2ND SUMMIT
RARE
DISEASES
COPAC

What Fabry cardiologists should know from the Nephrologist's point of view

sanofi

Disclosures

Consultant: Sanofi Genzyme, Freeline

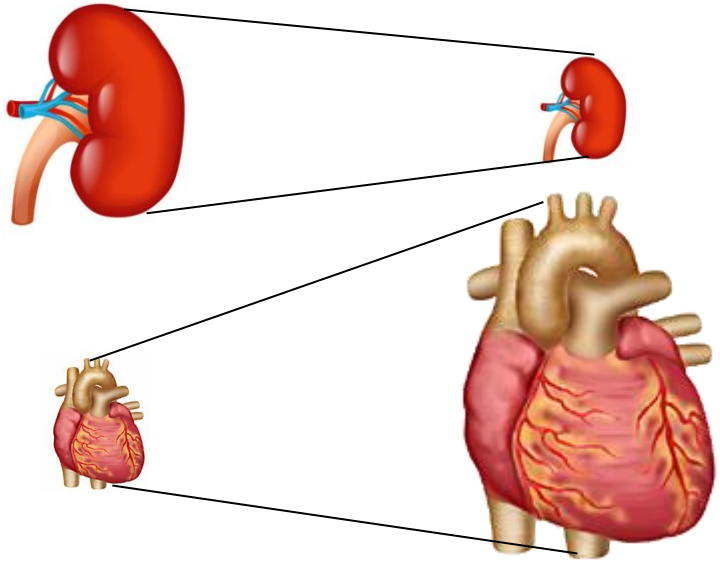
Speaker fees: Sanofi Genzyme, Shire, Amicus

FRASE DE SALVAMENTO

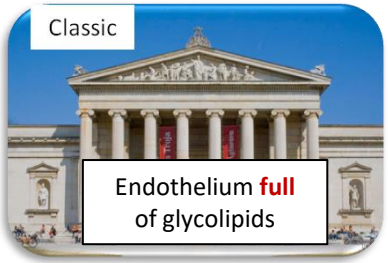
La información contenida en esta presentación está dirigida exclusivamente al cuerpo médico, con la intención de brindar información científica de interés y refleja las consideraciones del autor y no las de SANOFI. Cualquier indicación OFF LABEL mencionada será con el único objetivo de intercambio científico y no representa una promoción. SANOFI no recomienda indicaciones que no estén contenidas en la información para prescribir aprobada de sus productos en Colombia.

CODIGO PROMOMAT: MAT-CO-2202625

The central tenet of CKD



Fabry disease natural history in males



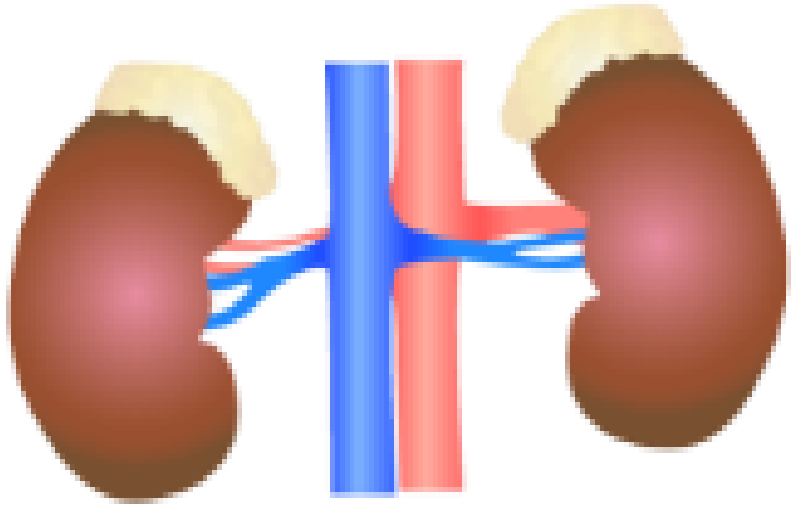
20y 40y

Death before 60 y

Persistent fever sign

The red spots in underwear sign: angiokeratoma

Ortiz A, et al. Nephrol Dial Transplant. 2010 Mar;25(3):769-75. Patel MR, et al. J Am Coll Cardiol. 2011 Mar 1;57(9):1093-9



Mean age at **RRT**: **40** years (males and females), but approx. 20-fold less females
Ortiz A, et al. Nephrol Dial Transplant. 2010 Mar;25(3):769-75

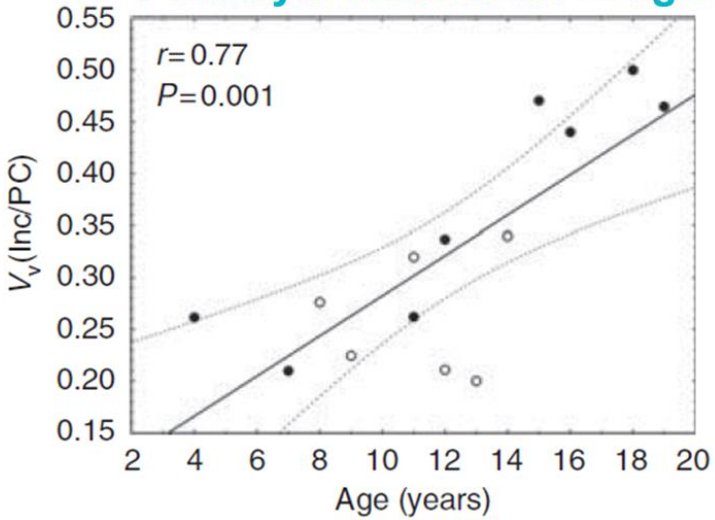
Mean age at **cardiac** event **45** and **54** years, males and females, respectively
Patel MR, et al. J Am Coll Cardiol. 2011 Mar 1;57(9):1093-9

https://upload.wikimedia.org/wikipedia/commons/4/48/201405_kidney.png

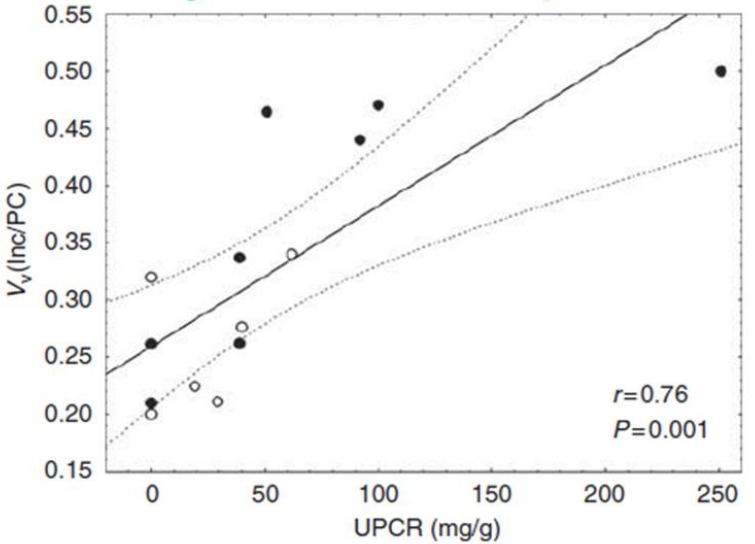
Progressive podocyte injury and globotriaosylceramide (GL-3) accumulation in young patients with Fabry disease

