

# Maladie cardiovasculaire et maladie rénale chronique chez l'enfant

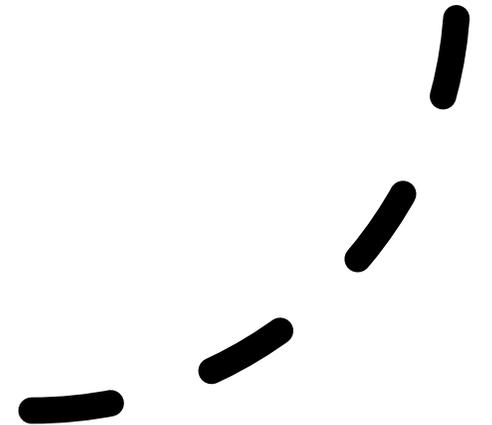
Dr Julie BERNARDOR

*Congrès SNP, Reims  
20 Novembre 2025*



# Outline

- **Épidémiologie**
- **Facteurs de risque et physiopathologie**
- **Prévention et prise en charge**
- **Recherche...**



# Survie pédiatrique



**USRDS**  
UNITED STATES RENAL DATA SYSTEM

- 1990-2010, N=23 400 en dialyse
- **39 décès/1000 patients/an** chez l'enfant > 5 ans
- **99 décès/1000 patients/an** chez l'enfant <5 ans
- Causes de décès
  - **MCV 35-38%**
  - Infections 16-19%

*Mistnefes et al. JAMA 2013*



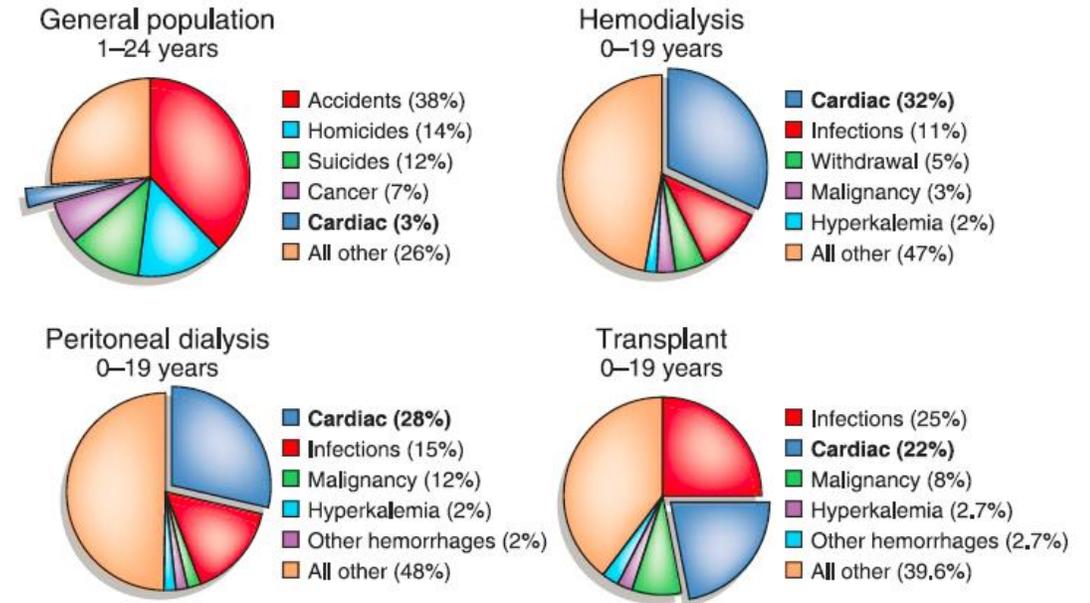
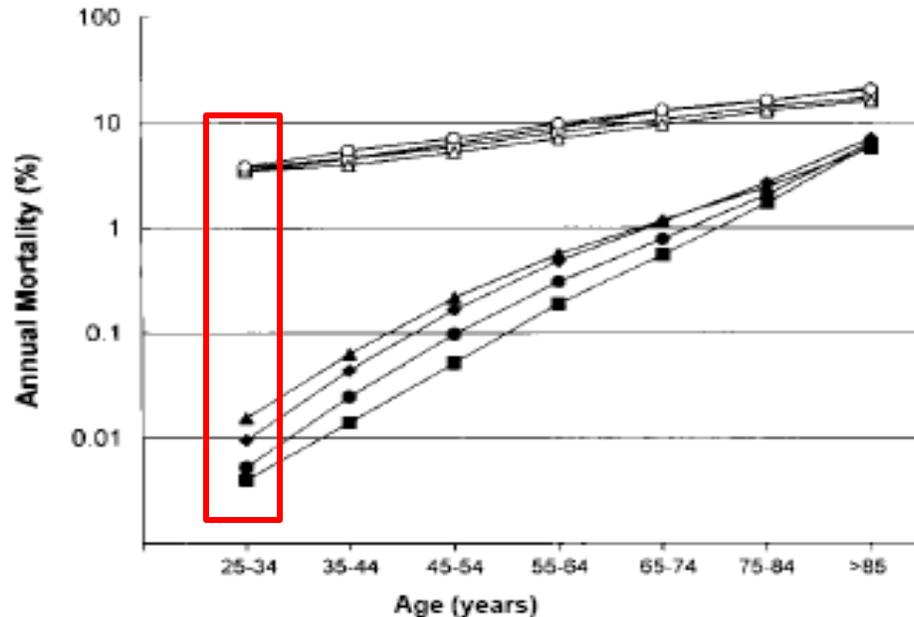
**ESPN/ERA-EDTA Registry**  
European Registry for Children on Renal Replacement Therapy

- 2000-2013, N=6 473 en dialyse
- Suivi médian= 2.17 ans
- Survie à 5 ans 89,5 %
- **16 décès/1000 patients/an** chez l'enfant > 5 ans
- **49 décès/1000 patients/an** chez l'enfant < 5 ans
- Causes de décès
  - **MCV 25%**
  - Infections 17%
- Facteur de risque
  - **0-5 ans ; 1ère année de vie en dialyse**

*Chesnaye et al. Kidney Int 2016*

# Mortalité cardiovasculaire en MRC pédiatrique

Exceedingly high CV mortality in young dialysis patients compared to the general population



**Figure 1.** Leading causes of death in general pediatric population and in children on renal replacement therapy. Data are presented as percentages. Data for dialysis and transplant patients are from the USRDS (2011).<sup>2</sup> Data for general pediatric population are from Mathews et al. (2011).<sup>1</sup>

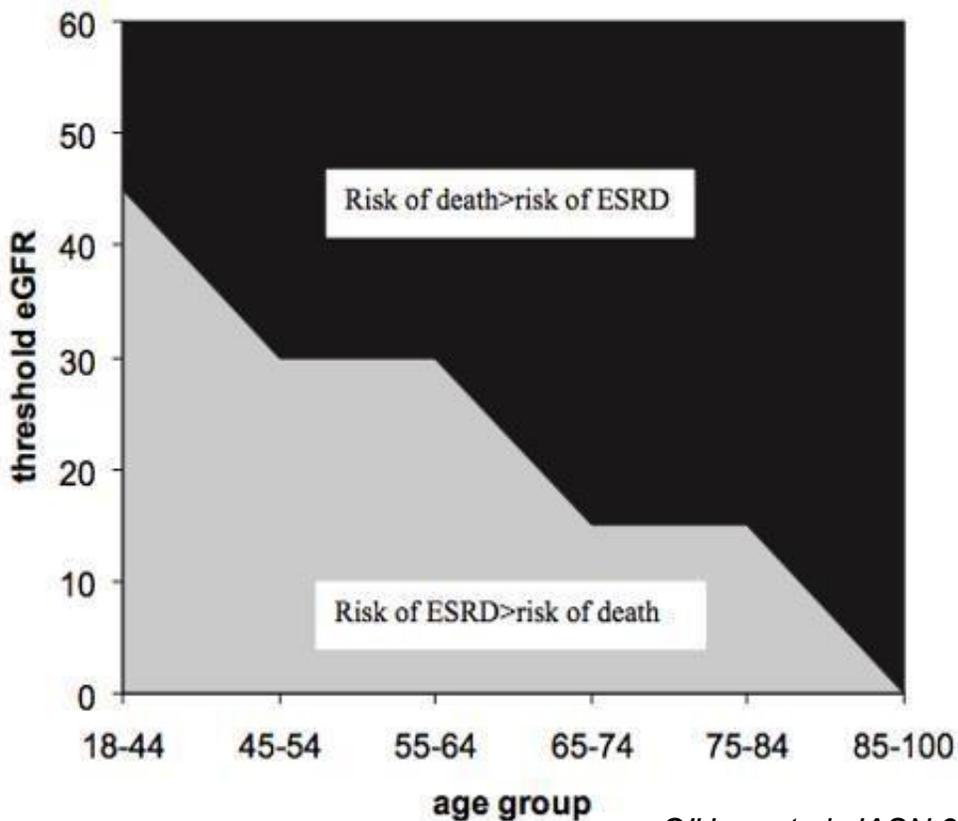
# Diminution de l'espérance de vie

**USRDS**  
UNITED STATES RENAL DATA SYSTEM

> 50 % de tous les décès sont liés à la MCV chez les patients adultes

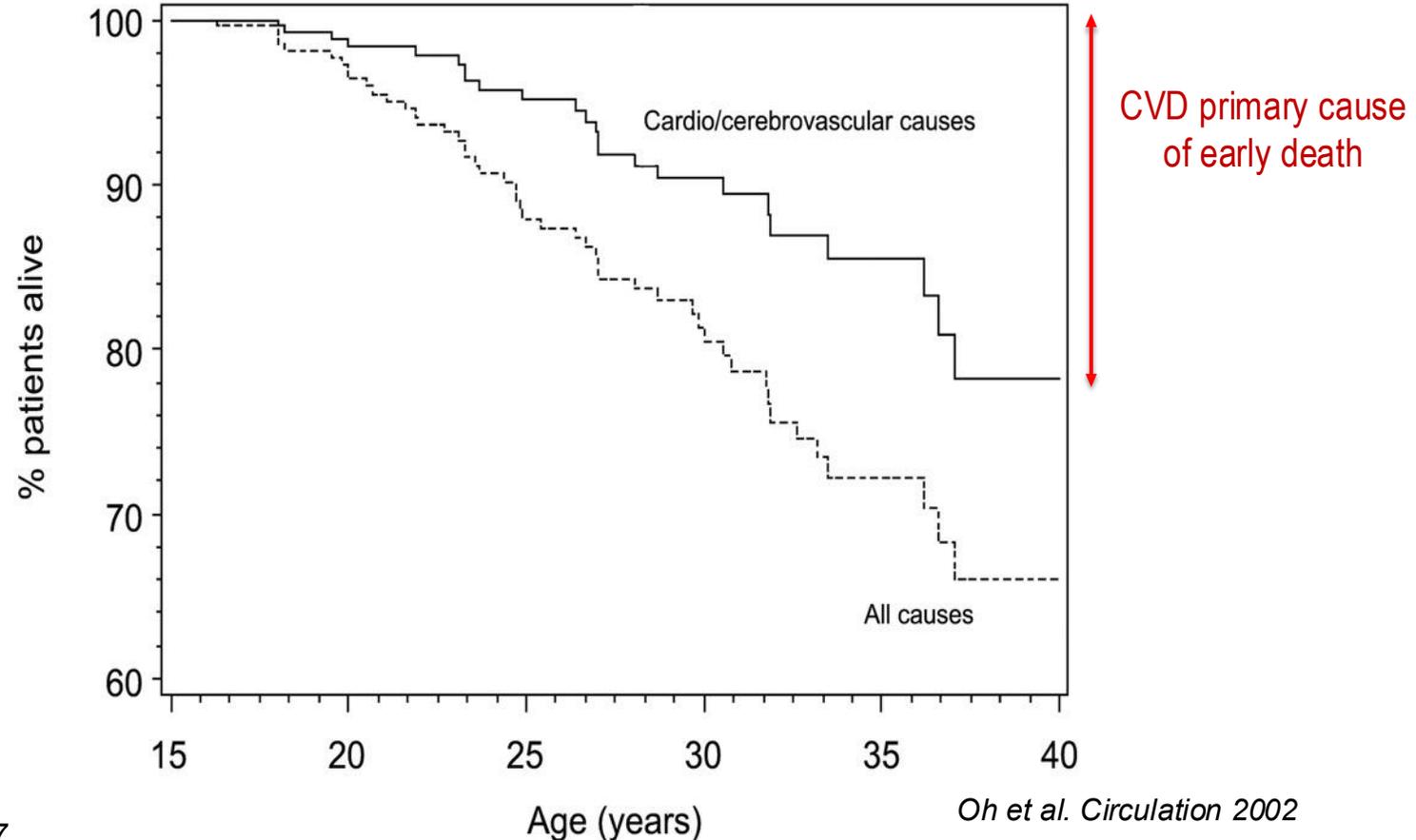
USRDS Annual Report 2020

Les patients adultes atteints d'IRC sont plus susceptibles de mourir de **MCV** que d'évoluer vers une IRT



