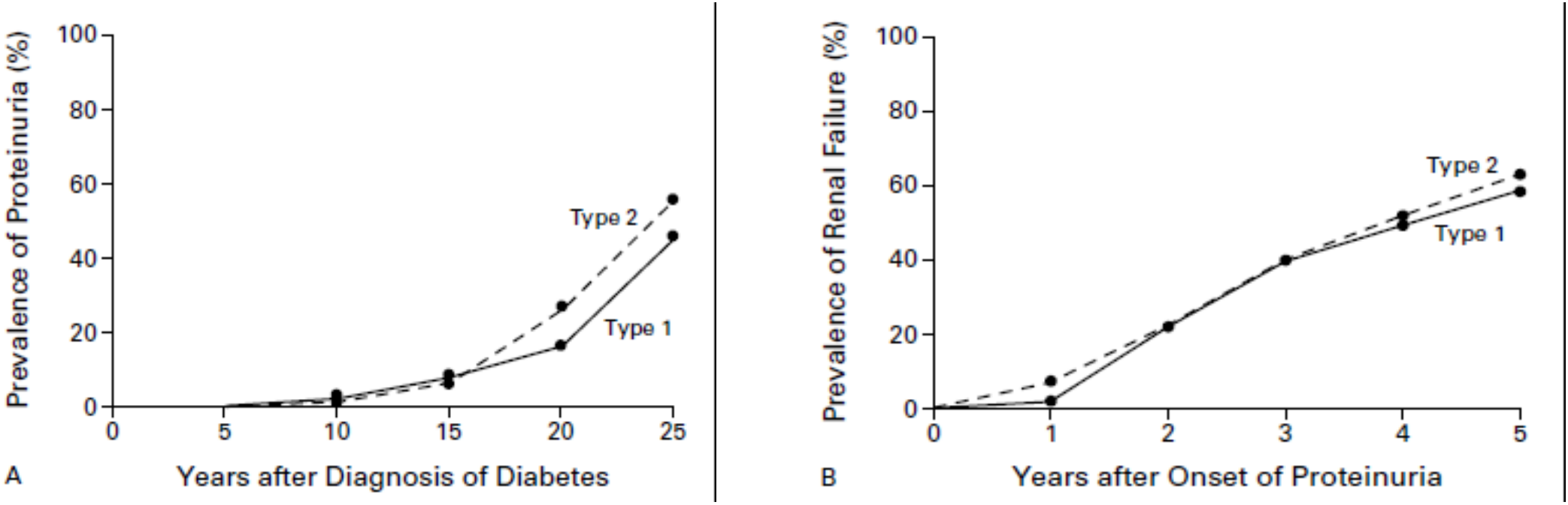


Figure 1. Cumulative Prevalence of Persistent Proteinuria among Patients with Type 1 or Type 2 Diabetes, According to the Duration of Diabetes (Panel A), and Cumulative Prevalence of Renal Failure among Patients with Type 1 or Type 2 Diabetes, According to the Duration of Proteinuria (Panel B).

Standards of Medical Care in Diabetes—2014

American Diabetes Association

Diabetes Care Volume 37, Supplement 1, January 2014

Détection MRD: dosage de créatinine sérique et albuminurie en g/g créatininurie

MDRD ou CKD-EPI

Table 12–Stages of chronic kidney disease

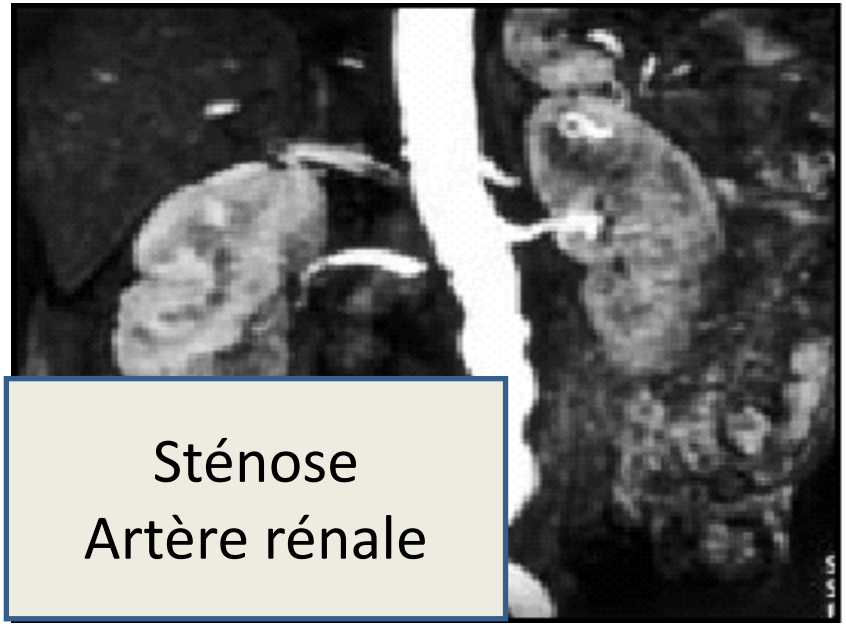
Stage	Description	GFR (mL/min/1.73 m^2 body surface area)
1	Kidney damage* with normal or increased GFR	≥90
2	Kidney damage* with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	<15 or dialysis

*Kidney damage defined as abnormalities on pathologic, urine, blood, or imaging tests. Adapted from Levey et al. (434).

Définition des valeurs normales d'albuminurie et de la Néphropathie Diabétique (ND)

K-DIGO (2012)	Stade	Echantillon	Récolte minutée	Urines de 24 heures
A1	Pas de ND	**< 30 mg/g créat. urinaire**	< 20 µg/min	< 30 mg/24 heures
A2 (**µalbuminurie**)	ND incipiens	**30 à < 300 mg/g créat. urinaire**	20 à < 200 µg/min	30 à < 300 mg/24 heures
A3 **(tigette +)**	ND avérée	**>= 300 mg/g créat. urinaire**	>= 200 µg/min	>= 300 mg/24 heures