Behzad Najafian [1], Einar Svarstad [2], Leif Bostad [3], Marie-Claire Gubler [4], Camilla Tøndel [5], Chester Whitley [6], Michael Mauer [7]

Podocyte inclusions vs age



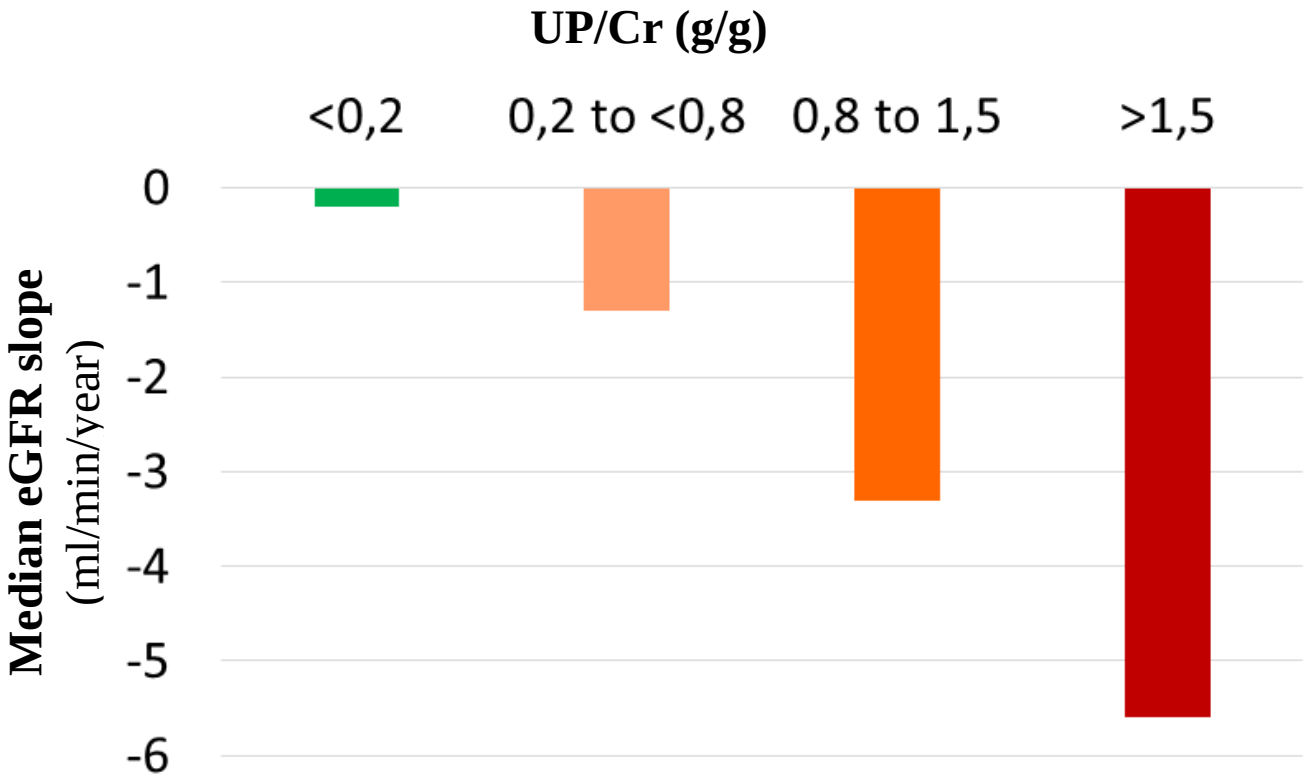
Podocyte inclusions vs proteinuria



Relationship between age and podocyte (Vv(Inc/PC)), and endotheli cell (Vv(Inc/Endo)) GL-3 fractional volume of inclusions per cytoplasi

Segmental foot process effacement
was present in **all glomeruli**

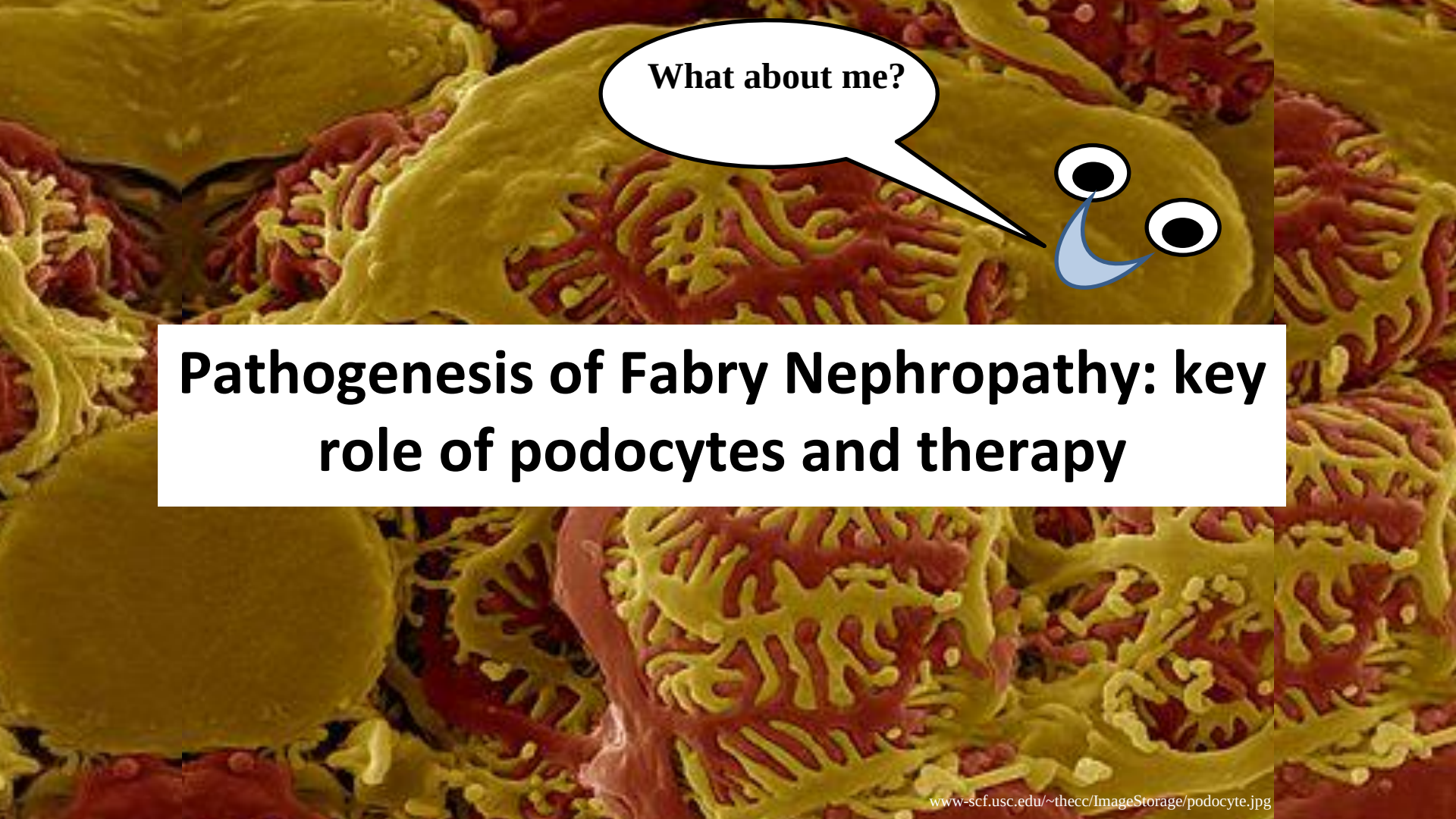
Proteinuria is a major **risk factor** for **CKD progression** in Fabry