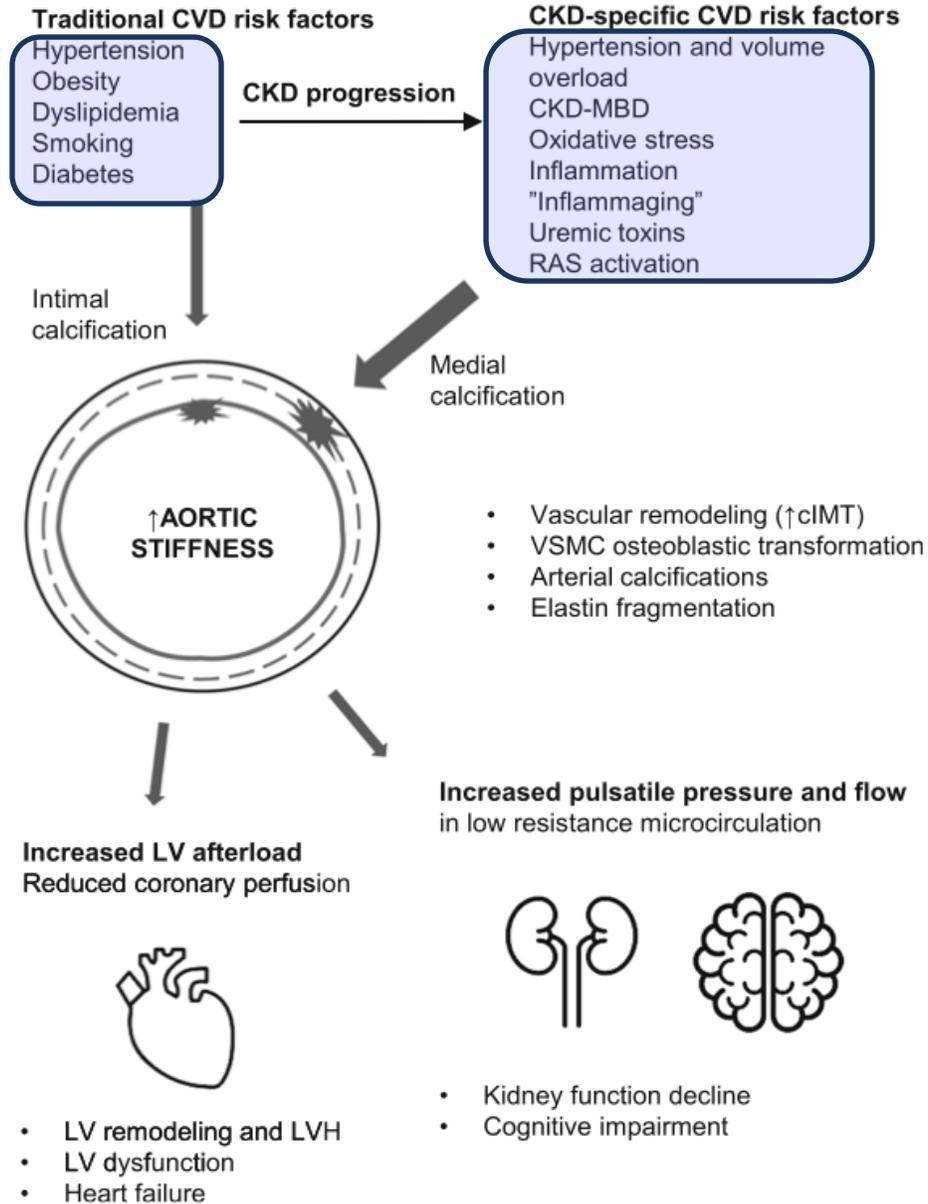
O'Hare et al. JASN 2007

Les MCV sont la principale cause de décès chez les adultes atteints d'IRC dans l'enfance



Oh et al. Circulation 2002

# Facteurs de risque de MCV



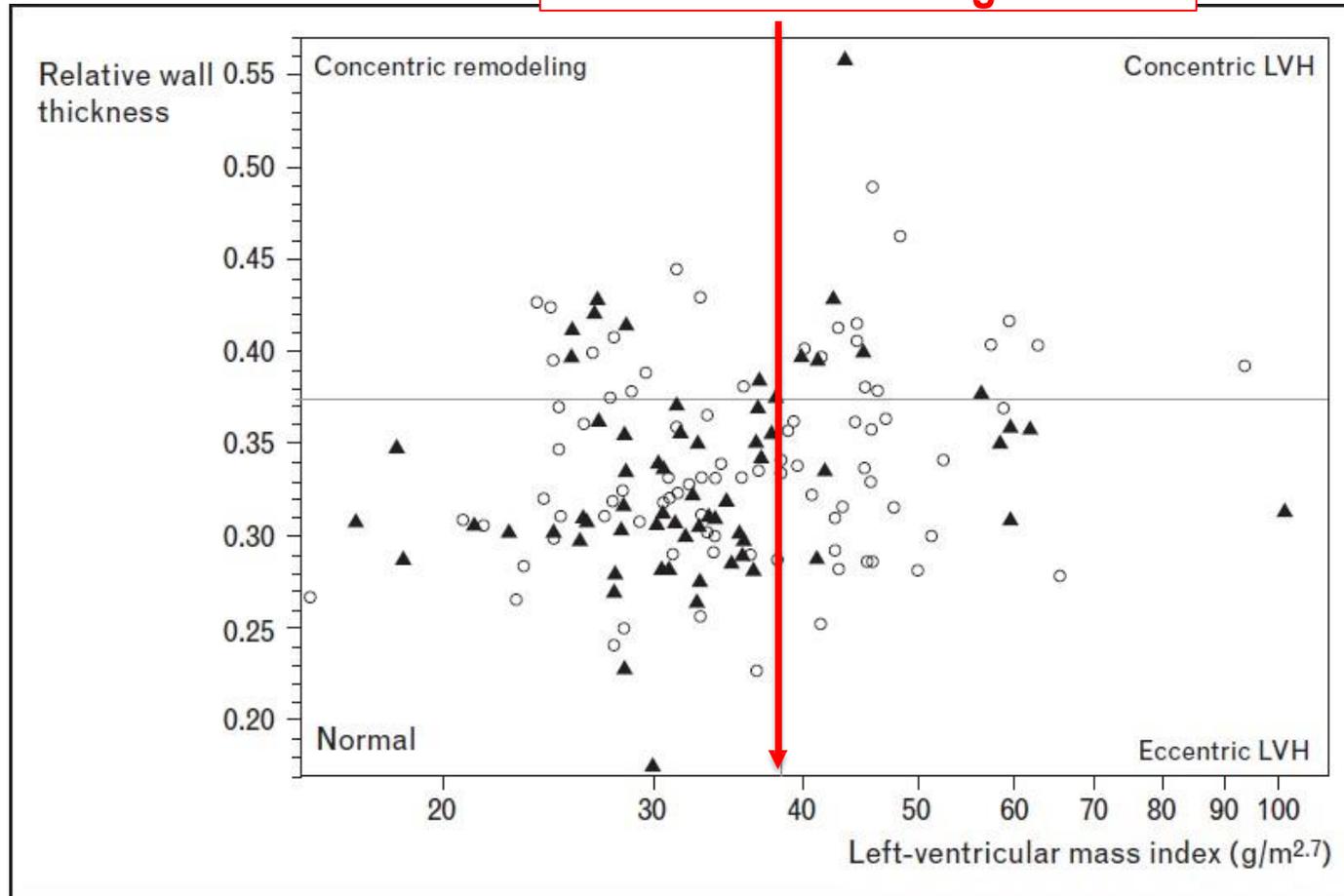
# Facteurs de risque de MCV en MRC pédiatrique

| Risk factors                       | CKD stages 2-5 (%) | Dialysis (%) | Kidney transplant (%) |
|------------------------------------|--------------------|--------------|-----------------------|
| <b>Traditional</b>                 |                    |              |                       |
| Hypertension                       | 50                 | 50-75        | 70-80                 |
| Dyslipidemia                       | 45                 | 40-90        | 55-85                 |
| Altered glucose metabolism         | 30                 | 50           | 30-60                 |
| Obesity                            | 30                 | 15           | 15-30                 |
| Sedentary lifestyle                |                    | 90           | 90                    |
| <b>Non traditional</b>             |                    |              |                       |
| Anemia                             | 20                 | 75           | 15                    |
| Increased Ca and/or P              | 30-40              | 50-80        |                       |
| HyperPTH                           | 30-45              | 50-60        | 75                    |
| Inflammation                       |                    | 75           | 15                    |
| Oxidative stress / RAAS activation |                    |              |                       |
| Volume overload                    |                    | >50          |                       |

# MCV: phénotype « précoce »

## ESCAPE Trial

LVH definition  $>38.5 \text{ g/m}^{2.7}$



HVG détectée chez  
1/3 des enfants avec  
une IRC légère à  
modérée

# MCV: phénotype « précoce »

Data from Cardiovascular Comorbidity in Children with CKD (4C) and Haemodiafiltration, Heart and Height (3H) studies

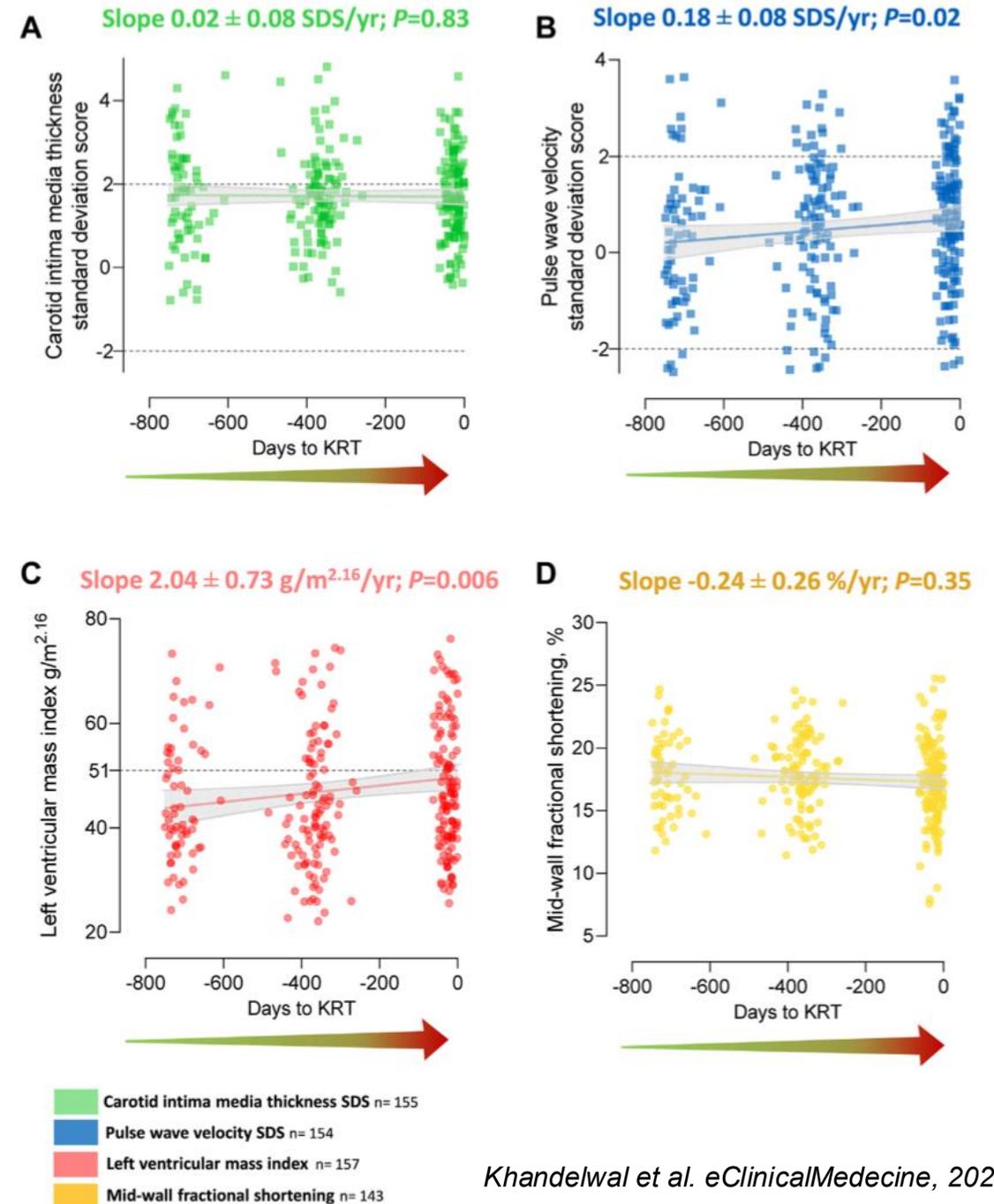
**75,8 %** des patients présentent au moins une anomalie cardiovasculaire à l'entrée en KRT