Multiple causes of nephropathy in type 2 diabetes



Sténose
Artère rénale

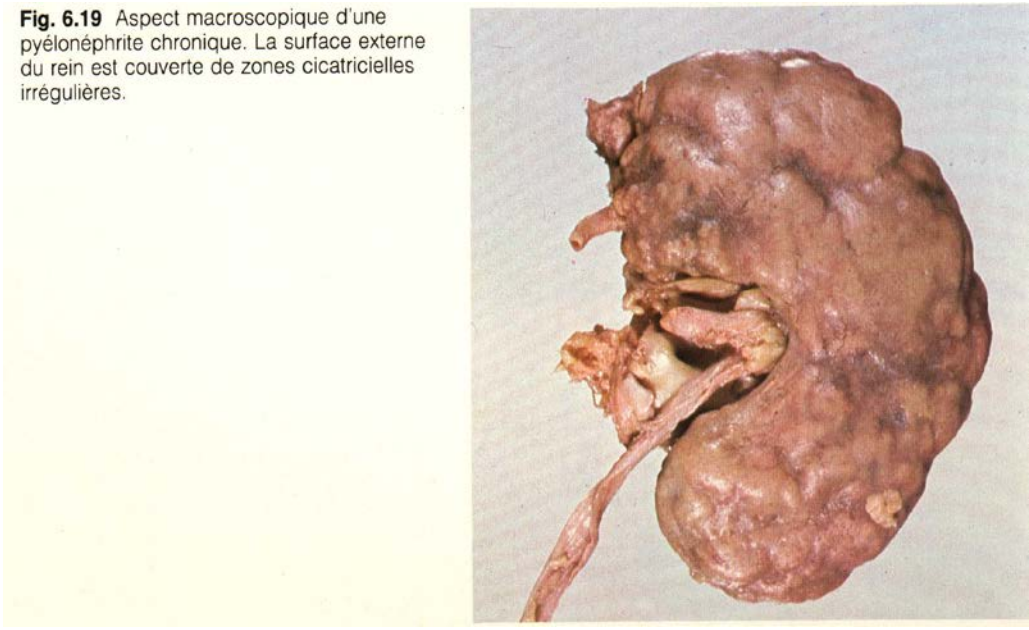


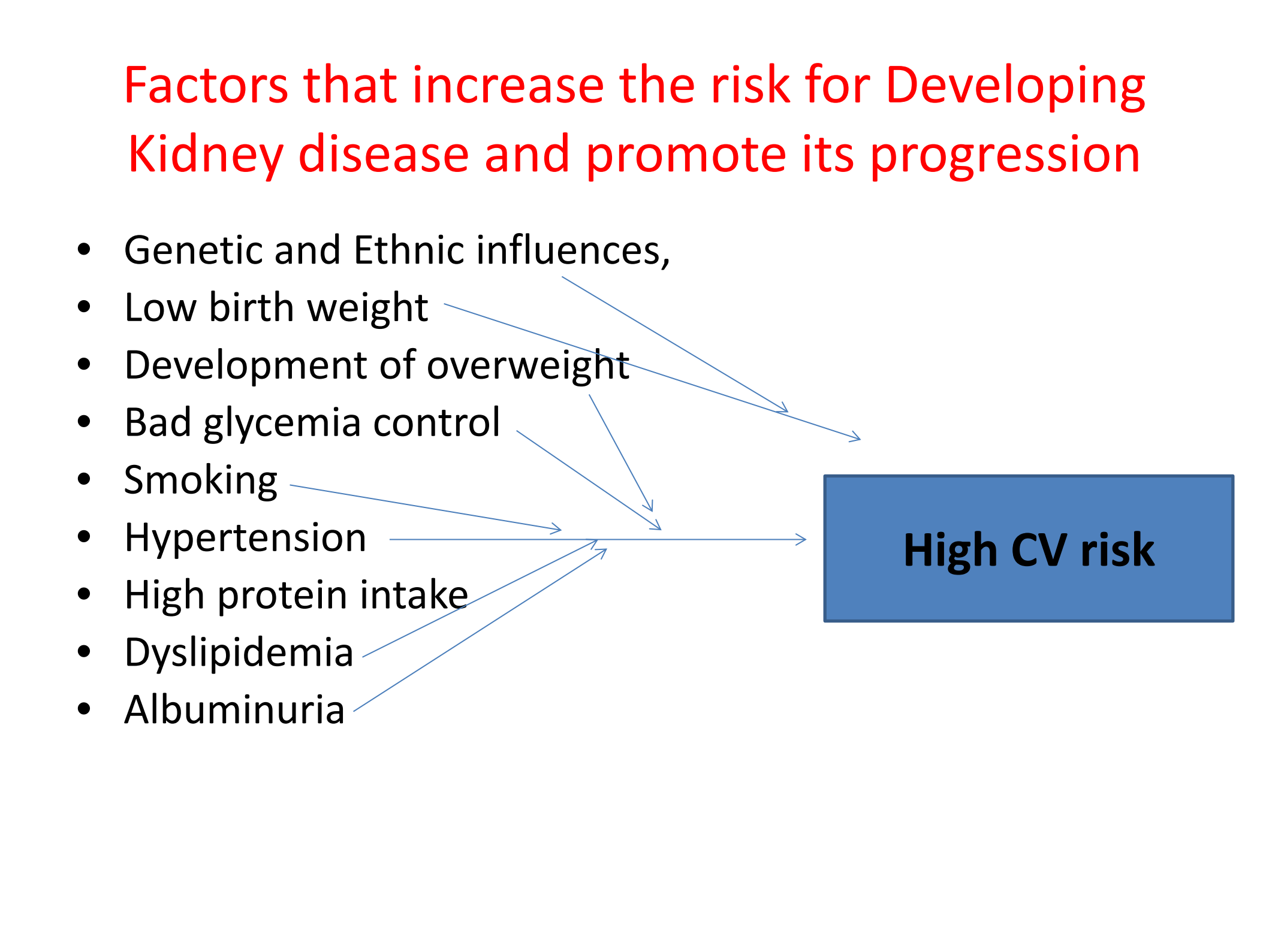
Fig. 6.19 Aspect macroscopique d'une pyélonéphrite chronique. La surface externe du rein est couverte de zones cicatricielles irrégulières.

- **classical DN (with retinopathy)**
- **hypertensive nephropathy**
- **ischaemic renal disease**
- **Pyelonephritis, T/I disease**