Natural history data from
121 men not on ERT
(Fabry Registry)

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ERT, enzyme replacement therapy; UP/Cr, urinary protein:creatinine ratio

Wanner et al. CJASN 2010 Dec;5(12):2220-8

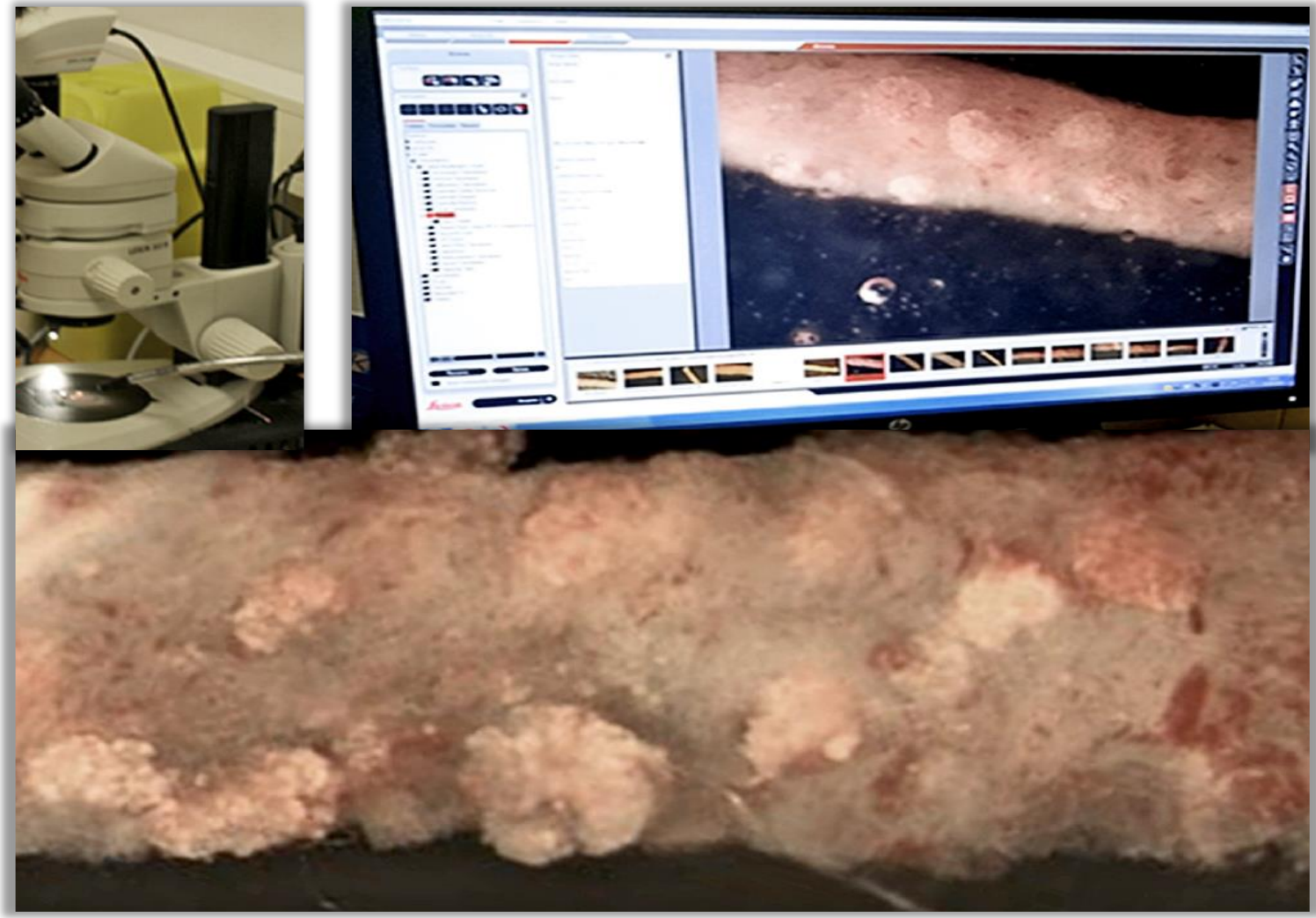


Pathogenesis of Fabry Nephropathy: key role of podocytes and therapy

www-scf.usc.edu/~thecc/ImageStorage/podocyte.jpg

https://upload.wikimedia.org/wikipedia/commons/4/46/Sea_anemone_on_the_Oregon_Coast_%283222020816%29.jpg

Fabry podocytes are fuuuuull of glycolipids



Svarstad E et al. *Nephron*. 2018;138(1):13-21.

This is not what it seems!!!!

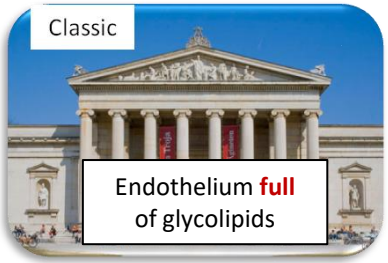
But they are **not** always immortal

Shplotch!

(podocyte crashing against toilet)

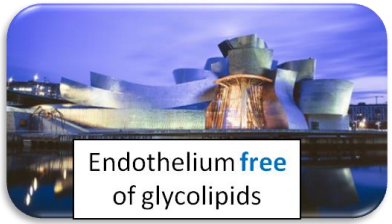
Podocyte farewell ceremony by cell biology scientist

Fabry disease natural history in males



20y 40y

Death before 60 y



20y 40y 60y

Death before 80 y

Ortiz A, et al. Nephrol Dial Transplant. 2010 Mar;25(3):769-75. Patel MR, et al. J Am Coll Cardiol. 2011 Mar 1;57(9):1093-9

https://commons.wikimedia.org/wiki/File:Ischemic_Stroke.svg?uselang=fr

Treatment decisions: who and when?