- cIMT (>2ds):, **42,6 %**
- PWV (>2 SDS): **24,8 %**
- HVG: **49,3 %**

**>50 %** des patients présentent des FdR CV à l'entrée en KRT

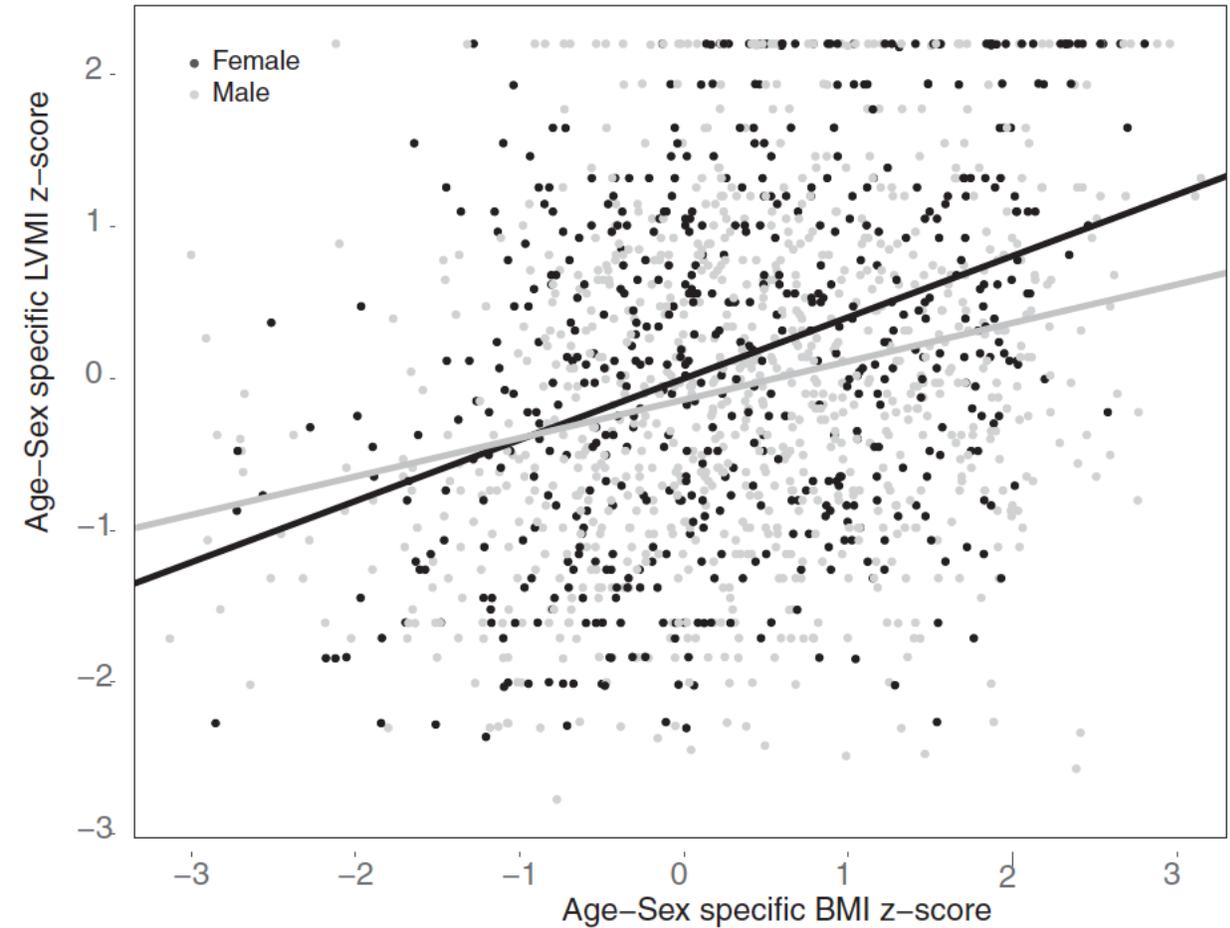
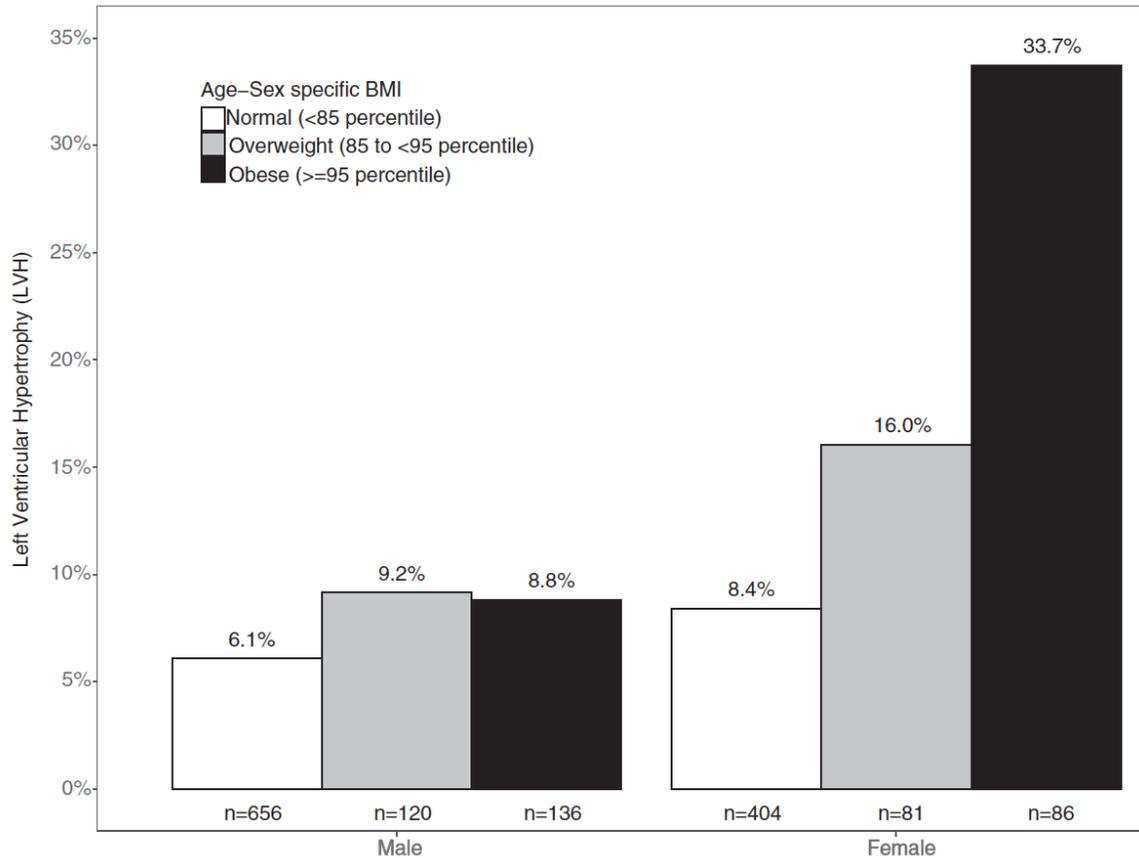
- HTA (HTA non contrôlée : 60%; masquée 14.5%)
- Anémie, acidose, hyperphosphatémie, HPT secondaire, dyslipidémie; obésité

La santé cardiovasculaire se dégrade significativement dans les 2 années précédant la KRT



# Role de l'obésité

Suivi median 3.3 ans



L'adiposité (IMC) constitue un **facteur indépendant de dommage myocardique** chez les enfants avec CKD, **plus marqué chez les filles** (persiste après ajustement DFG et TA)

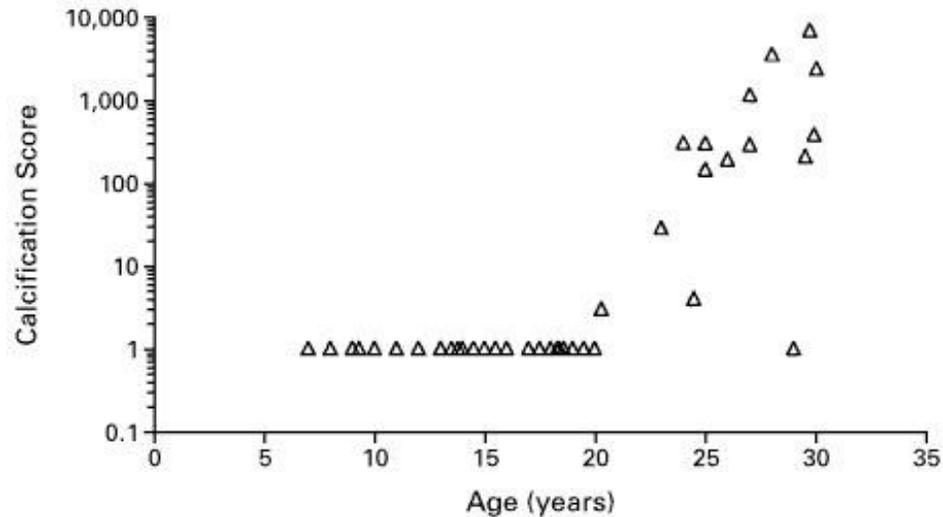
# Phénotype « tardif »: Calcifications vasculaires (CV)

“CV damage in the form of athero- and arteriosclerosis”



## Coronary-Artery Calcification in Young Adults with End-Stage Renal Disease Who Are Undergoing Dialysis

William G. Goodman, M.D., Jonathan Goldin, M.D., Ph.D., Beatriz D. Kuizon, M.D., Chun Yoon, M.D., Ph.D., Barbara Gales, R.N., Donna Sider, R.N., Yan Wang, Ph.D., Joanie Chung, M.S., Aletha Emerick, Lloyd Greaser, M.P.H., Robert M. Elashoff, Ph.D., and Isidro B. Salusky, M.D.



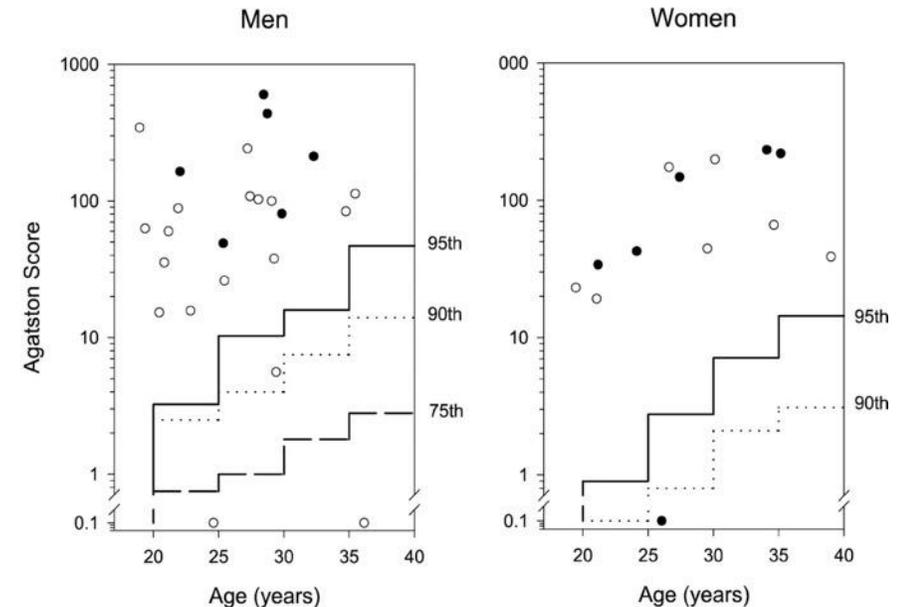
- 39 enfants et jeunes adultes < 30 ans
- Durée moyenne dialyse :  $7 \pm 6$  ans (range 0,3 à 21)
- Aucun des 23 patients <20 ans n'a eu de CAC
- mais 14 /16 patients âgés de 20 à 30 ans avaient CAC

## Circulation

Volume 106, Issue 1, 2 July 2002; Pages 100-105  
<https://doi.org/10.1161/01.CIR.0000020222.63035.CO>