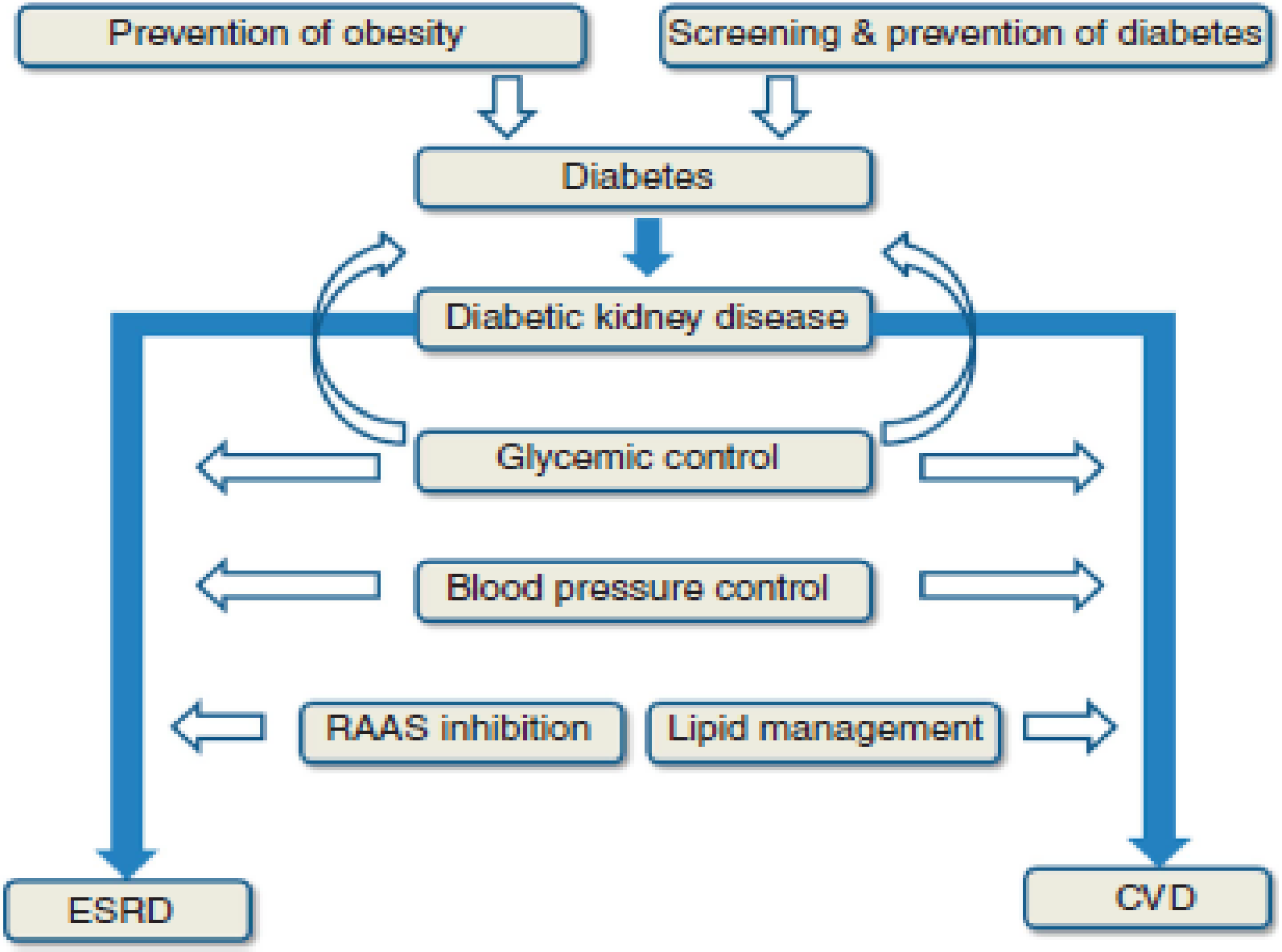
If no proteinuria, check for another cause than classical DN

Factors that increase the risk for Developing Kidney disease and promote its progression

- Genetic and Ethnic influences,
- Low birth weight
- Development of overweight
- Bad glycemia control
- Smoking
- Hypertension
- High protein intake
- Dyslipidemia
- Albuminuria



Prise en charge du diabète



Kidney International (2015) **87**, 20–30

Risks of strict glycaemic control in diabetic nephropathy

Martin H. de Borst and Gerjan Navis

Nat. Rev. Nephrol. **11**, 5–6 (2015); published online 4 November 2014;

Table 1 | Trials comparing intensive versus standard glycaemic control in T2DM

	ADVANCE[1]	ADVANCE-ON[3]	ACCORD[2]	Papademetriou *et al.*[4]
Number of patients	11,140	8,494	10,251	10,136
Follow-up (years)	5.0	5.4 (post-trial)	3.4	3.4
Comparison	Intensive versus standard glucose control	Intensive versus standard glucose control	Intensive versus standard glucose control	Intensive versus standard glucose control in CKD and non-CKD subgroups*
HbA_{1c} at study end (%)	6.5 versus 7.3	7.2 versus 7.4	6.3 versus 7.3	CKD: 6.3 versus 7.4 Non-CKD: 6.3 versus 7.5
Primary end point(s) (HR [95% CI])	Major macrovascular or microvascular events (0.90 [0.82–0.98])‡	All-cause mortality (1.00 [0.92–1.08]) Major macrovascular events (1.00 [0.92–1.08])	Nonfatal myocardial infarction, stroke or cardiovascular mortality (0.90 [0.78–1.04])	Cardiovascular or all-cause mortality in CKD versus non-CKD subgroups (1.86 [1.65–2.11])‡
Renal end point (HR [95% CI])	ESRD (0.35 [0.15–0.83])‡	ESRD (0.54 [0.34–0.85])‡	ESRD§ (0.95 [0.73–1.24])	NA
Cardiovascular mortality (HR [95% CI)]	0.88 [0.74–1.04]	0.97 [0.86–1.10]	1.35 [1.04–1.76]‡	CKD: 1.41 [1.05–1.89]‡ Non-CKD: 1.14 [0.82–1.58]
All-cause mortality (HR [95% CI])	0.93 [0.83–1.06]	1.00 [0.92–1.08]	1.22 [1.01-1.46]‡	CKD: 1.31 [1.07–1.60]‡ Non-CKD: 1.08 [0.87–1.34]

HRs indicate the risk to reach an end point for intensive versus standard glucose control. *ACCORD participants with CKD (n=3,636) versus those without CKD (n=6,506). ‡Significant HR. §This end point was analysed in a separate publication.[10] Abbreviations: ACCORD, Action to Control Cardiovascular Risk in Diabetes; ADVANCE, Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation; ADVANCE-ON, ADVANCE-observational study; CKD, chronic kidney disease; ESRD, end-stage renal disease; HR, hazard ratio; NA, not available; T2DM, type 2 diabetes mellitus.