Appendix A. **Renal** involvement in adult patients with Fabry disease: manifestations, assessments, and management

Appendix B. **Cardiac** involvement in adult patients with Fabry disease: manifestations, assessments, and management

Appendix C. **Peripheral nervous system** involvement in adult patients with Fabry disease: manifestations, assessments, and management

Appendix D. **Central nervous system** involvement in adult patients with Fabry disease: manifestations, assessments, and management

Appendix E. Involvement of **other** organ systems in adult patients with Fabry disease: manifestations, assessments, and management

Appendix F. Enzyme replacement therapy **infusion setting** for adult patients with Fabry disease

Appendix G. Impact of enzyme replacement therapy **dose** in the treatment of patients with Fabry disease

Appendix H. **Pregnancy and lactation** in adult patients with Fabry disease

Ortiz A et al. *Mol Genet Metab* 2018;123:416–27

Treatment decisions: who and when?

The European Fabry Working Group Consensus Document

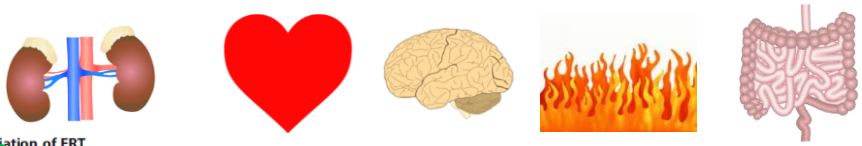


Table 3 Consensus criteria for initiation of ERT

	No signs or symptoms	Renal*	Cardiac*	CNS*	Pain*	GI*
Classical FD, males	if ≥ 16 years of age (Class IIB)	- microalbuminuria† (Class I) - proteinuria† (Class I) - renal insufficiency (GFR 60–90)‡ (Class I) - renal insufficiency (GFR 45–60)‡ (Class IIB)	- cardiac hypertrophy (MWT > 12 mm) without (or only minimal signs of) fibrosis (Class I)	- WMLs (Class IIB) - TIA/stroke (Class IIA)	- neuropathic pain (Class IIA) - neuropathic pain even if	GI symptoms (Class IIA if < 16 years of age, Class IIB if > 16 years of age)
Non-classical FD, males		- microalbuminuria† (Class I) - proteinuria† (Class I) - renal insufficiency (GFR 60–90)‡ (Class IIA) - renal insufficiency (GFR 45–60)‡ (Class IIB)	- signs of cardiac rhythm disturbances§ (Class I)	- hearing loss, corrected for age (Class IIB)	completely controlled (not interfering with daily activities) with pain medication (Class IIB)	
Classical FD, females		- microalbuminuria† (Class IIB) - proteinuria† (Class IIB) - renal insufficiency (GFR 60–90)‡ (Class IIA) - renal insufficiency (GFR 45–60)‡ (Class IIB)				
Non-classical FD, females		- microalbuminuria† (Class IIB) - proteinuria† (Class IIB) - renal insufficiency (GFR 60–90)‡ (Class IIB) - renal insufficiency (GFR 45–60)‡ (Class IIB)	(Class I)	for age (Class IIB)	activities) with pain medication (Class IIB)	

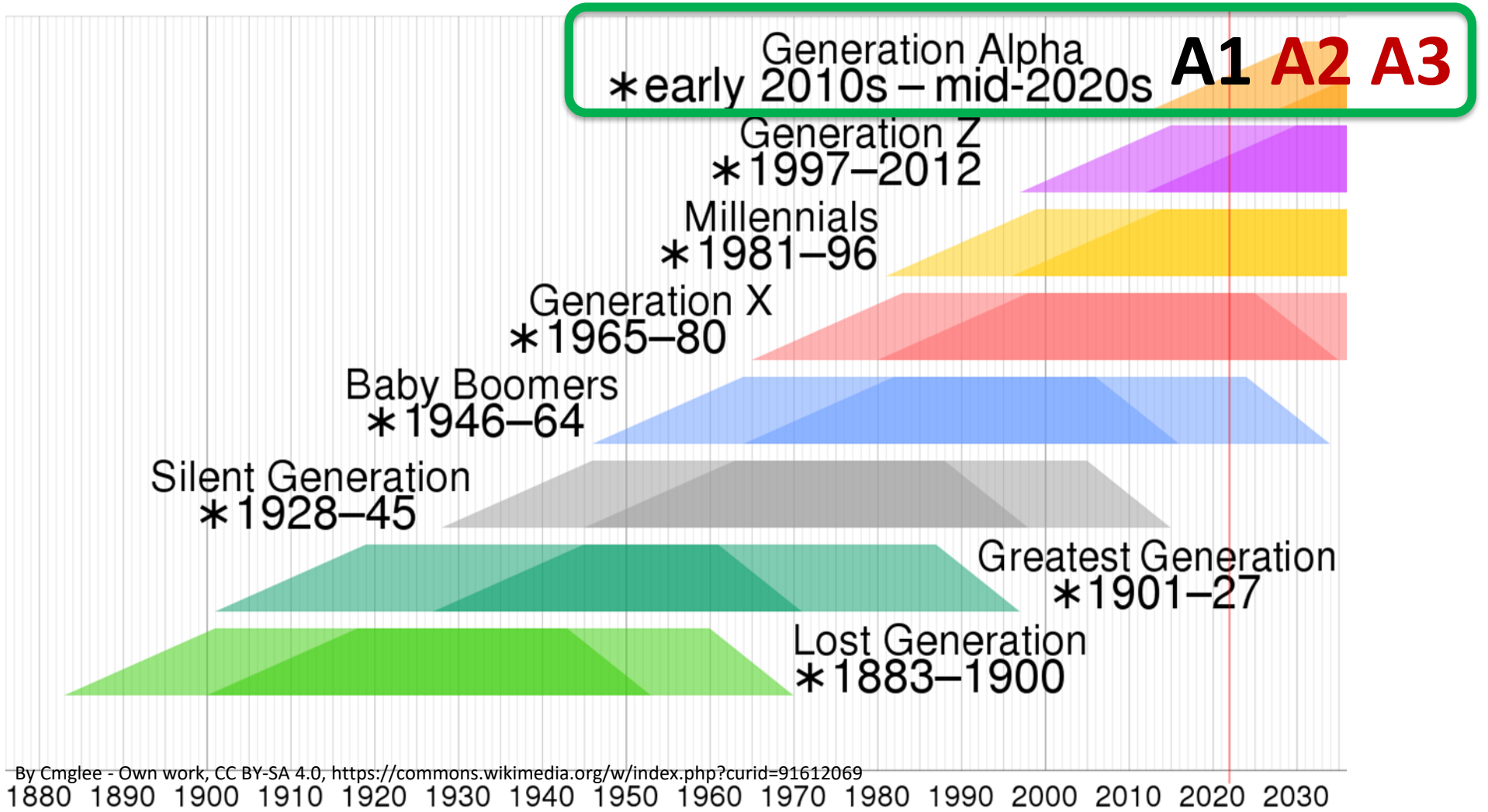
*consistent with FD and not fully explained by other pathology; †according to international guidelines of kidney disease, KDIGO criteria; ‡in ml/min/1.73 m² corrected for age (>40 years: −1 ml/min/1.73 m²/year); §sinus bradycardia, AF, repolarization disorders; ERT = enzyme replacement therapy; GFR = glomerular filtration rate; MWT = maximal wall thickness; CNS = central nervous system; WMLs = white matter lesions; TIA = transient ischemic attack; GI = gastrointestinal.