## CLINICAL INVESTIGATION AND REPORTS

### Advanced Coronary and Carotid Arteriopathy in Young Adults With Childhood-Onset Chronic Renal Failure

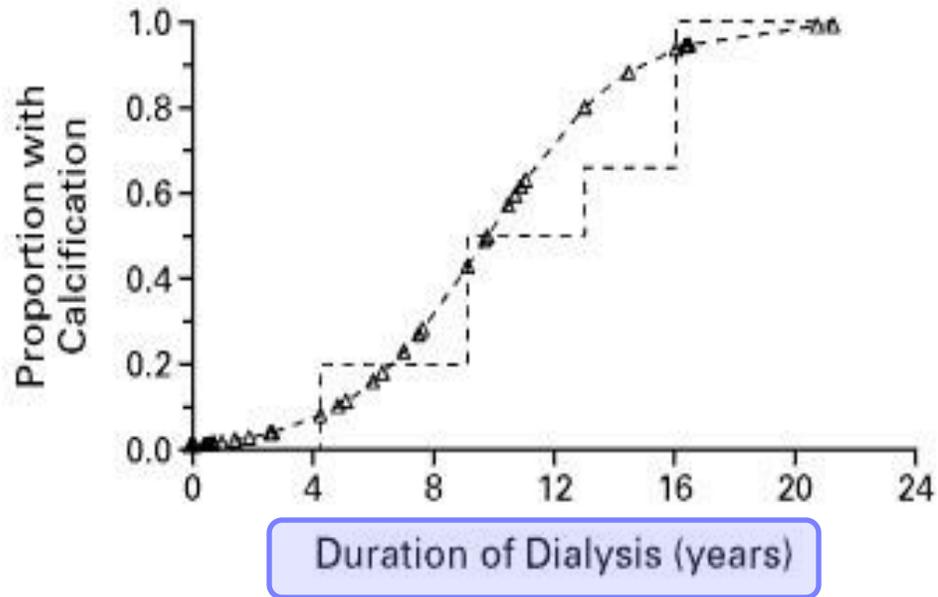


- 39 adultes atteints d'IRC infantile
- 92 % avec calcifications vasculaires

# Dialyse et CAC

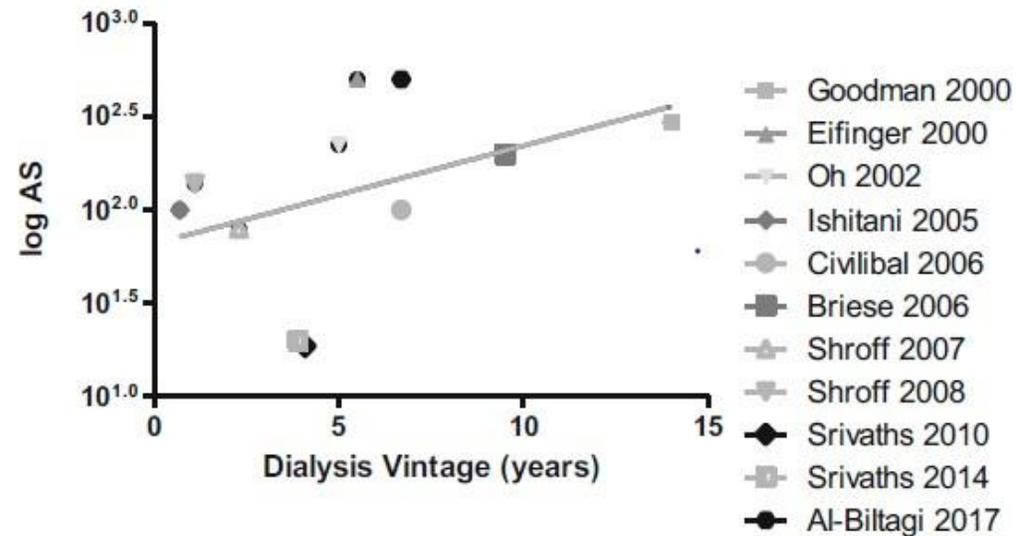
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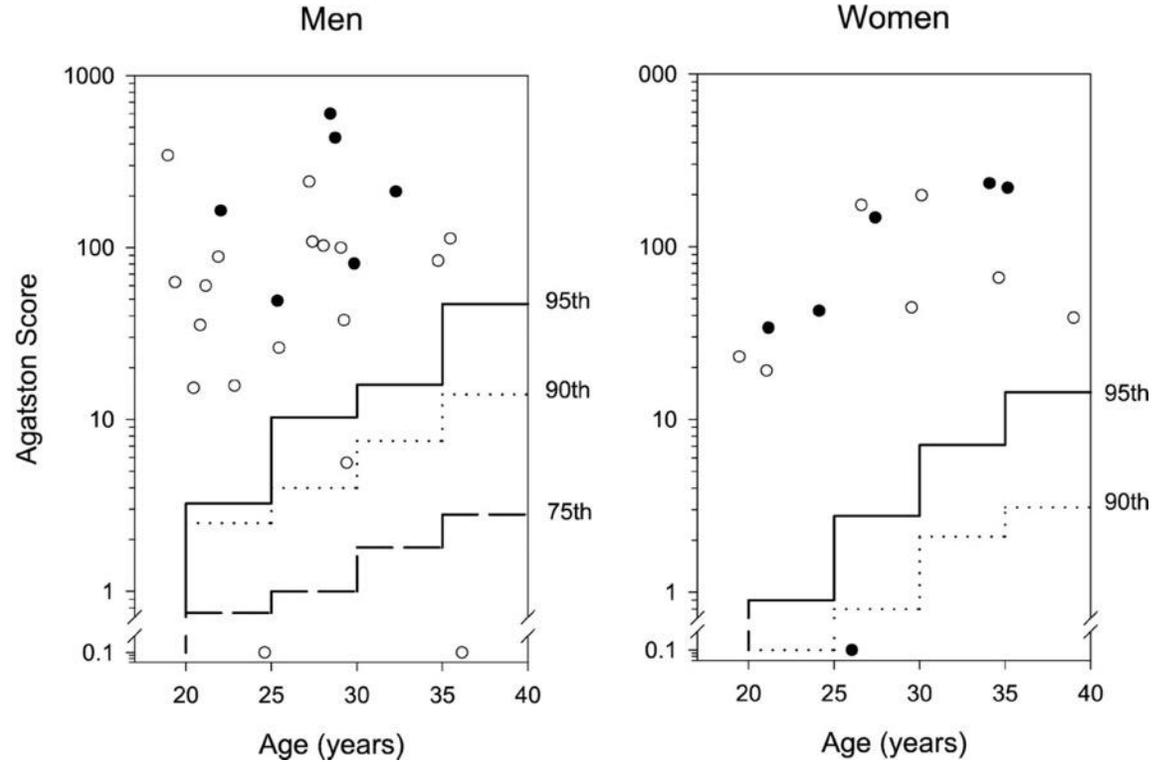
Goodman et al. NEJM 2000

## Coronary Calcifications in Young Patients with ESKD

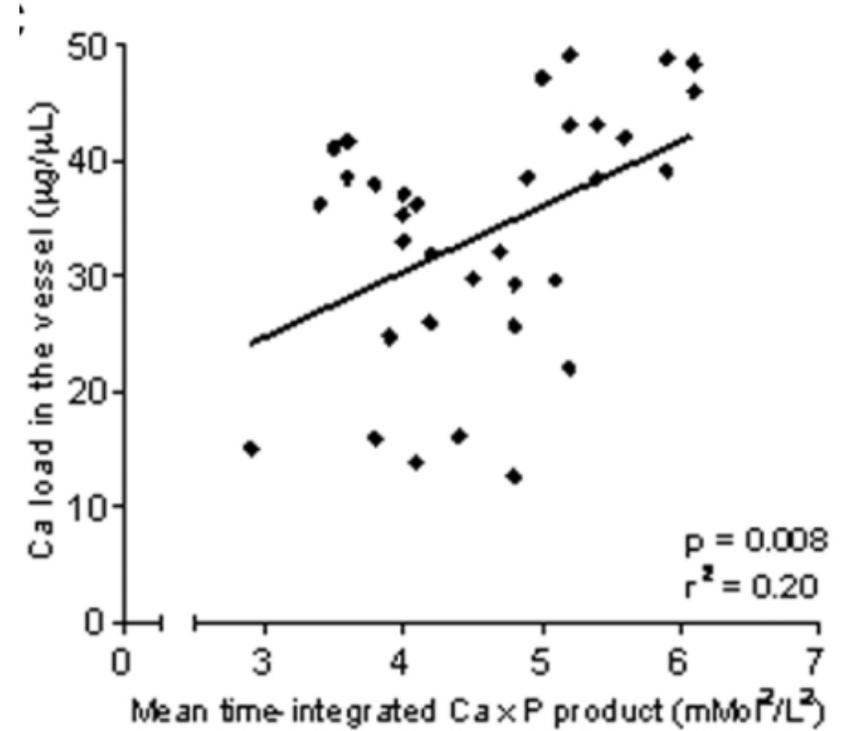


Querfeld & Schaefer. Pediatr Nephrol 2019

# CKD-MBD et CAC

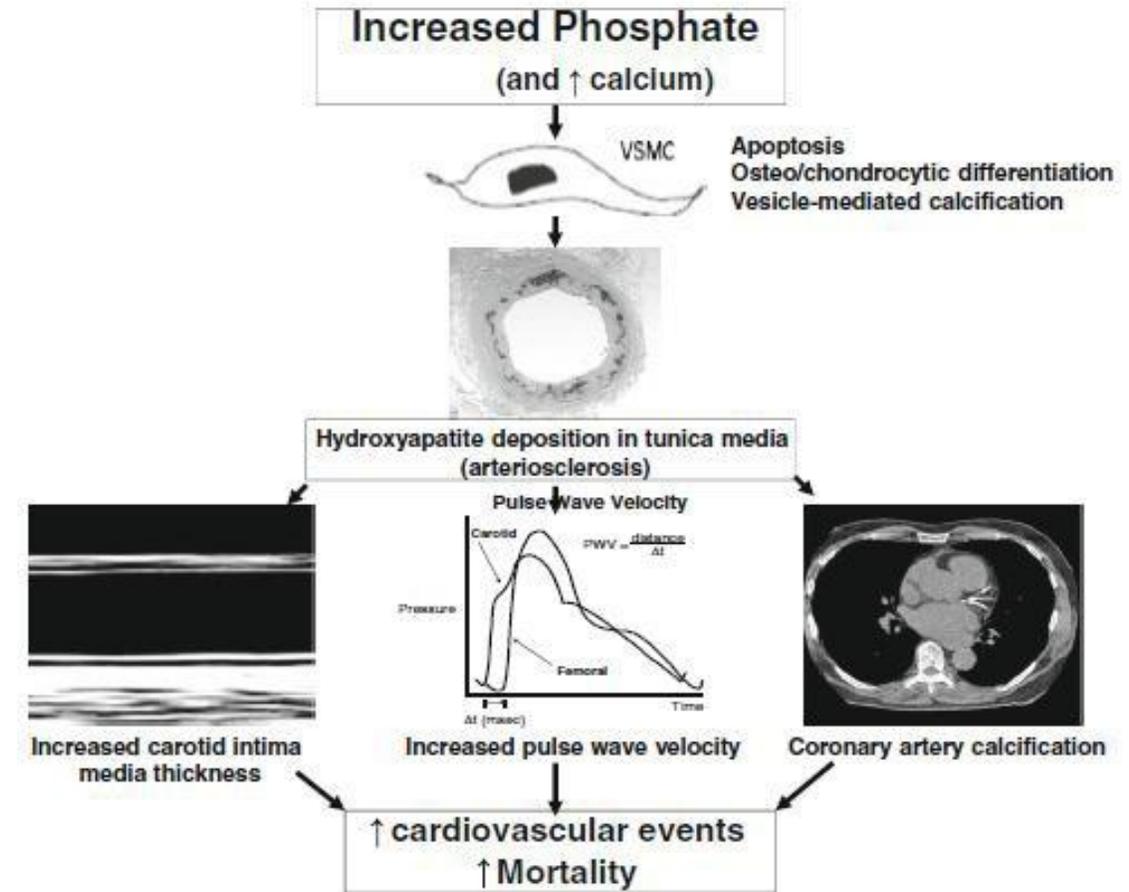
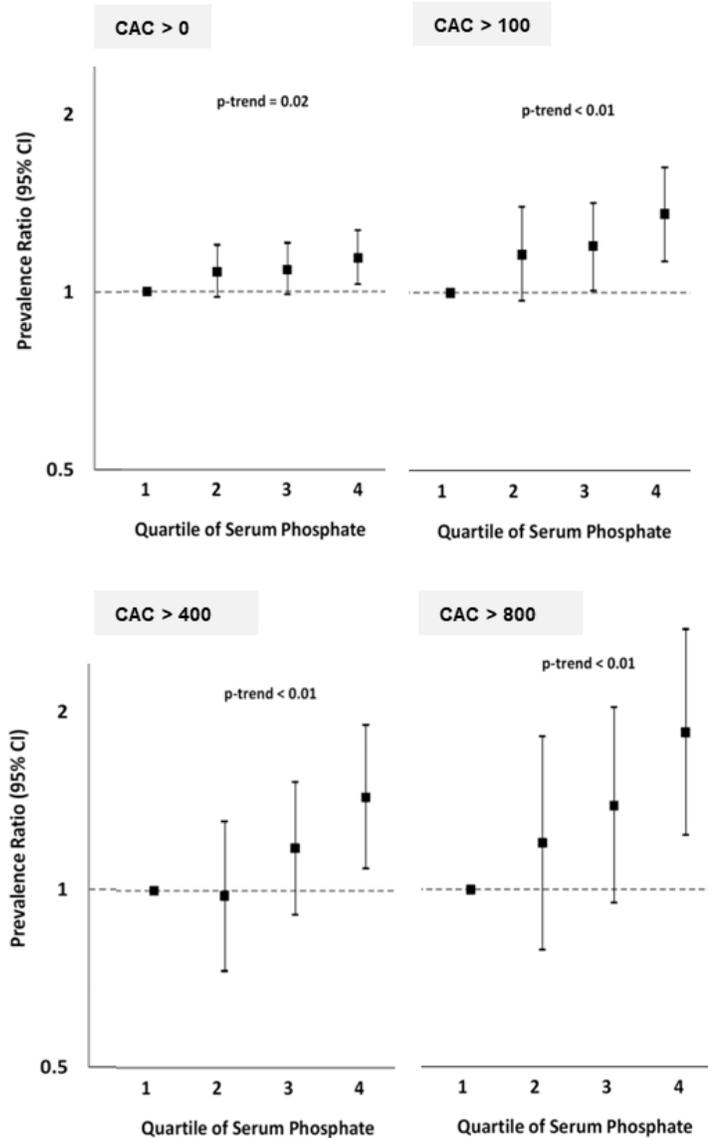


Association avec hyperPTH,  
Ca-P overload, inflammation



Predialysis: Ca-P overload

# Phosphate: “silent killer”



Chez 1501 patients avec MRC

# Comment évaluer la MCV?

## Risques CV traditionnels

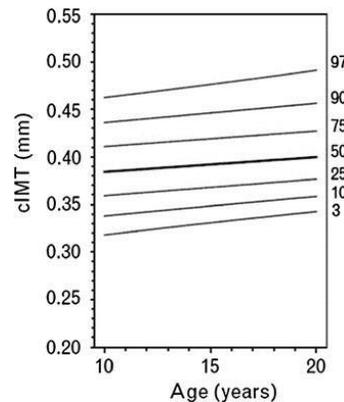
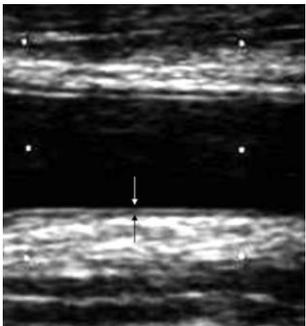
- Age sexe, BMI
- Dyslipidémie
- Tension artérielle
- Diabète , tabac