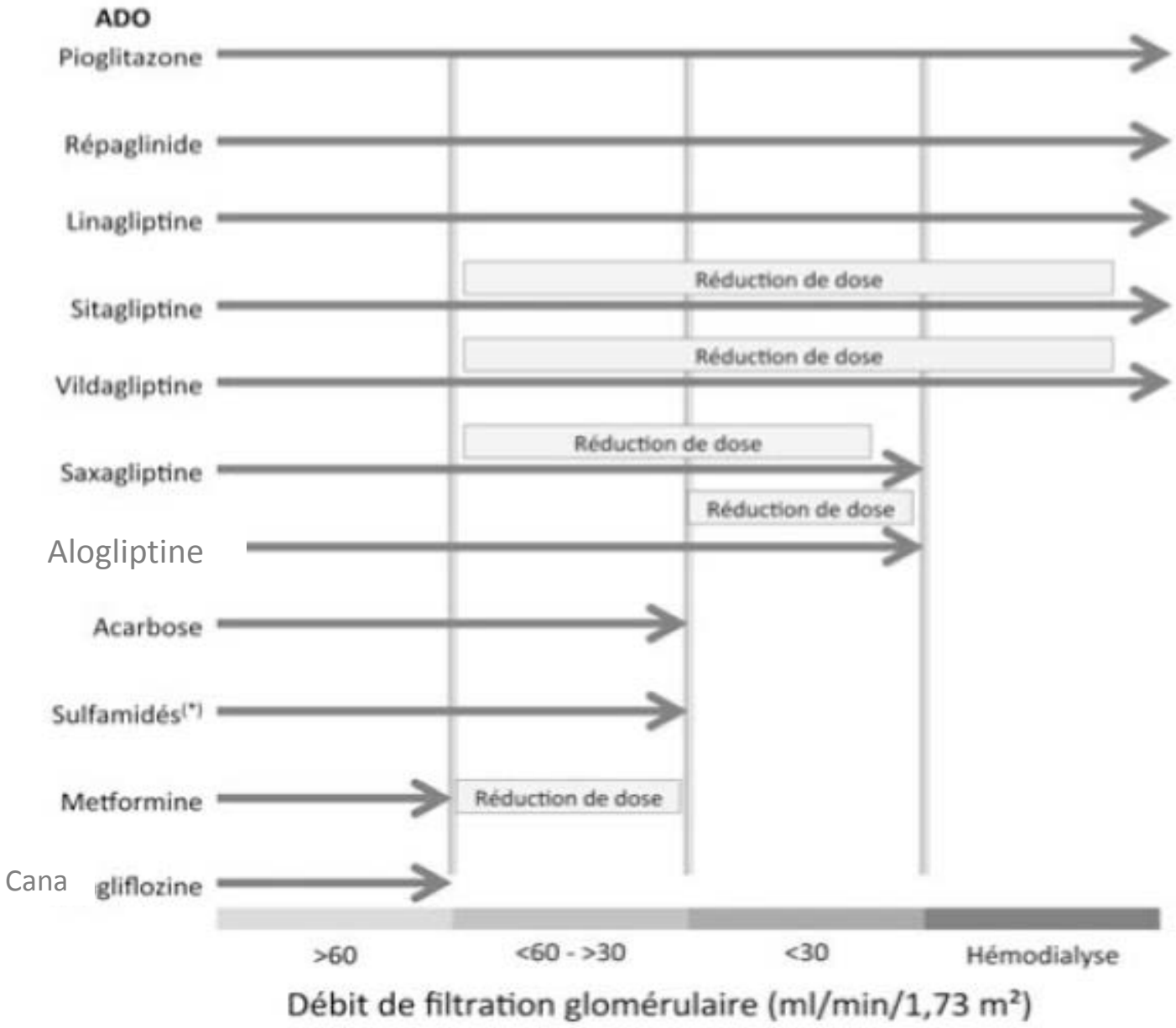
Contrôle strict de la glycémie chez le Diabétique

- Protection significative contre les complications microvasculaires
- Moins convaincant en termes de protection CV
- Le bénéfice CV d'une HbA1C < 7% plutôt que 8% diminue avec
  - l'âge,
  - la durée du diabète et
  - les co-morbidités.

André J. Scheen

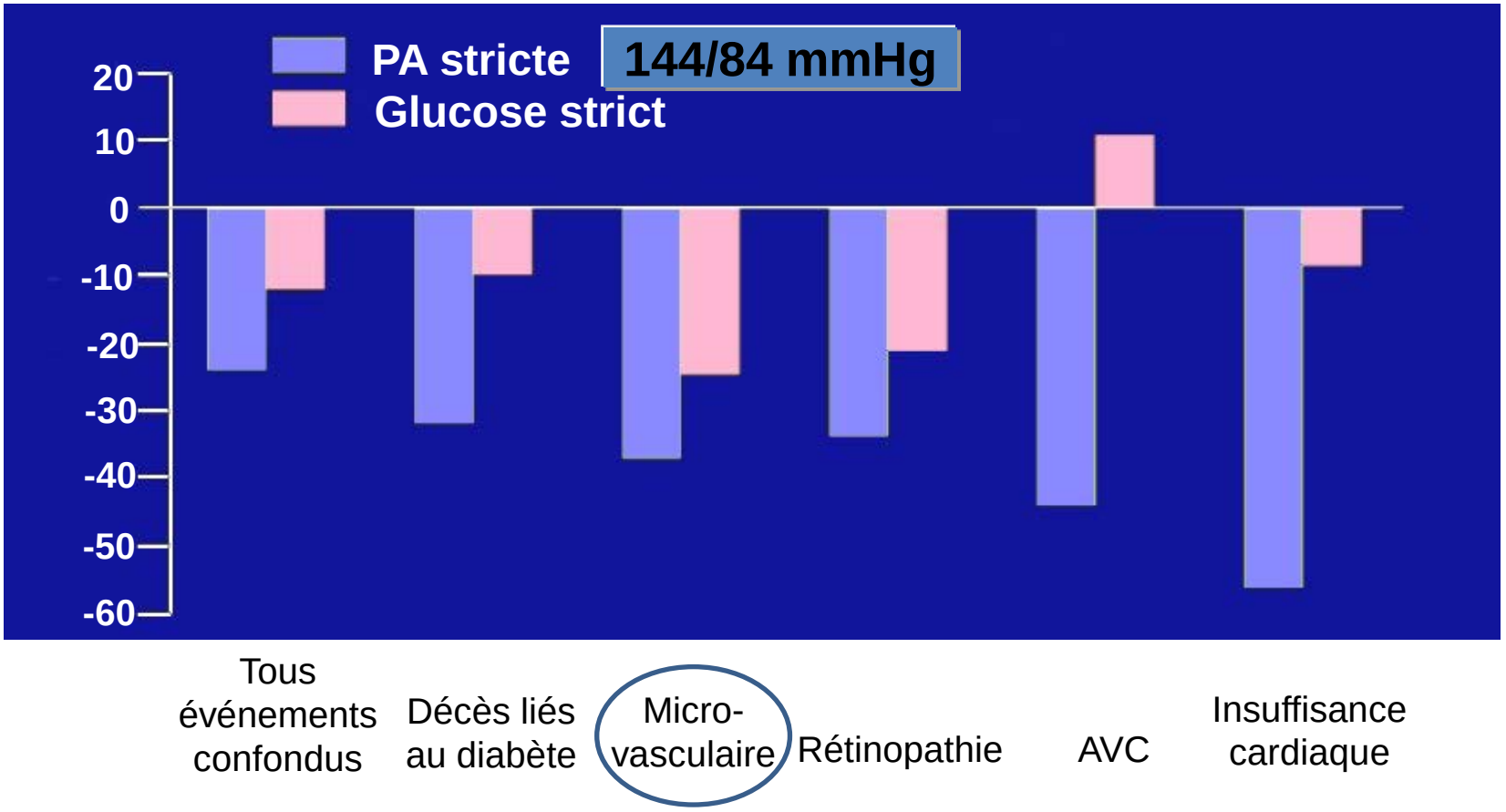
Utilisation des antidiabétiques oraux en cas d'insuffisance rénale