Microalbuminuria

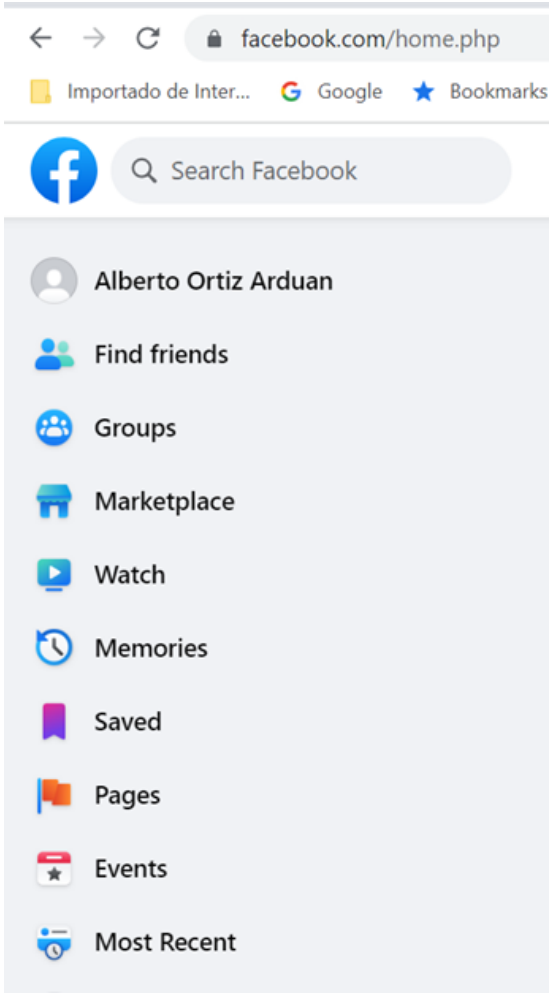
Microalbuminuria is sooooo last century!

Biegstraaten M et al. *Orphanet J Rare Dis* 2015;10:36

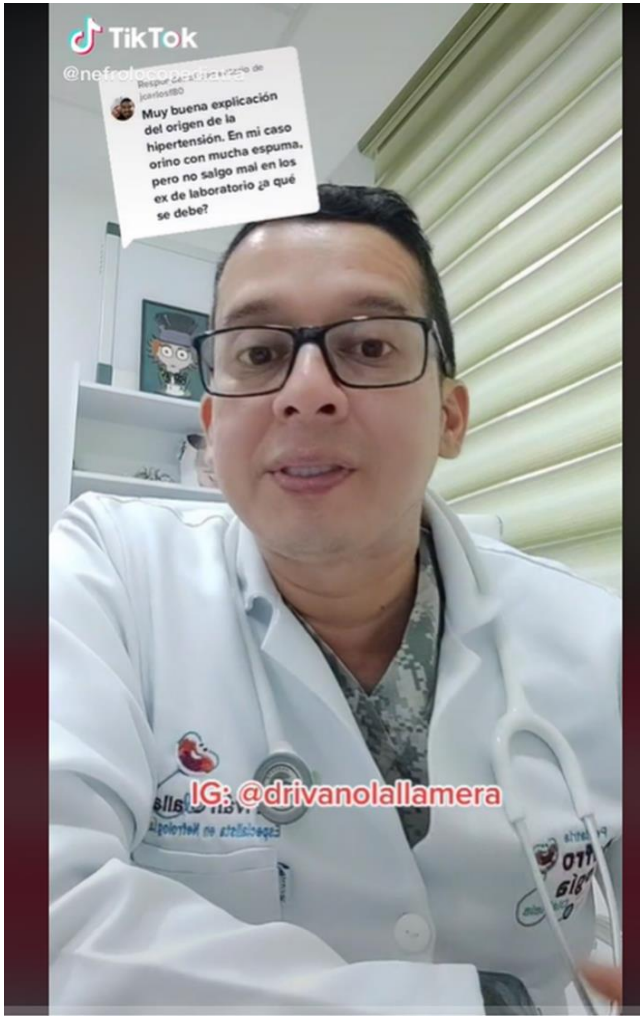

Microalbuminuria is
soooooo last century!



That was then



This is now



That was then

This is now

Fabry Disease: Renal Involvement Limited to Podocyte Pathology and Proteinuria in a Septuagenarian Cardiac Variant. Pathologic and Therapeutic Implications

Shane M. Meehan, MD, Tipsuda Junsanto, MD, James J. Rydel, MD, and Robert J. Desnick, PhD, MD

Am J Kidney Dis. **2004** Jan;43(1):164-71.

N215S

At age 75 years
he had significant **proteinuria** (1 g/L),
mildly decreased renal function
(serum creatinine, 1.8 mg/dL)
presumably secondary to hypertensive arteriosclerosis.

Blood pressure 114/72 mmHg

At age 65, **urinary protein** 0.3 g/L

UACR at least 500 mg/g

eGFR 36 ml/min/1.73 m2

????