## Risque CV spécifiques

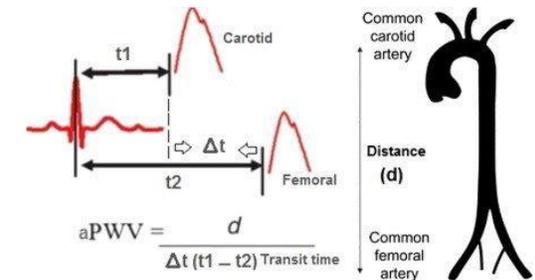
- GFR, albuminurie
- Ph-Ca-PTH
- Anémie
- Hypoalbuminémie, inflammation

## Évaluation CV

- TA, MAPA
- Échographie cardiaque



**En recherche**  
FGF23, cIMT, PWV,  
Fetuin A, pyrosphosphate, MGP



# Peut-on prévenir la maladie cardiovasculaire ?



## Contrôle de la pression artérielle

Pour prévenir le phénotype « précoce »  
(LVH)



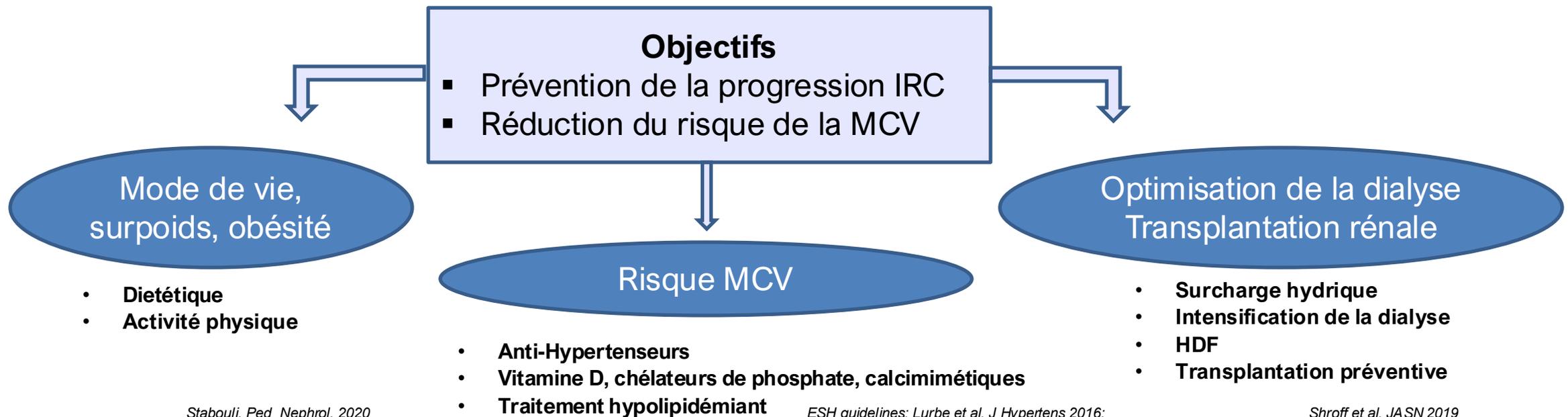
## CKD-MBD

Pour maintenir un équilibre adéquat Ca/Ph



## Optimisation de la dialyse

Pour diminuer la période de dialyse



# Traitement de la MCV

## Management of CV risk factors in children with CKD2-5

Figure 2

Step 1

### Lifestyle modification



Healthy plant-slant diet, maintain normal weight, age-appropriate physical activity and sleep duration, limit screen time, avoid smoking and second-hand smoke exposure

Step 2

### Pharmacotherapy



#### BP pressure control

Target BP

- <75<sup>th</sup> pc in stages 2-5 CKD without proteinuria
- <50<sup>th</sup> pc in stages 2-5 CKD with proteinuria

**1st line** ACEi or ARBs

**2nd line** Calcium Channel Blockers, Beta Blockers or Diuretics

MAPA annuel

#### Dyslipidemia

Consider if LDL is persistently above 190 mg/dL

**1st line** statins and/or ezetimibe in all children with CKD CKD2-5D,T

Consider if triglycerides above 200 mg /dL

**1st line** omega-3 supplements

#### Glycemic control

Consider if glucose targets are not met, pharmacological treatment as per American Diabetes Association 2023 with advice of pediatric endocrinologist

Anti-SGLT2  
>10ans

#### CKD MBD

- Ca and P within the age- and sex-related normal ranges, PTH within the CKD-stage dependent target range
- Haemoglobin levels at the lower limit of normal range

- Maintain 25(OH)D >75 nmol/L with cholecalciferol
- Use lowest effective doses of active vitamin D to prevent hypocalcemia and for PTH control
- Correct metabolic acidosis

Treat proteinuria

# Équilibre nutritionnel pour la prise en charge du CKD-MBD

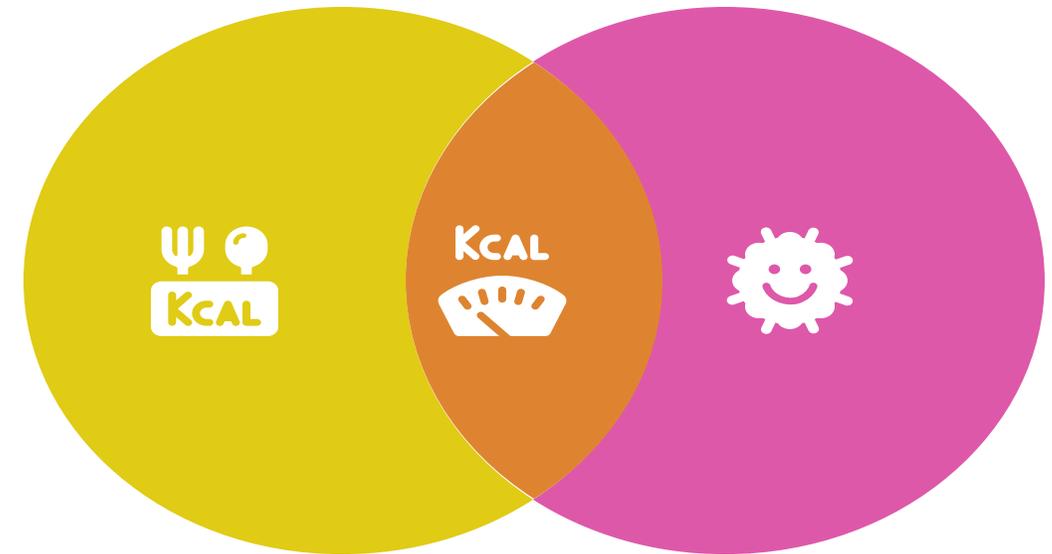
## Apport calorique et protéique adéquat

**Table 1** Energy and protein requirements for infants, children and adolescents with CKD2–5D aged 0–18 years

SDI for energy and protein: birth<sup>a</sup> to 18 years

| Month | SDI <sup>b</sup> energy (kcal/kg/day) | SDI protein (g/kg/day) | SDI protein (g/day)    |                              |
|-------|---------------------------------------|------------------------|------------------------|------------------------------|
| 0     | 93–107                                | 1.52–2.5               | 8–12                   |                              |
| 1     | 93–120                                | 1.52–1.8               | 8–12                   |                              |
| 2     | 93–120                                | 1.4–1.52               | 8–12                   |                              |
| 3     | 82–98                                 | 1.4–1.52               | 8–12                   |                              |
| 4     | 82–98                                 | 1.3–1.52               | 9–13                   |                              |
| 5     | 72–82                                 | 1.3–1.52               | 9–13                   |                              |
| 6–9   | 72–82                                 | 1.1–1.3                | 9–14                   |                              |
| 10–11 | 72–82                                 | 1.1–1.3                | 9–15                   |                              |
| 12    | 72–120                                | 0.9–1.14               | 11–14                  |                              |
| Year  | SDI energy (kcal/kg/day)              |                        | SDI protein (g/kg/day) | SDI protein (g/day)          |
| –     | Male                                  |                        |                        |                              |
| 2     | 81–95 <sup>c</sup>                    |                        | 0.9–1.05               | 11–15                        |
| 3     | 80–82                                 |                        | 0.9–1.05               | 13–15                        |
| 4–6   | 67–93                                 |                        | 0.85–0.95              | 16–22                        |
| 7–8   | 60–77                                 |                        | 0.9–0.95               | 19–28                        |
| 9–10  | 55–69                                 |                        | 0.9–0.95               | 26–40                        |
| 11–12 | 48–63                                 |                        | 0.9–0.95               | 34–42                        |
| 13–14 | 44–63                                 |                        | 0.8–0.9                | 34–50                        |
| 15–17 | 40–55                                 |                        | 0.8–0.9                | Male: 52–65<br>Female: 45–49 |

## Optimal Nutritional Management



**Collaborate with a pediatric renal dietitian**

For children with poor growth, reference to the SDI for height age may be appropriate. Height age is the age that corresponds to an individual's height when plotted on the 50th centile on a growth chart

# Apport alimentaire adéquat en phosphate et en calcium



**Evaluer les apports en Ca et Ph**

Regular assessment ensures intake aligns with dietary guidelines.



## Provenant du lait, de l'alimentation, des médicaments

The Ca requirement may need to exceed **twice the SDI** in infants with rapid growth or those with mineral depleted bone



**Maintain Total Ca Intake**

Keeping Ca intake within SDI supports growth and bone health.




**Maintain Dietary P Intake**

Adhering to SDI for P prevents imbalances.



## Maintenir le phosphate sérique dans les valeurs normales pour l'âge (sans compromettre l'apport en protéines)

|                     | iCa mmol/L | Ca mg/dL | Ca mmol/L | P mg/dL  | P mmol/L  |
|---------------------|------------|----------|-----------|----------|-----------|
| 0–14 days           | 1.22–1.40  | 8.5–11.0 | 2.13–2.75 | 5.6–10.5 | 1.81–3.39 |
| 15–30 days          | 1.22–1.40  | 8.5–11.0 | 2.13–2.75 | 4.8–8.4  | 1.55–2.71 |
| 30 days to 6 months | 1.22–1.40  | 8.5–11.0 | 2.13–2.75 | 4.8–8.4  | 1.55–2.71 |
| 6 months to 1 year  | 1.20–1.40  | 8.5–11.0 | 2.13–2.75 | 4.8–8.4  | 1.55–2.71 |
| 1 to 2 years        | 1.22–1.32  | 9.2–10.5 | 2.30–2.63 | 4.3–6.8  | 1.39–2.20 |

Results are presented as lower and upper limit. For calcium, the conversion factor measured calcium (mmol/L) and serum albumin (g/L) is the following:  $CaC = Ca / (0.55 + P/16)$ . For phosphate, the conversion factor is to multiply by 88.4. In the CALIPER database, albumin was assessed with bro

**Table 7** Summary of SDI (suggested dietary intake) for calcium and phosphate in children with CKD2-5D

| Age (years)   | SDI calcium (mg) | SDI phosphate (mg) |
|---------------|------------------|--------------------|
| 0–< 4 months  | 220              | 120                |
| 4–< 12 months | 330–540          | 275–420            |
| 1–3 years     | 450–700          | 250–500            |
| 4–10 years    | 700–1000         | 440–800            |
| 11–17 years   | 900–1300         | 640–1250           |

Bacchetta et al for the ESPN CKD-MBD and dialysis working groups, *Pediatr Nephrol* 2023

# Nouvelles recommandations pour la supplémentation en vitamine D native chez les enfants et les adultes atteints d'IRC



ERA  
NEPHROLOGY DIALYSIS TRANSPLANTATION

## The role of nutritional vitamin D in CKD-MBD in children and adults with CKD, on dialysis, and after kidney transplantation – a European consensus statement

The focus of the study was to address whether to screen for, and correct, vitamin D deficiency in patients with chronic kidney disease.