Rev Med Suisse 2012;8:1614-1620



Restrictions éventuelles de l'utilisation des antidiabétiques oraux (ADO) en fonction des différents stades de l'insuffisance rénale chronique estimés par le débit de filtration glomérulaire (DFG ou eGFR)

UKPDS :
Importance du contrôle strict de la PA et de la glycémie sur le risque de complications liées au diabète



UKPDS Group, *The Lancet, 1998;352:837-853*

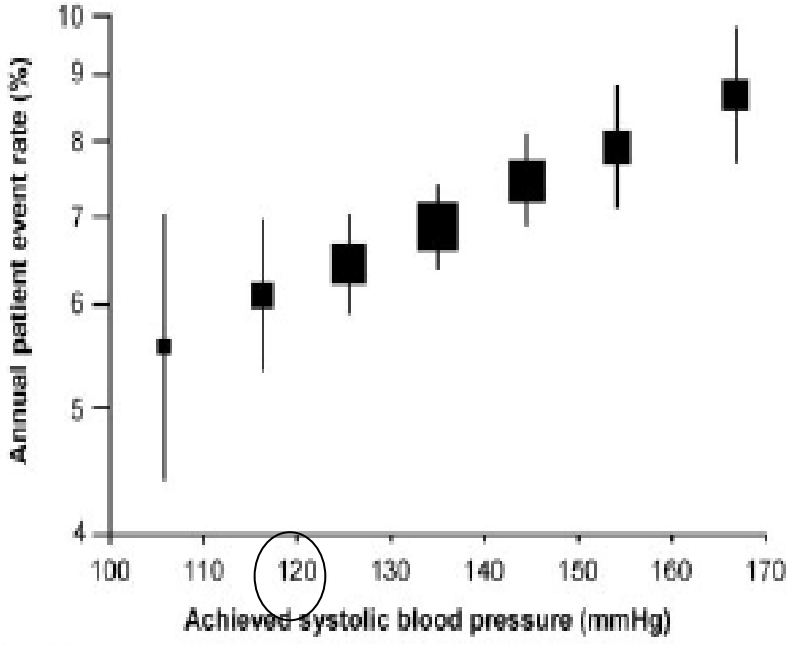
UKPDS Group, *BMJ,1998*;317:703-713

Lowering Blood Pressure Reduces Renal Events in Type 2 Diabetes

Bastiaan E. de Galan,*† Vlado Perkovic,* Toshiharu Ninomiya,* Avinesh Pillai,* Anushka Patel,* Alan Cass,* Bruce Neal,* Neil Poulter,‡ Stephen Harrap,§ Carl-Erik Mogensen,‖ Mark Cooper,¶ Michel Marre,** Bryan Williams,†† Pavel Hamet,‡‡ Giuseppe Mancia,§§ Mark Woodward,* Paul Glasziou,‖‖ Diederick E. Grobbee,¶¶ Stephen MacMahon,* and John Chalmers,*
on behalf of the ADVANCE Collaborative Group

JASN 2009; 20: 883

ADVANCE: renal protection until SBP of 120 mmHg

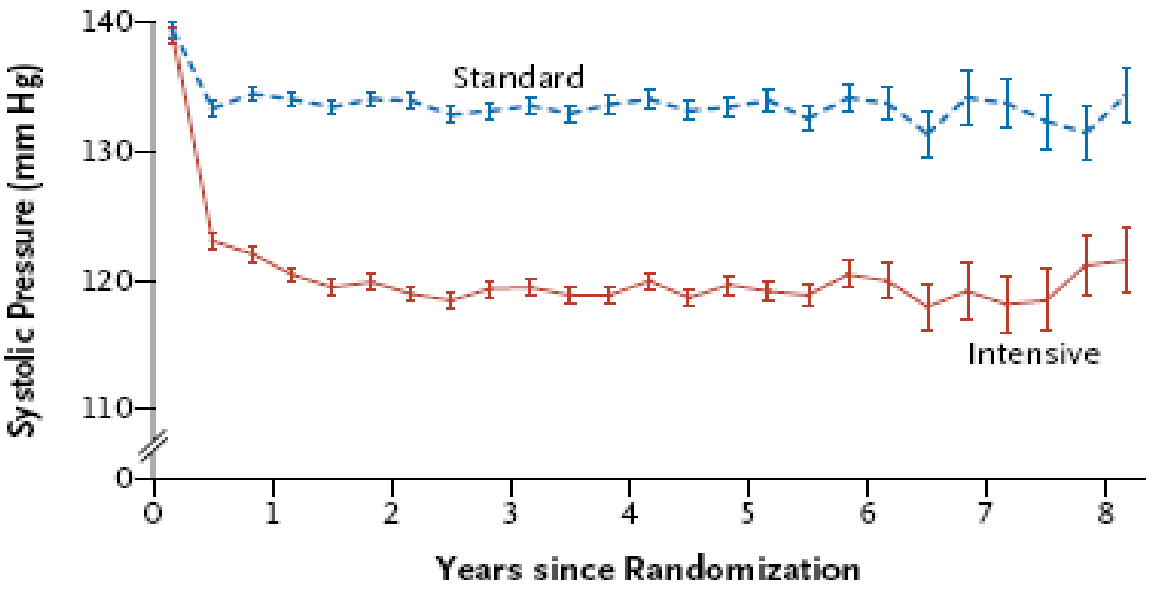


Median systolic blood pressure (mmHg)	106	116	125	135	144	154	168
No. of person-years	1431	4266	8974	11983	9138	4942	3470

Figure 4. Incidence of all renal events according to achieved BP levels, adjusted for age, gender, duration of diabetes, glycosylated hemoglobin, currently treated hypertension, history of macrovascular disease, electrocardiogram abnormalities (ventricular hypertrophy, Q waves, or atrial fibrillation), triglycerides, LDL cholesterol, HDL cholesterol, body mass index, current smoking,

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*



Mean No. of Medications Prescribed								
Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3
No. of Patients								
Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

Figure 1. Mean Systolic Blood-Pressure Levels at Each Study Visit.

133/70

119/64

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*

ABSTRACT

BACKGROUND

There is no evidence from randomized trials to support a strategy of lowering systolic blood pressure below 135 to 140 mm Hg in persons with type 2 diabetes mellitus. We investigated whether therapy targeting normal systolic pressure (i.e., <120 mm Hg) reduces major cardiovascular events in participants with type 2 diabetes at high risk for cardiovascular events.