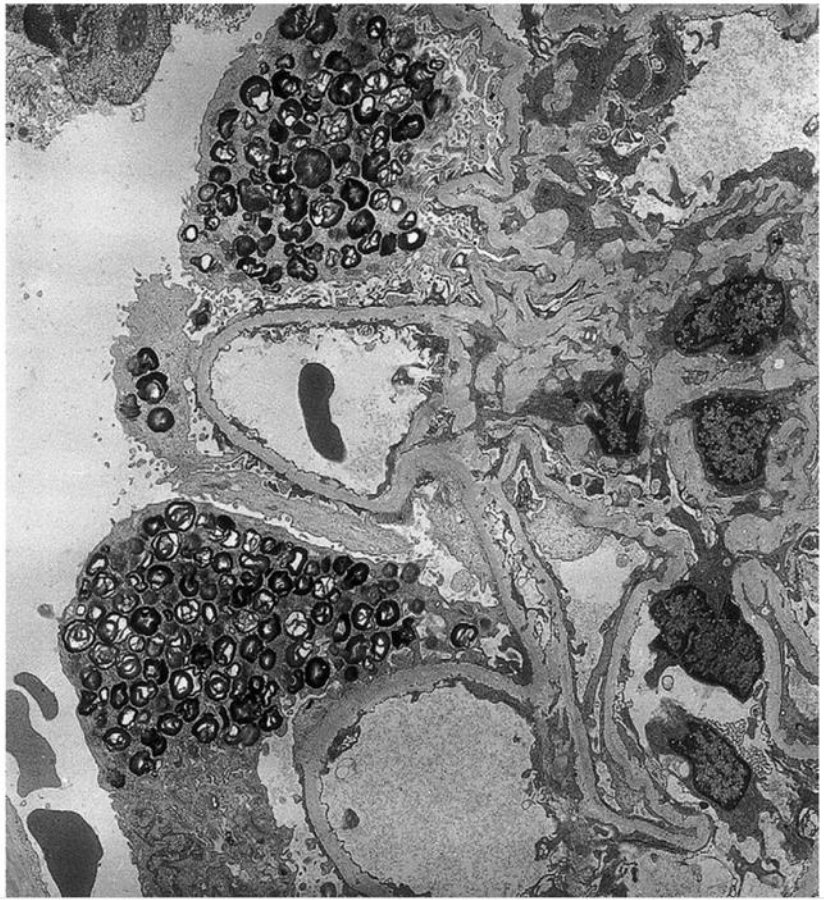
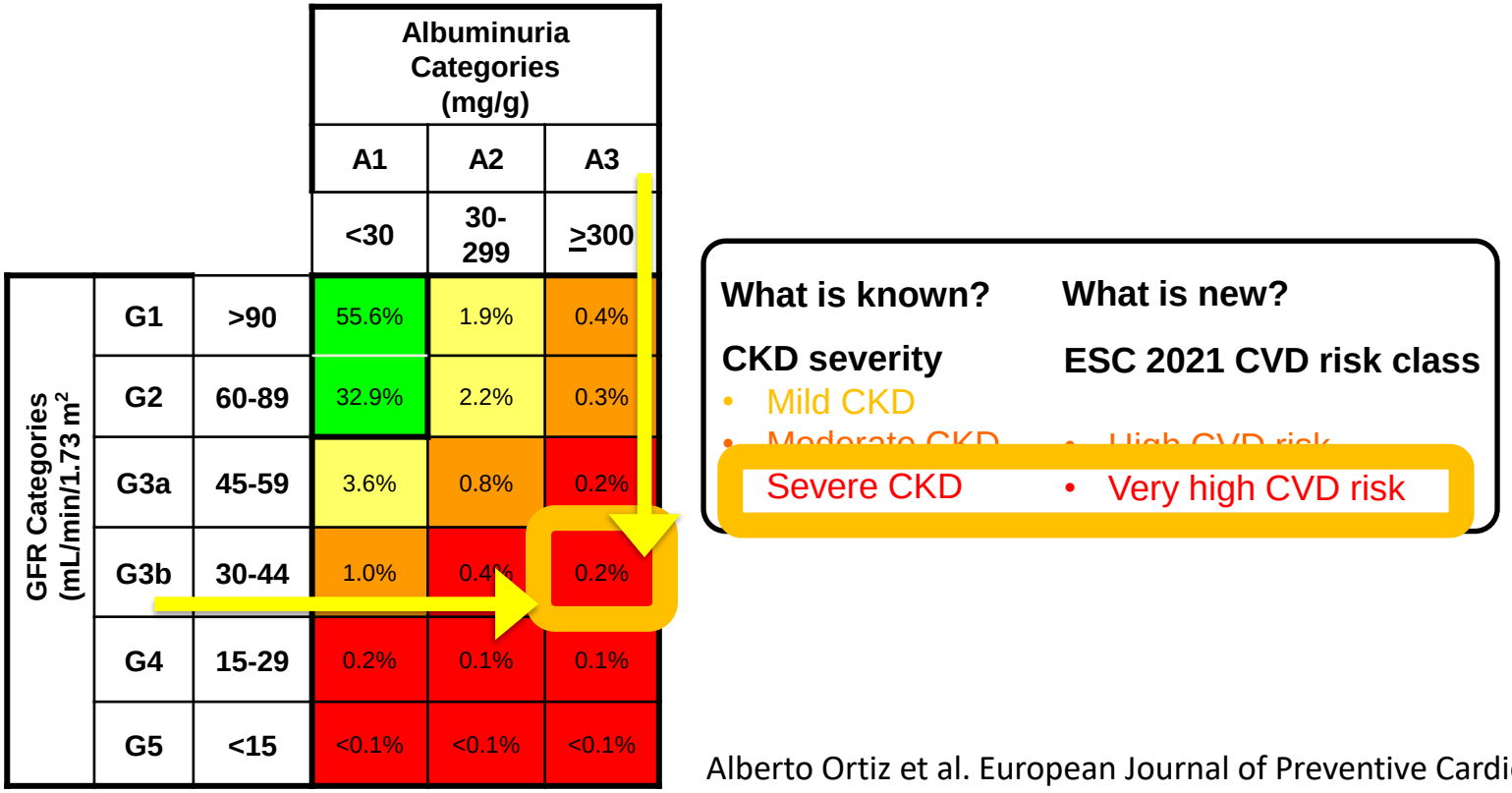


Fig 4. Electron microscopy shows abundant electron-dense myelin figures within the podocyte cytoplasm. The podocyte foot processes are largely effaced. These inclusions were absent from the glomerular and peritubular capillary endothelium, and vascular smooth muscle. (Original magnification ×5,700.)