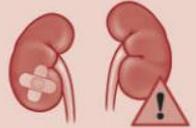
### Methods

Literature review by expert panel

Delphi survey

Revision based on survey replies

### Results

- **Nutritional vitamin D**
- **Chronic kidney disease**
- **CKD-associated osteoporosis**
- **Cardiovascular complications**

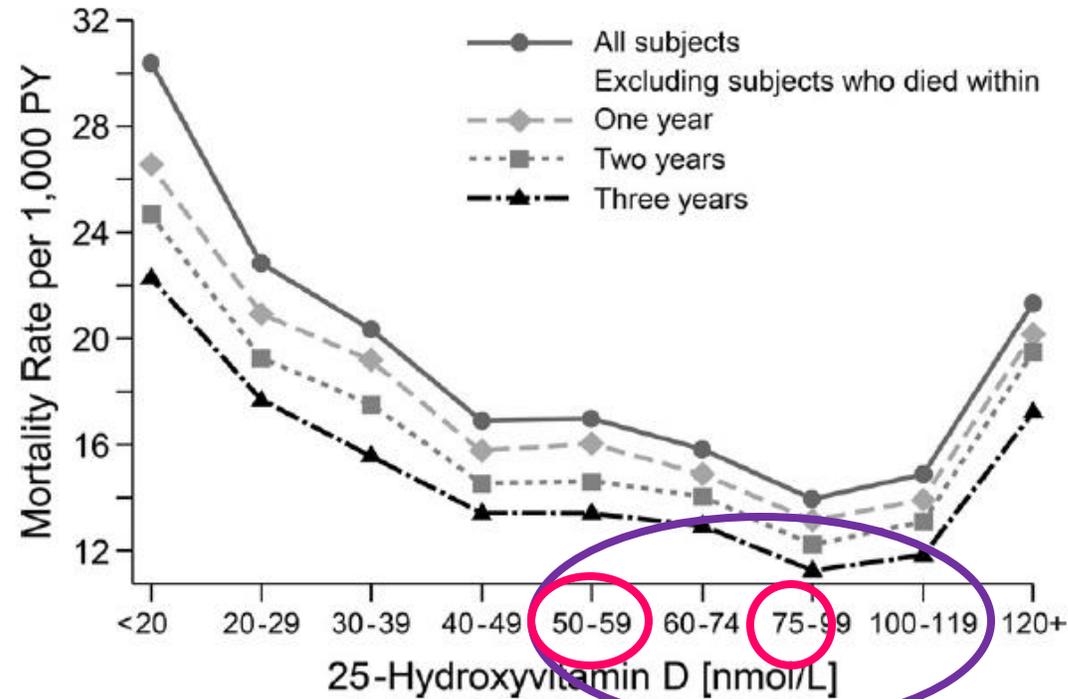
### Key recommendations

-  **Target 25(OH)D >75 nmol/L (>30 ng/mL) in CKD, dialysis and post-transplant**
-  **Avoid Vitamin D mega-doses (>100,000 IU) and 25(OH)D >150–200 nmol/L (60–80 ng/mL)**

Jørgensen, H. S. et al.  
NDT (2024)  
@NDTSocial

**This consensus provides key evidence and clinical practice points, as well as future research recommendations, on vitamin D supplementation in children and adults with CKD, on dialysis, and after kidney transplantation.**

# Trop de contrôle du CKD-MBD?



**Figure 2.** Mortality rate adjusted for age, sex, race/ethnicity, and season by serum 25(OH)D concentration (nanomoles per liter): 15-year follow-up of NHANES III through 2006 (n = 15 099).

Le patient ne meurt pas d'une maladie osseuse  
*Faible dose de vitamine D active + cinacalcet*

Lorsque vous traitez l'os de manière adéquate ...

Bone Mineral Density and Vascular Calcification in Children and



La croissance staturale peut être un facteur important



Multicenter longitudinal study



Tibial cortical and trabecular peripheral quantitative CT

Participants with statural growth had lower annualized cIMT & PWV Z-score change ( $p < 0.0001$  &  $p = 0.02$ )

10% CAC

Le squelette en croissance est capable de tamponner et d'absorber l'excès de calcium ?

84% structural changes



CKD stages 4-5 or on dialysis



- Coronary artery calcification
- Pulse wave velocity (PWV)
- Carotid distensibility
- Carotid intima-media thickness (cIMT)

trabecular BMD predicted annualized cIMT increase ( $p = 0.03$ )

KI REPORTS  
Kidney International Reports

Lalayiannis A et al., 2022

Visual abstract by:  
Eric Au, MBBS MPH FRACP  
@EricAu

**Conclusion** This hypothesis generating study suggests that children and young adults with CKD or on dialysis may develop vascular calcification even as BMD increases. A presumed buffering capacity of the growing skeleton may offer some protection against extrasosseous calcification.

# Ne surtraitez pas votre patient...

- 99,9 % du Ca se trouve dans l'os, un énorme tampon
- Le dépassement du traitement CKD-MBD supprime la formation osseuse et bloque le réservoir de Ca



**CKD-MBD  
management**

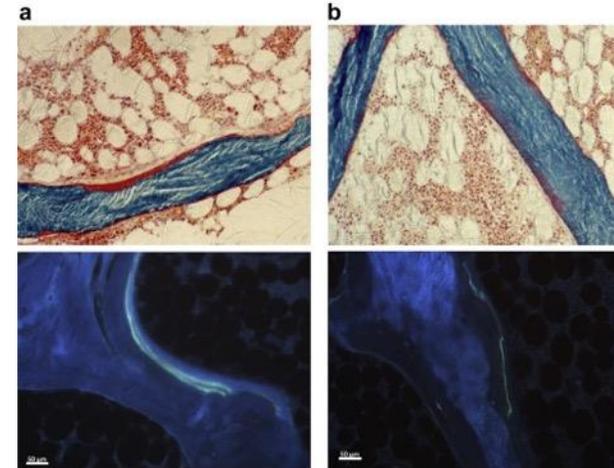
## Calcifications extra-osseuses



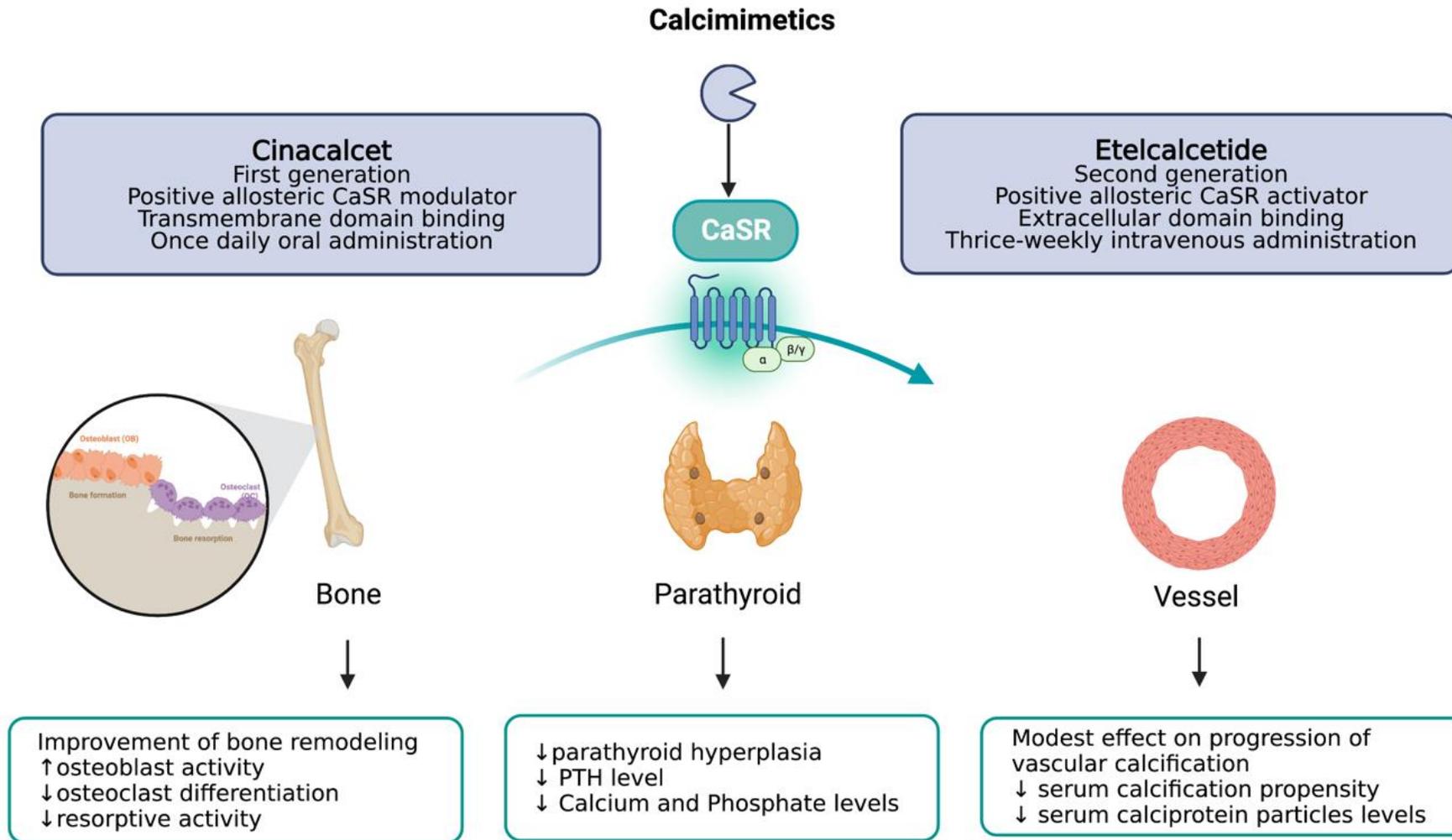
## Os adynamique

Résistance de l'os à la PTH

Cible PTH : 2 fois la normale supérieure



# Calcimimétiques



## ... sur les vaisseaux



### Modèles animaux

- Diminution de Ca, Ph, PTH
- Diminution des calcifications aortiques
- Diminution des marqueurs ostéoblastiques
- Anti-HTN



### ADVANCE trial

- 360 adultes en hémodialyse
- Cinacalcet versus placebo+SOC
- Similar Agaston score (p=0.07)
- **Diminution de la calcification cardiaque et diminution de la progression des calcifications de l'artère coronaire**



### EVOLVE trial results

- Mêmes événements cardiovasculaires et mortalité cardiovasculaire

*Kawata T, Kidney Int. 2008  
Odenwald T, American Society of Nephrology; 2006  
Raggi P, Nephrol Dial Transplant, 2011  
EVOLVE Trial Investigators N Engl J Med. 2012*

Les expériences et les études cliniques sont incohérentes ; mais probablement quelques avantages cardiovasculaires

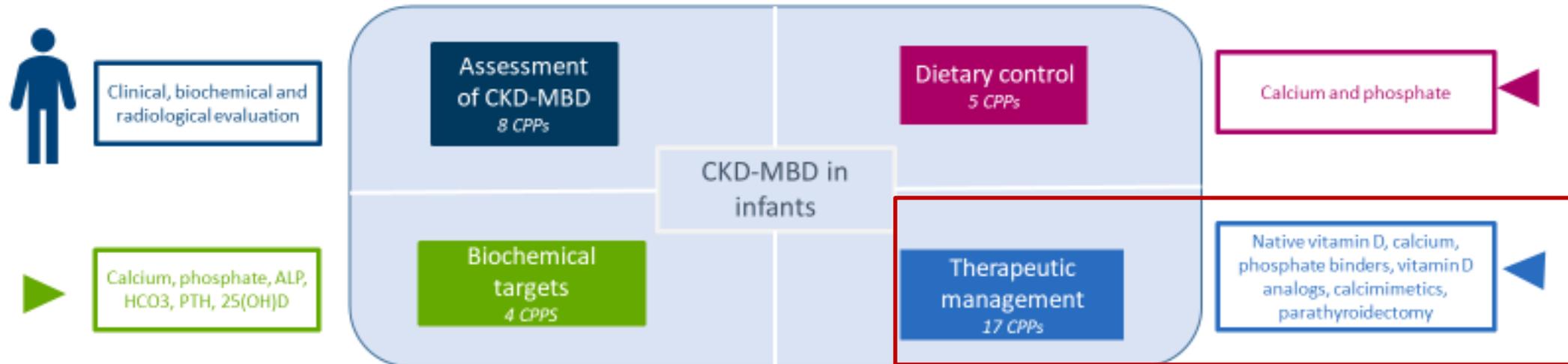
# Chez le nourrisson : période de croissance la plus rapide

Diagnosis and management of mineral and bone disorders in infants with CKD: clinical practice points from the ESPN CKD-MBD and dialysis working groups and the Pediatric Renal Nutrition Taskforce



**HYPOTHESIS:** Infants with CKD form a vulnerable population who are highly prone to mineral and bone disorders

**DESIGN & OUTCOMES:** Position paper with 34 Clinical Practice Points (CPPs) on the diagnosis and management of CKD-MBD in infants less than 2 years



**CONCLUSION:** Due to rapid bone growth and difficulties with nutrition, an adequate control of CKD-MBD in infants is particularly challenging. Given that there are very few high quality studies to guide evidence-based practice, these statements must be carefully considered by the treating physician and adapted to individual patient needs as appropriate.