CONCLUSIONS

In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events. (ClinicalTrials.gov number, NCT00000620.)

This article (10.1056/NEJMoa1001286) was published on March 14, 2010, at NEJM.org.

N Engl J Med 2010.

Standards of Medical Care in Diabetes—2014

American Diabetes Association

Diabetes Care Volume 37, Supplement 1, January 2014

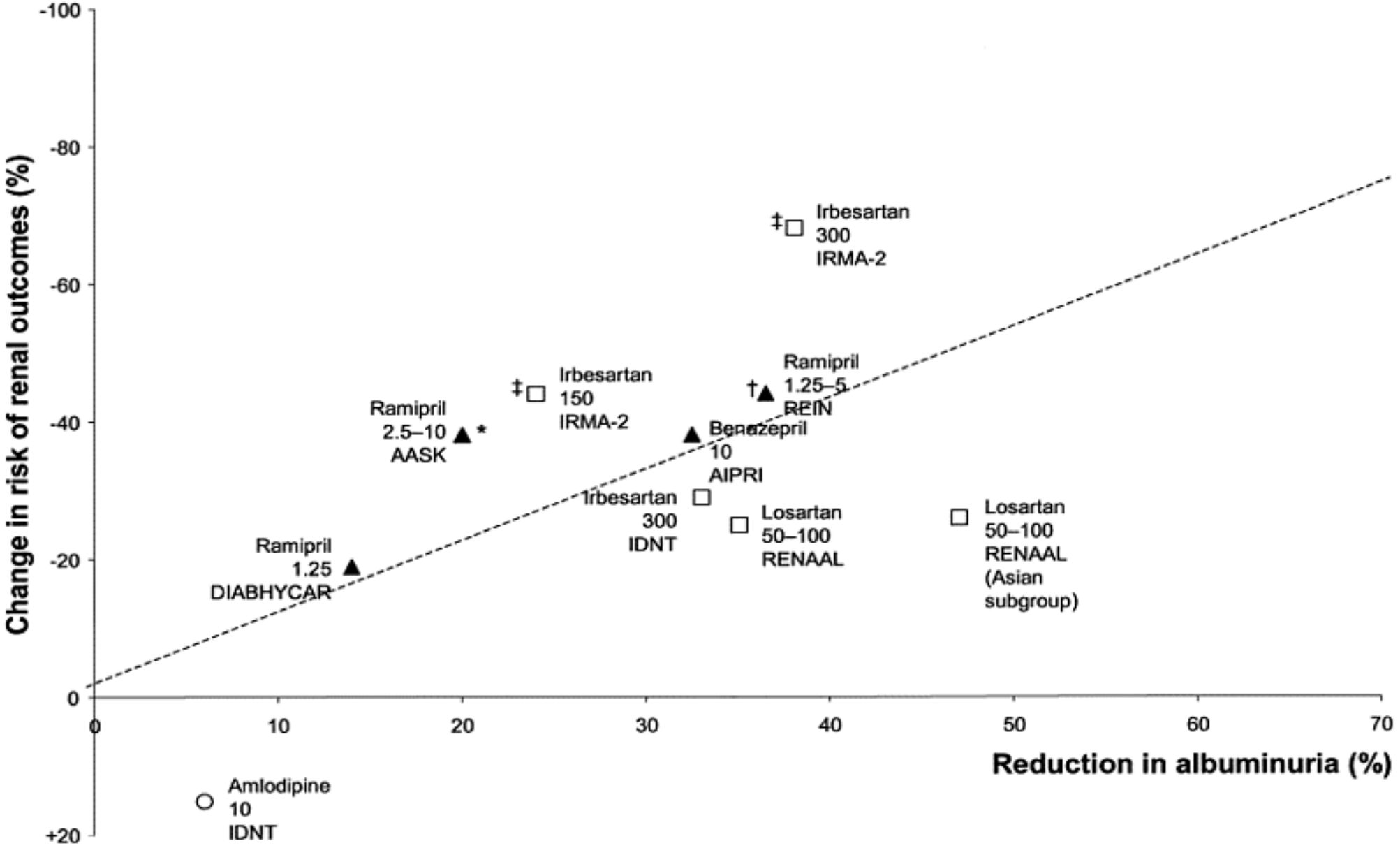
Cibles recommandées pour le contrôle des FR du Diabète

Table 10—Summary of recommendations for glycemic, blood pressure, and lipid control for most adults with diabetes

A1C	<7.0%*
Blood pressure	<140/80 mmHg**
Lipids	
LDL cholesterol	<100 mg/dL (<2.6 mmol/L)† Statin therapy for those with history of MI or age over 40 plus other risk factors

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations. **Based on patient characteristics and response to therapy, lower SBP targets may be appropriate. †In individuals with overt CVD, a lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/L), using a high dose of a statin, is an option.

Change in risk for renal outcomes associated with treatment-induced decreases in **albuminuria** (Basi and Lewis AJKD 2006)