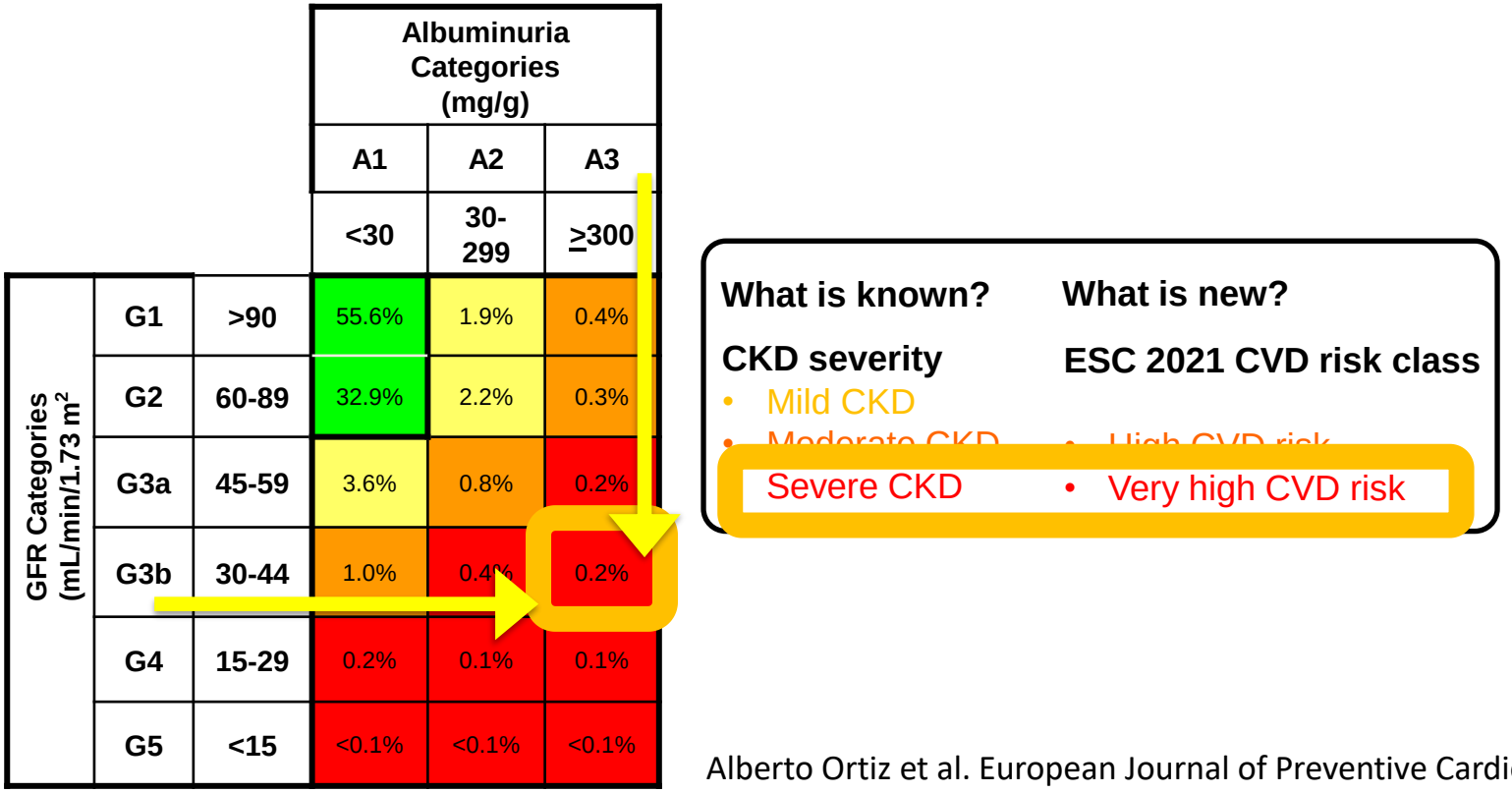
Meehan et al. Am J Kidney Dis. **2004** Jan;43(1):164-71.

Figure 1. Translation of chronic kidney disease (CKD) risk classes (as defined by KDIGO in 2012) into cardiovascular (CVD) risk classes as defined by the European Society of Cardiology in the 2021 guideline on CVD prevention. Numbers within cells represent prevalence in the general population.



Alberto Ortiz et al. European Journal of Preventive Cardiology. 2022 (accepted)

Figure 1. Translation of chronic kidney disease (CKD) risk classes (as defined by KDIGO in 2012) into cardiovascular (CVD) risk classes as defined by the European Society of Cardiology in the 2021 guideline on CVD prevention. Numbers within cells represent prevalence in the general population.



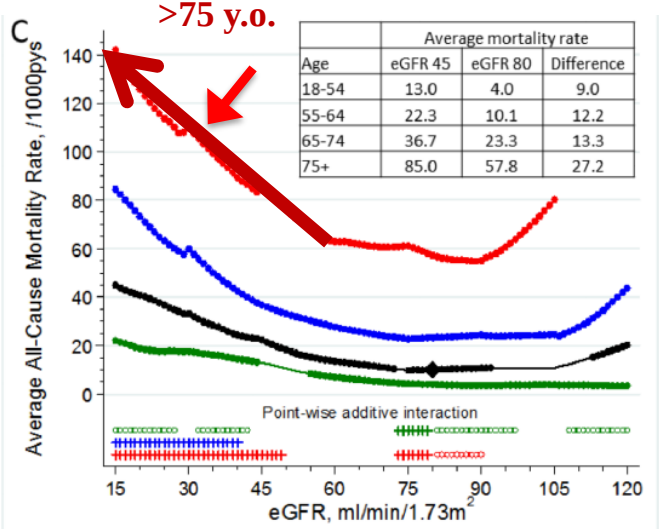
Alberto Ortiz et al. European Journal of Preventive Cardiology. 2022 (accepted)

eGFR and risk of death in the elderly

JAMA. 2012 December 12; 308(22): 2349–2360. doi:10.1001/jama.2012.16817.

Age and the Association of Kidney Measures with Mortality and End-Stage Renal Disease

Stein I. Hallan, MD, PhD, Kunihiro Matsushita, MD, PhD, Yingying Sang, MS, Bakhtawar K.



	Average mortality rate		
Age	eGFR 45	eGFR 80	Difference
18-54	13.0	4.0	9.0
55-64	22.3	10.1	12.2
65-74	36.7	23.3	13.3
75+	85.0	57.8	27.2

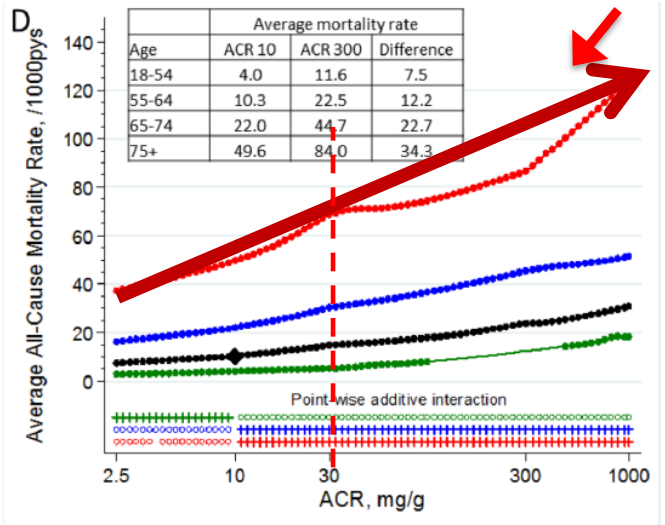
Hallan SI, Matsushita K, Sang Y, et al. Age and association of kidney measures with mortality and end-stage renal disease. JAMA. 2012;308(22):2349-2360.

UACR and risk of death in the elderly

JAMA. 2012 December 12; 308(22): 2349–2360. doi:10.1001/jama.2012.16817.