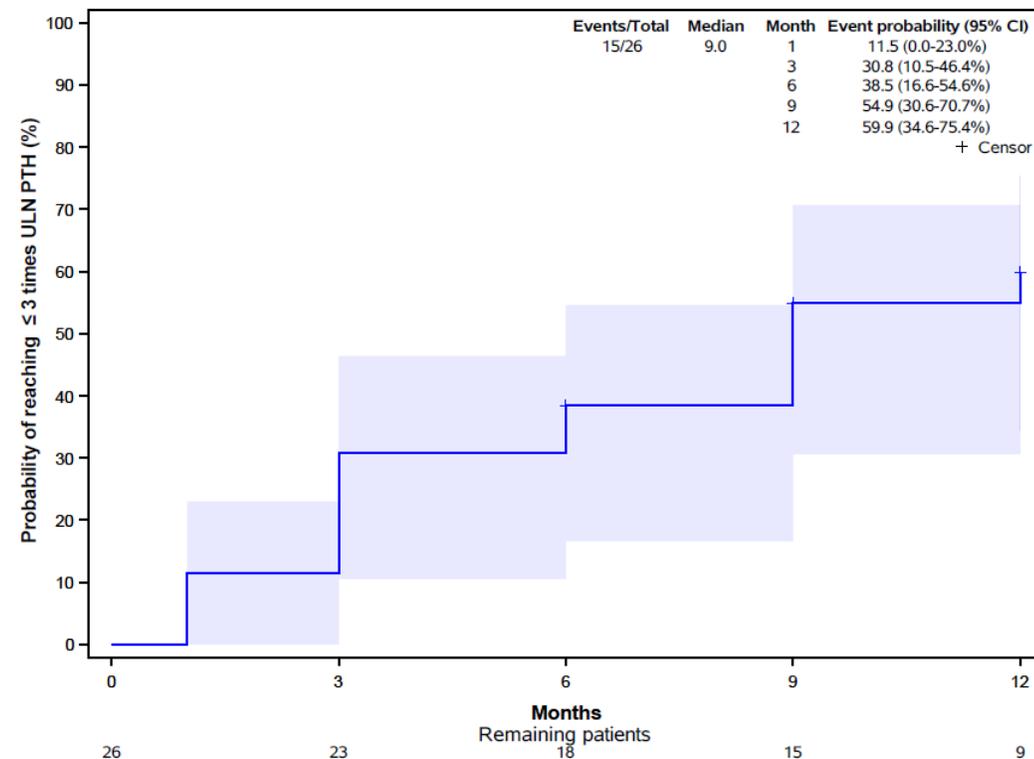
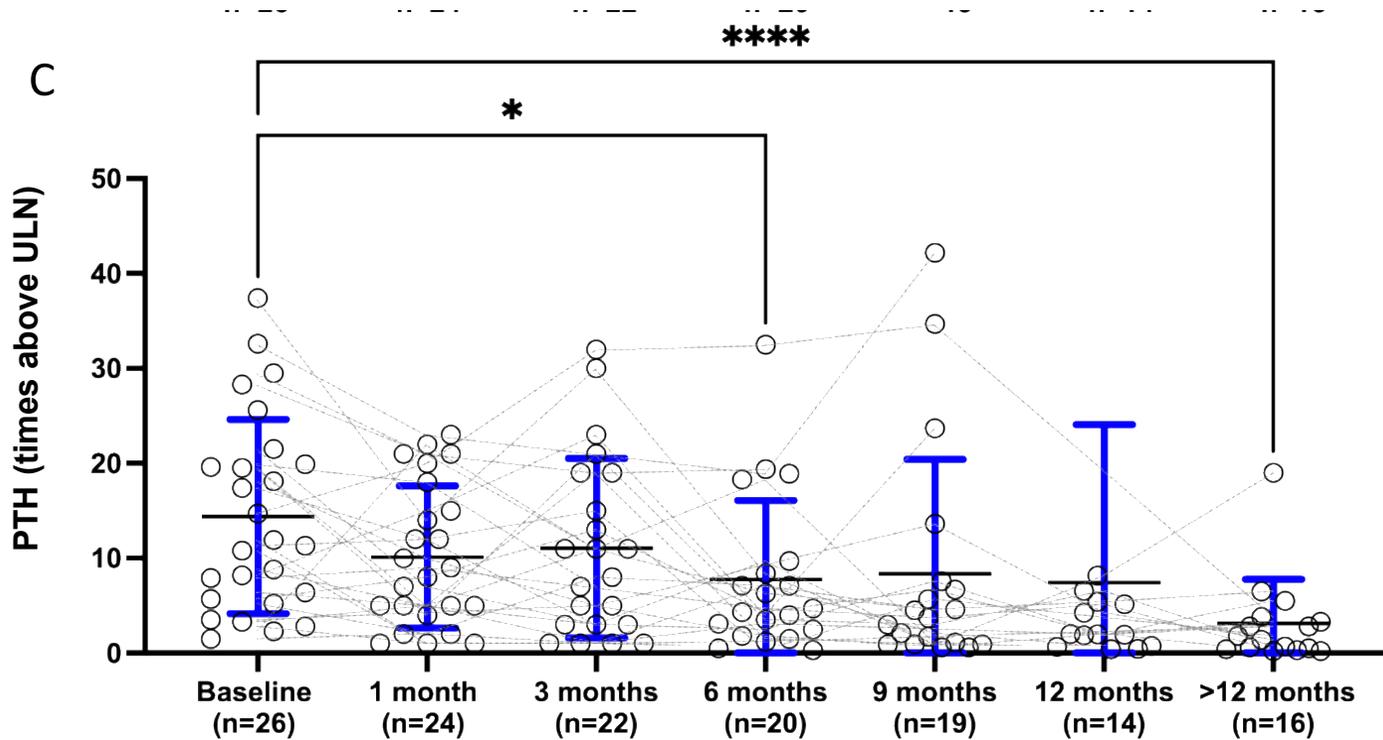
J Bacchetta et al. 2022



**Pediatric Nephrology**

Journal of the  
International Pediatric Nephrology Association

# Cinacalcet chez le nourrisson : effets sur la PTH



The probability of achieving serum PTH in the target range (i.e.,  $<3$  times ULN) increased over time and was above 50% after 9 months

# Chez le nourrisson : bonne tolérance et sécurité

- **Side effects**

- Hypocalcémie

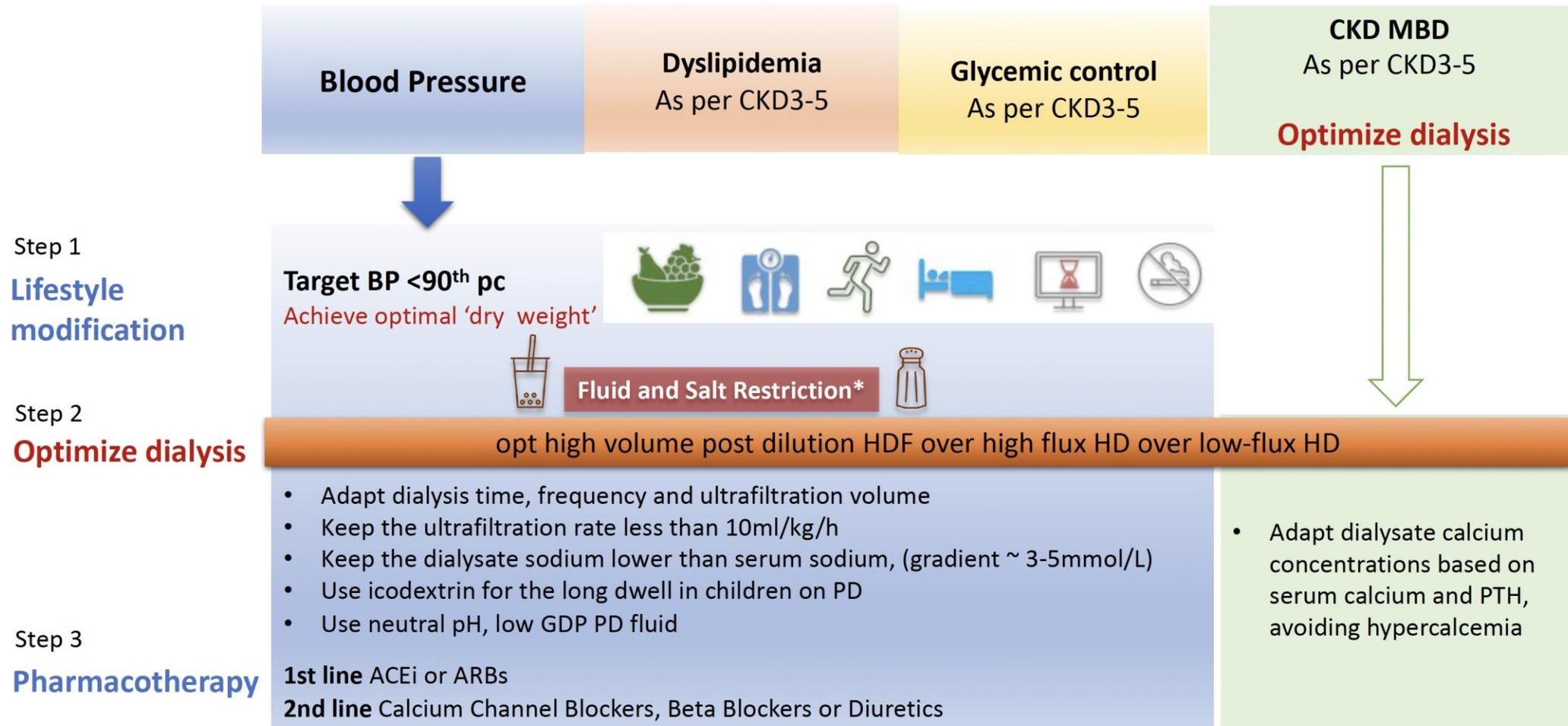
<2.1 mmol/L      n=7 // 10 episodes

- Tertiary HPT with high prevalence of hypercalcemia together with a very PTH!
- Impact sur le risque de calcification vasculaire ?
- Suggérez de commencer le cinacalcet plus tôt maintenant
- Les épisodes d'hypocalcémie ne sont pas plus fréquents que chez les enfants plus âgés atteints d'IRC5D
- Un contrôle méticuleux de l'équilibre calcique est obligatoire !

# Traitement de la MCV

Figure 3

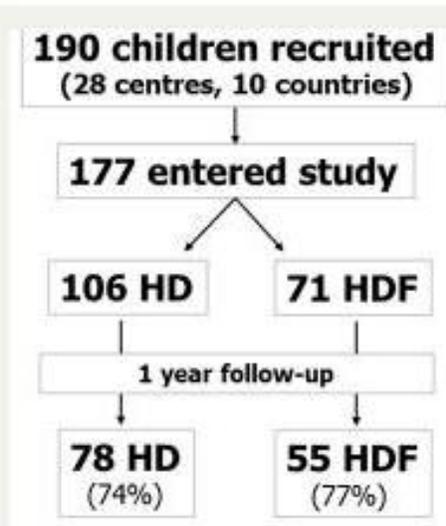
## Management of CV risk factors in children with CKD5D



\*Fluid and salt restriction may not need in children with CAKUT or salt losing nephropathies

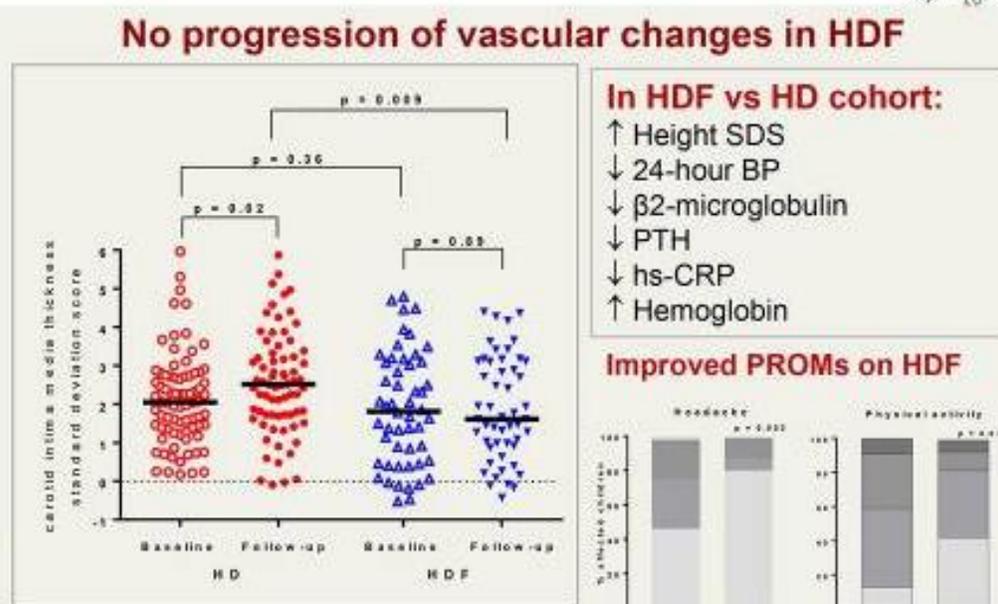
# Le HDF atténue les facteurs de risque de MCV

Cardiovascular risk, growth and patient-related outcome measures in children: an observational comparison of hemodiafiltration to conventional hemodialysis – the HDF, Heart and Height (3H) study



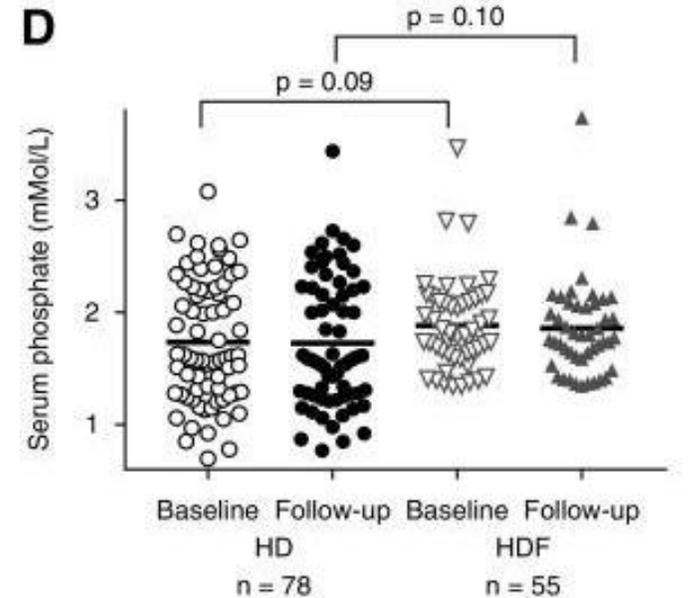
## Methods

1. Vascular measures –carotid intima-media thickness, pulse wave velocity, 24-hour BP, ECHO
2. Height SDS
3. Biochemistry
4. Patient related outcome measures (PROMs)



**CONCLUSION** 3H suggests an association between HDF modality with lack of progression in vascular measures, increase in height and improved patient-related outcomes compared to HD. This correlated with improved BP control and clearances on HDF. Confirmation through randomised trials is required.