Intérêt des bloqueurs du SRA dans la MRD

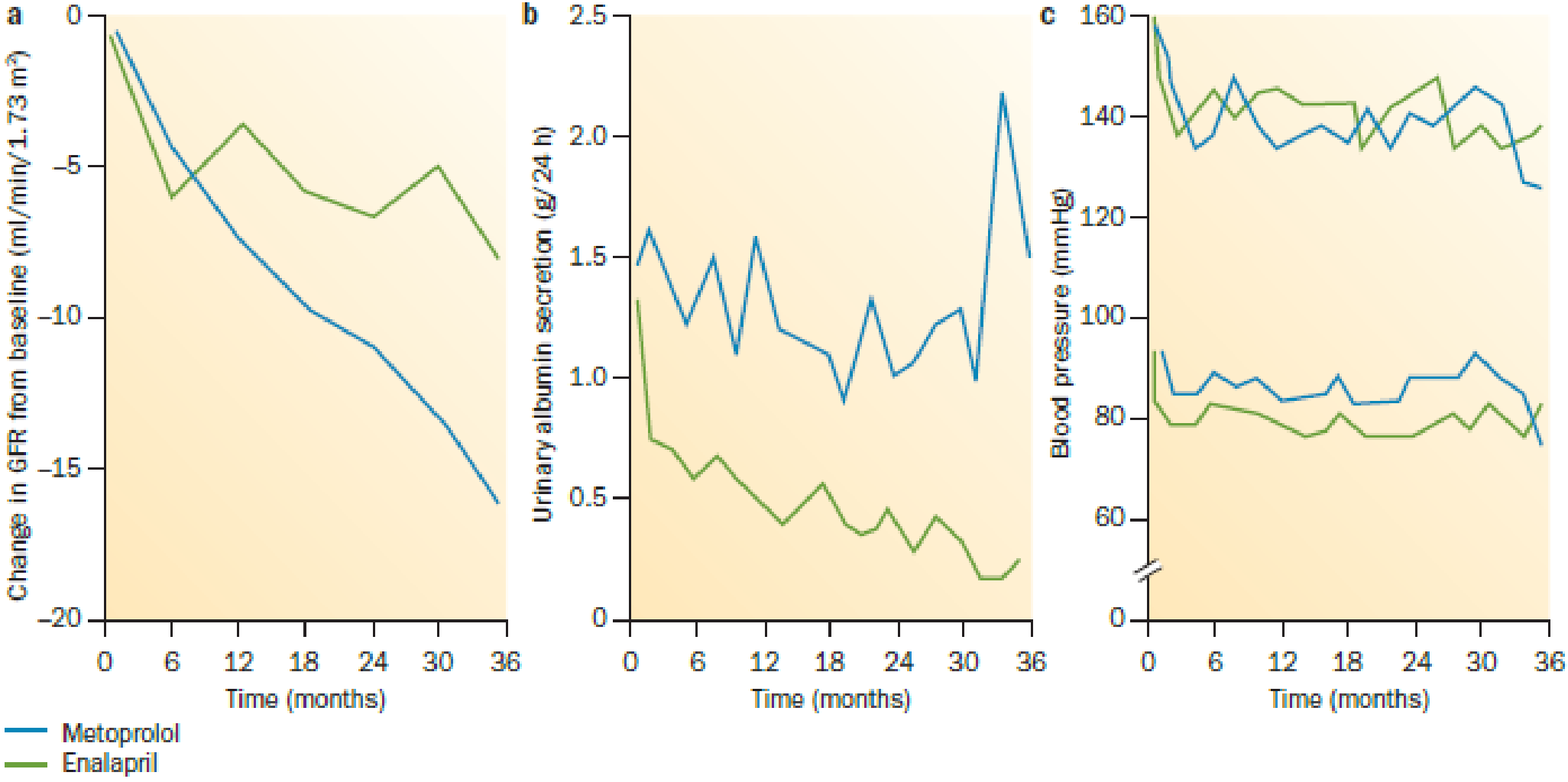


Figure 3 | The effect of enalapril versus metoprolol on surrogate outcomes in patients with type 1 diabetes ($n = 40$). Enalapril **a** | attenuated the decline in glomerular filtration rate and **b** | reduced urinary albumin excretion compared with metoprolol. **c** | Blood pressure control was similar between the treatment groups. Reproduced from © Björck *et al. BMJ* **304**, 339–343 (1992), with permission from BMJ Publishing Group Ltd.

Treatment strategies in patients with diabetes

BP target 140/80 mmHg

Journal of Hypertension 2013, 31:1281–1357

All classes of antihypertensive agents are recommended and can be used in patients with diabetes; RAS blockers may be preferred, especially in the presence of proteinuria or microalbuminuria.	I	A
It is recommended that individual drug choice takes comorbidities into account.	I	C
Simultaneous administration of two blockers of the RAS is not recommended and should be avoided in patients with diabetes.	III	B

Précaution d'emploi des inhibiteurs du système Rénine angiotensine

Complications : hyperkaliémie et insuffisance rénale aigüé hémodynamique

→ contrôle de la créatinine et du potassium après introduction, à J2 et J10 si terrain vasculaire, pour dépister une SAR mais aussi lors de tout événement qui modifie les pressions vasculaires au niveau du rein : Déshydratation, fièvre, diarrhée…..

→ ne pas associer avec d'autres molécules hyperkaliémiantes : diurétiques épargneurs potassiques , AINS, sels potassiques .

L'augmentation de la dose d'ARA2 au delà de la dose préconisée n'a pas d'effet sur la TA mais permet dans certains cas une majoration de l'effet anti protéinurique de 30%.

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Etude STENO

Glycémie
PA
Lipides
Tabac

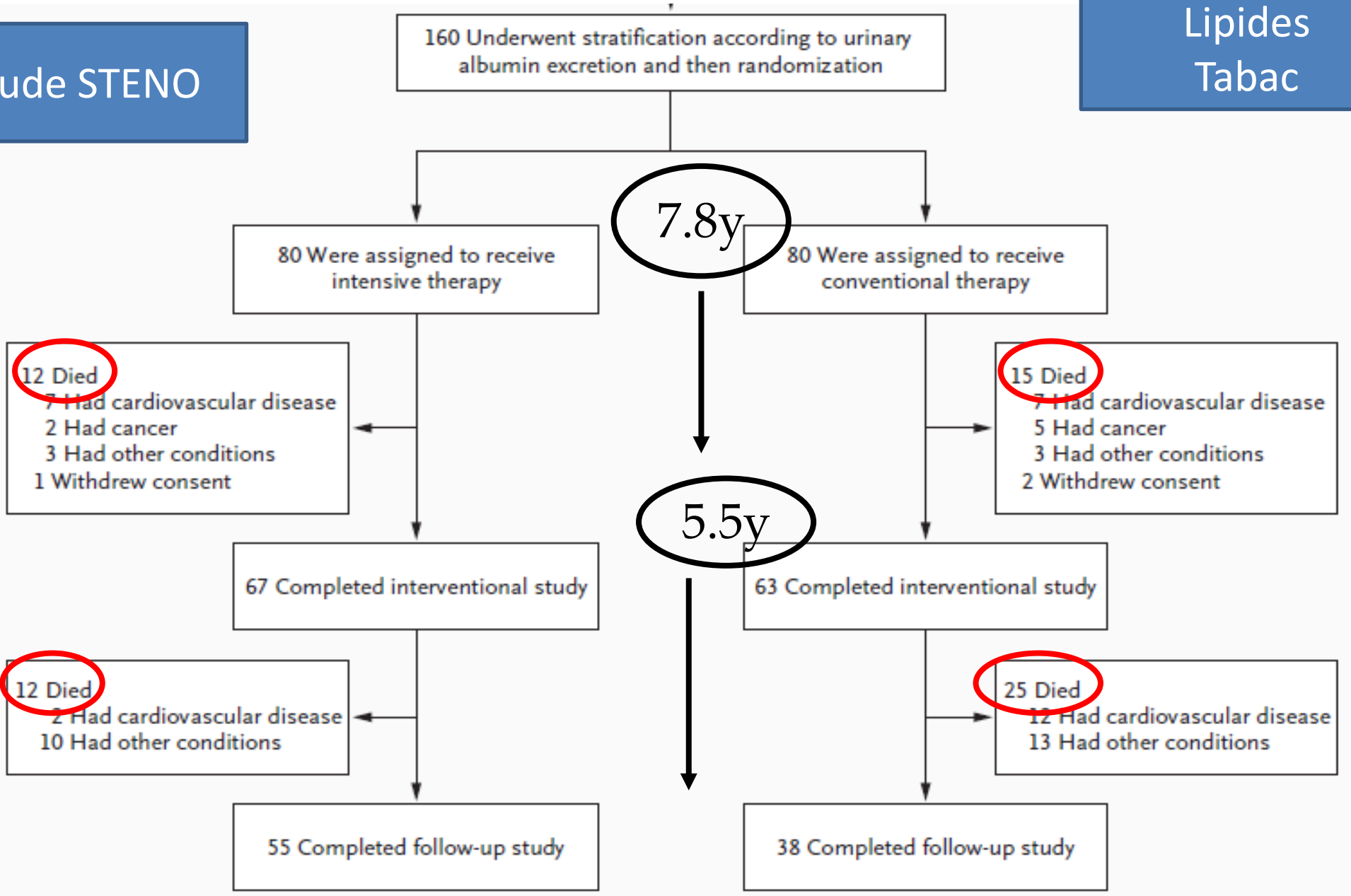


Figure 1. Enrollment and Outcomes.

Approche multifactorielle diabète tpe 2 (STENO)

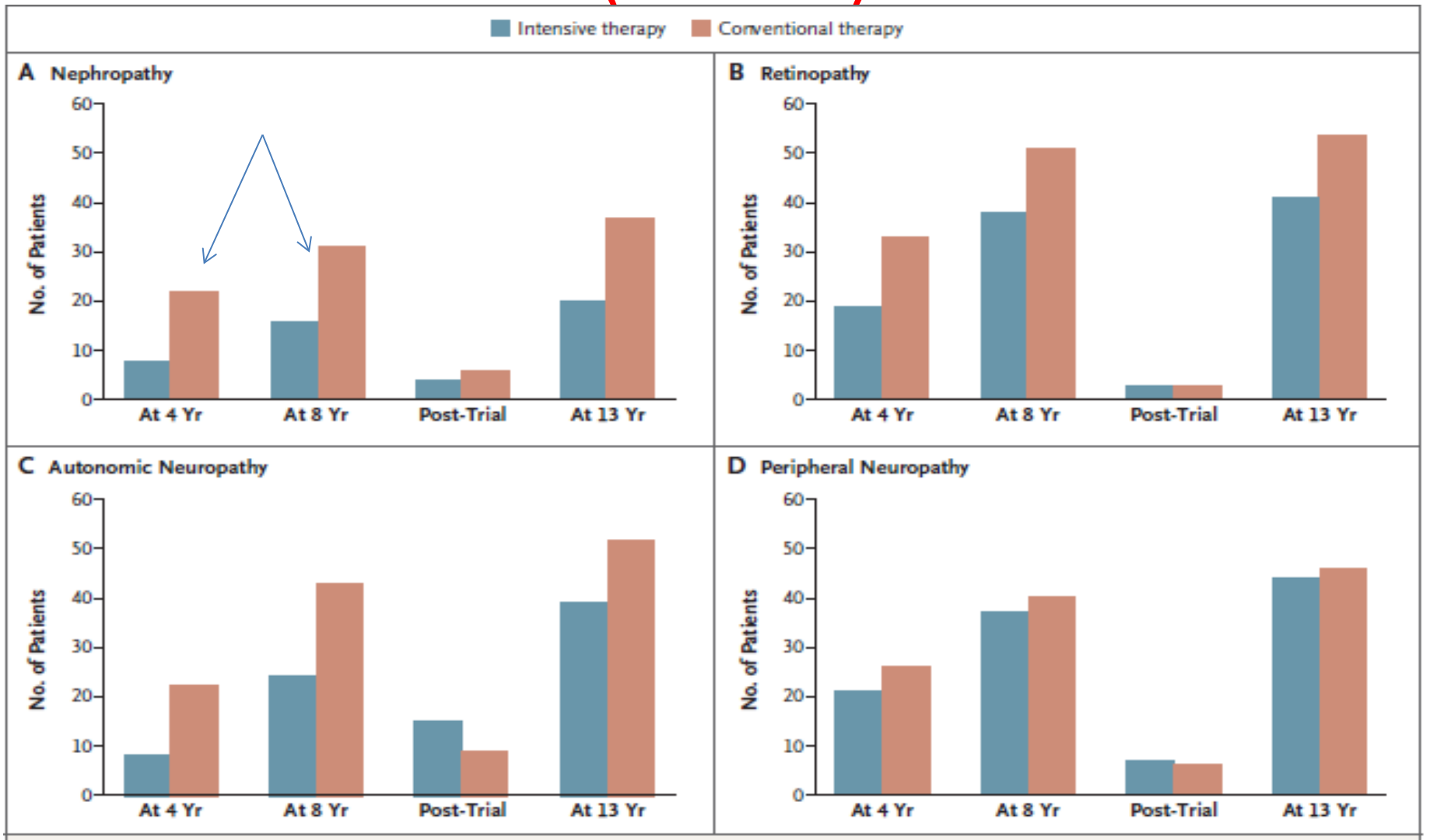


Figure 4. Patients with Development or Progression of Diabetic Nephropathy, Retinopathy, Autonomic Neuropathy, and Peripheral Neuropathy.

The bars labeled "Post-Trial" refer to the number of patients in whom the condition progressed during the period from the end of the original intervention trial to the end-point examination after an average of 13.3 years of study and follow-up.

Comment prendre en charge la MRD

Table 13—Management of CKD in diabetes

GFR	Recommended
All patients	Yearly measurement of creatinine, urinary albumin excretion, potassium
45–60	Referral to a nephrologist if possibility for nondiabetic kidney disease exists (duration of type 1 diabetes <10 years, heavy proteinuria, abnormal findings on renal ultrasound, resistant hypertension, rapid fall in GFR, or active urinary sediment on ultrasound) Consider need for dose adjustment of medications Monitor eGFR every 6 months Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly Assure vitamin D sufficiency Consider bone density testing Referral for dietary counseling
30–44	Monitor eGFR every 3 months Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin, weight every 3–6 months Consider need for dose adjustment of medications
<30	Referral to a nephrologist

Suivi biologie
DFG
< 60 : 6 mois
< 30 : 3 mois

Diabetes Care Volume 37, Supplement 1, January 2014

Conclusions

- Diabète = grand risque Maladie rénale
- Maladie rénale = risque CV>
- Approche multifactorielle nécessaire: non médicamenteuse et médicamenteuse
- Dépistage précoce nécessaire
- Adaptation posologique des ADO
- Rôle majeur joué par le MG!
- Collaboration multidisciplinaire indispensable!
- Trajet de Soin en Néphrologie à proposer!

Merci pour votre attention

FIGURE 2: Suggested use and dose adaptation of glucose-lowering drugs according to the CKD stages (see also Table 1 for details)