**JASN**





## Comparison of measured vs kinetic-model predicted phosphate removal during hemodialysis and hemodiafiltration

John T. Daugirdas

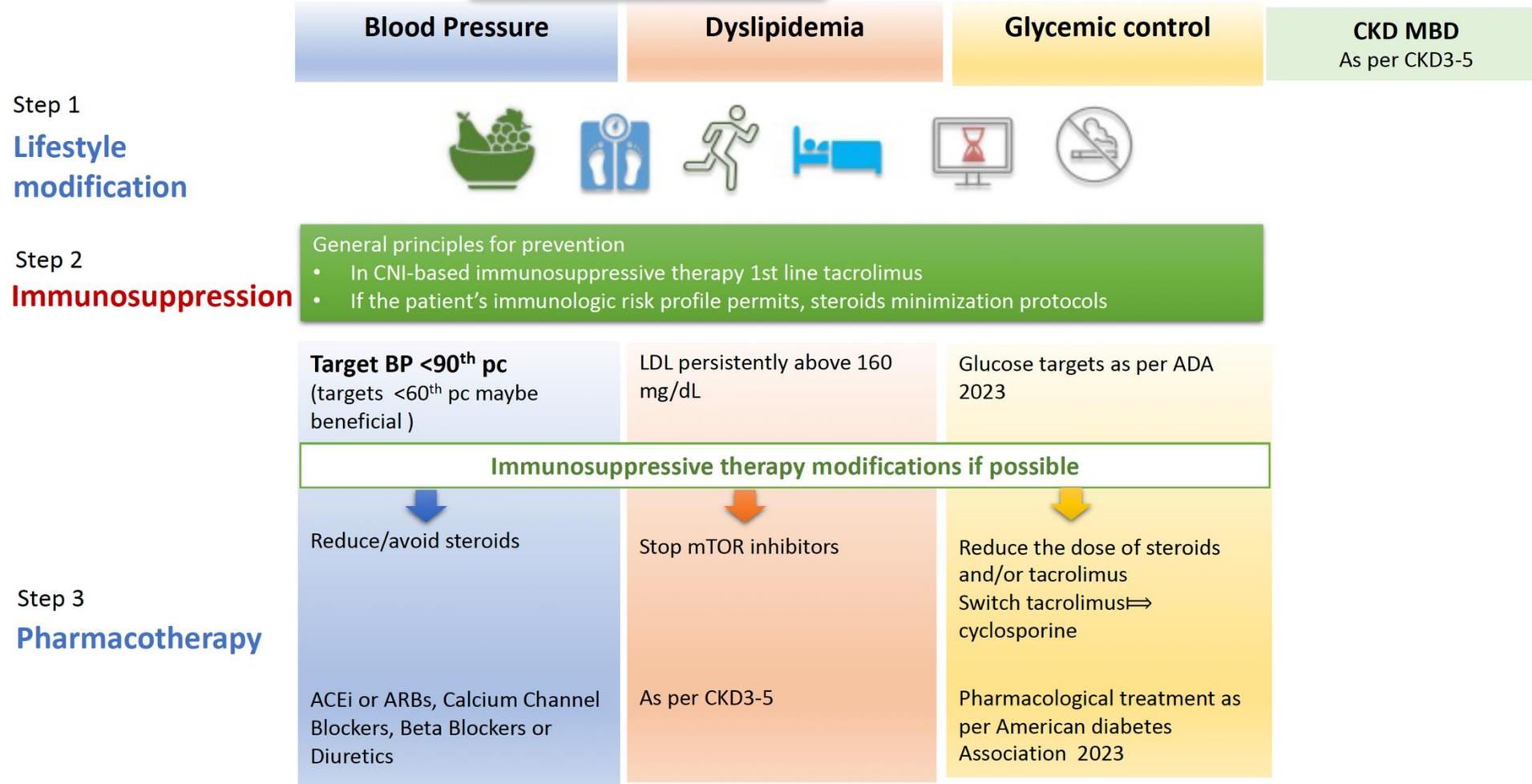
| Study             | Modality | Measured removal (mg) | Predicted removal (mg) | Measured removal HDF:HD |
|-------------------|----------|-----------------------|------------------------|-------------------------|
| Minutolo 2002 [6] | HD       | 814                   | 1098                   |                         |
|                   | HDF      | 1171                  | 1196                   | 1.44                    |
| Lornoy 2006 [7]   | HD       | 972                   | 1055                   |                         |
|                   | HDF      | 1159                  | 1192                   | 1.19                    |
| Nagaoka 2011 [8]  | HD       | 1020                  | 934                    |                         |
|                   | HDF      | 1088                  | 1012                   | 1.07                    |
| Cornelis 2014 [9] | HD       | 875                   | 913                    |                         |
|                   | HDF      | 932                   | 1020                   | 1.06                    |
| Švára 2016 [10]   | HD       | 1173                  | 1218                   |                         |
|                   | HDF      | 1187                  | 1286                   | 1.01                    |
| Average           |          | 1039                  | 1092                   | 1.155                   |
| SD                |          | 136                   | 127                    | 0.222                   |

**Élimination du phosphate 15,5 % plus élevée avec le HDF par rapport au HD**

# Traitement de la MCV

## Management of CV risk factors in children with CKD5T

Figure 4

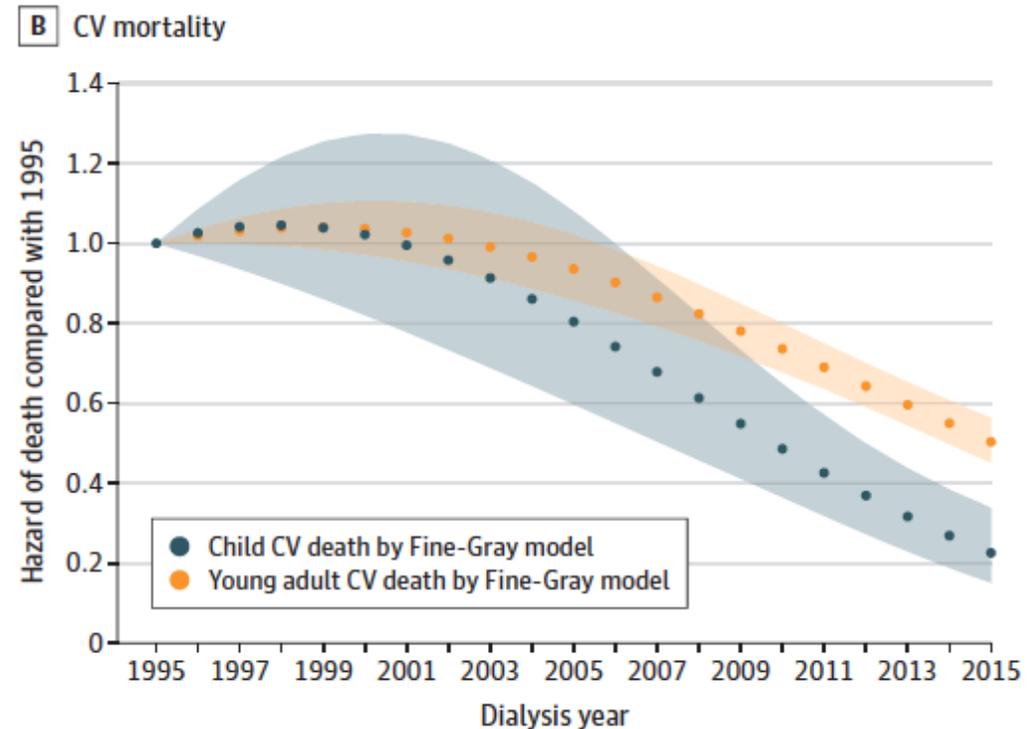
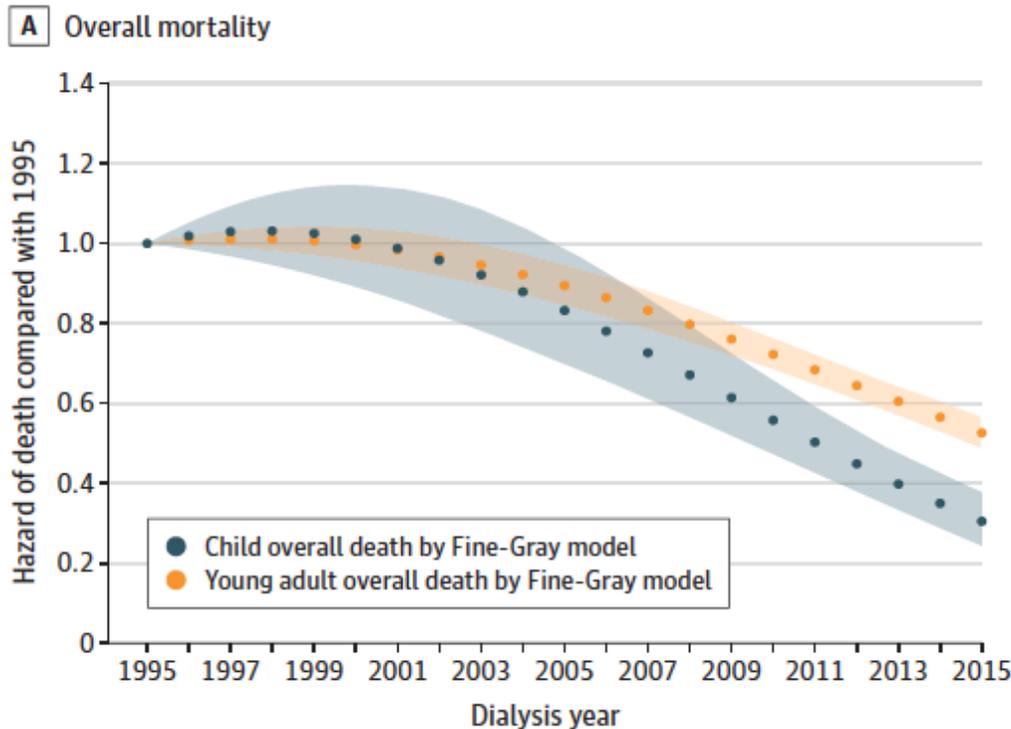


# Conclusion

## Cardiovascular mortality in young dialysis patients (1995-2015)

Risk of sudden cardiac death improved steadily for all age groups

- Children (SHR, 0.31; 95% CI, 0.20-0.47)
- Young adults (SHR, 0.64; 95% CI, 0.56-0.73)



Potential factors that may have contributed to the improvement in survival rates

# TAKE HOME MESSAGES

## MCV : DÉFI POUR LES NÉPHROLOGUES PÉDIATRIQUES !

1 Diminution de l'espérance de vie

2 Prévention en agissant sur les Fdr CV

3 Traitez l'os de manière adéquate

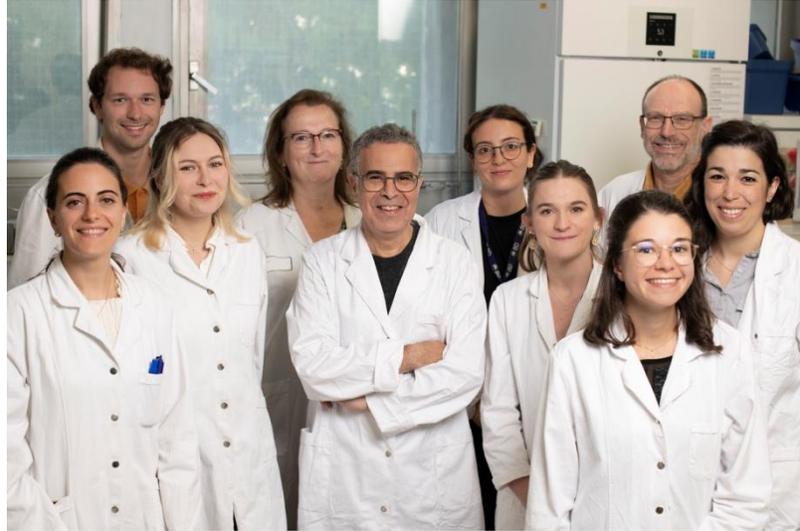
4 Low-Cinacalcet / low active vitamin D

5 Optimisation de la dialyse

6 Treat-to-target

Merci pour votre attention

- Dr Faudeux Camille
- Dr Magnavacca Marie
- Dr De Guillebon Jean-Marie
- Prof. Bérard Etienne
- Dr Battista Jennifer
- Dr Larché Elise



- And all the **Claudine Blin** team (M. Rouleau, M Materozzi, V Rezapova, A Mahler, C Girolet, A Wakkach, C Blin-Wakkach)



### LP2M

- Dr Stoyan Ivanov
- Dr Alexandre Gallerand
- Zackarya Caillot
- Dr Isabelle Rubera
- Pr Georges Leftheriotis
- Dr Christophe Durantou

### Heidelberg

- Prof. Claus Peter Schmitt
- Dr Maria Bartosova
- CERTAIN registry
- ERK-Net team

### Maastricht

- Prof. Leon Schurgers
- Dr Armand Jaminon



### Lyon

- Prof. Justine Bacchetta
- Dr David Magne
- Prof Gilles Rautureau



### ESPN

- *CKD-MBD working group, ESPN mentoring program, YPNN, ESPN grant 2022*