Age and the Association of Kidney Measures with Mortality and End-Stage Renal Disease

Stein I. Hallan, MD, PhD, Kunihiro Matsushita, MD, PhD, Yingying Sang, MS, Bakhtawar K.



Why is the **death** risk already increased at GFR category **G1**?

GFR is normal!

Who is the killer?

This is an easy one!

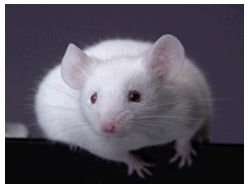
~~GFR~~

If the GFR is normal…. then the killer must be…

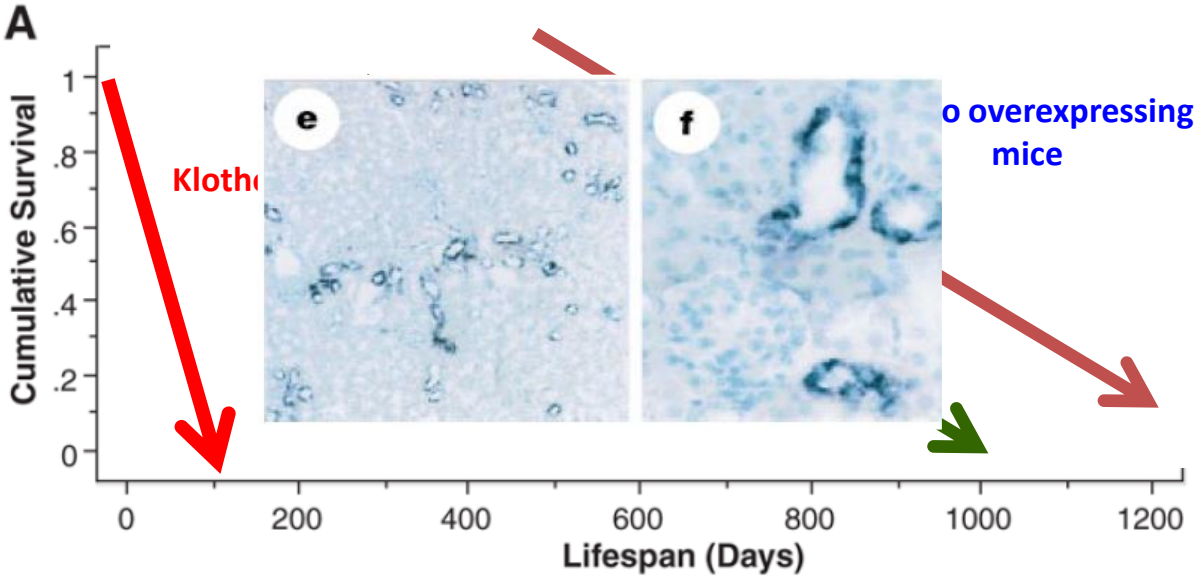
Albuminuria
(proteinuria)

Mr GFR **Detective** **Miss Albuminuria**

Suppression of Aging in Mice by the Hormone Klotho



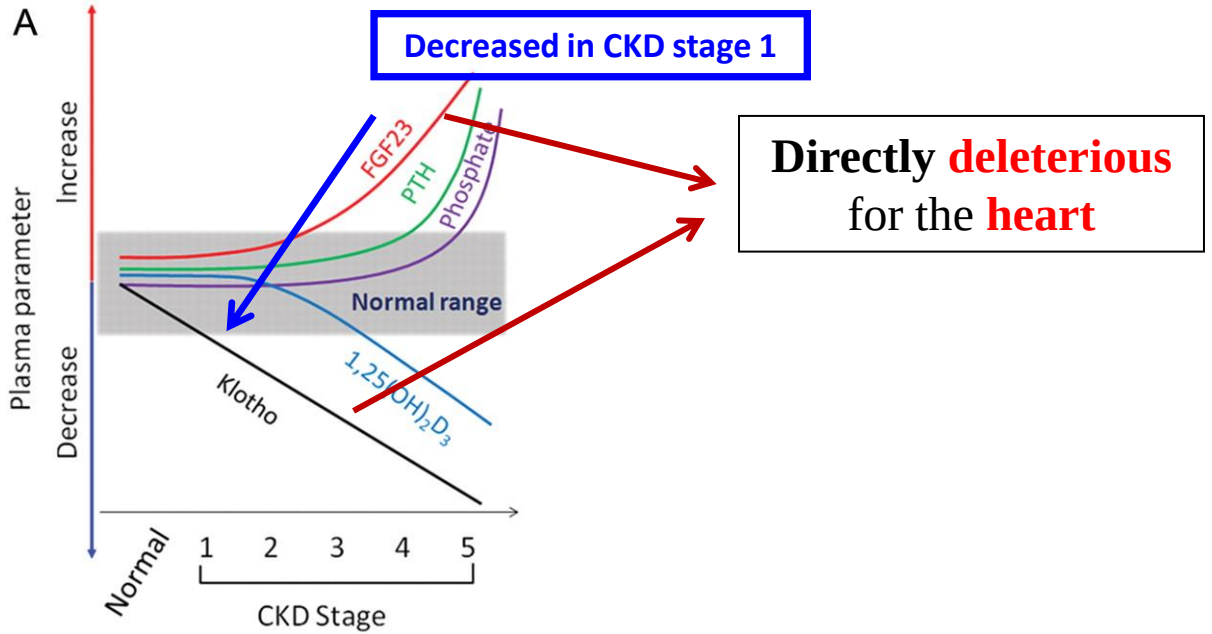
Hiroshi Kurosu[1], Masaya Yamamoto[1], Jeremy D. Clark[1], Johanne V. Pastor[1], Animesh Nandi[1], Prem Gurnani[1], Owen P. McGuinness[3], Hirotaka Chikuda[4], Masayuki Yamaguchi[4], Hiroshi Kawaguchi[4], Iichiro Shimomura[5], Yoshiharu Takayama[2], Joachim Herz[2], C. Ronald Kahn[6], Kevin P. Rosenblatt[1], and Makoto Kuro-o[1,*]



Science. 2005 September 16; 309(5742): 1829–1833.

Kuro-o M. Nature. 1997

Bone mineral metabolism and CKD progression. Early decrease in Klotho and subsequent increase in FGF23

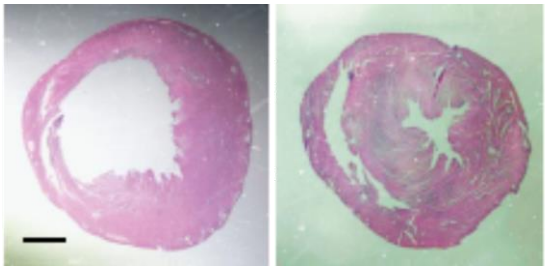


Hu M C et al. Nephrol. Dial. Transplant. 2012;27:2650-2657

NDT Nephrology Dialysis Transplantation

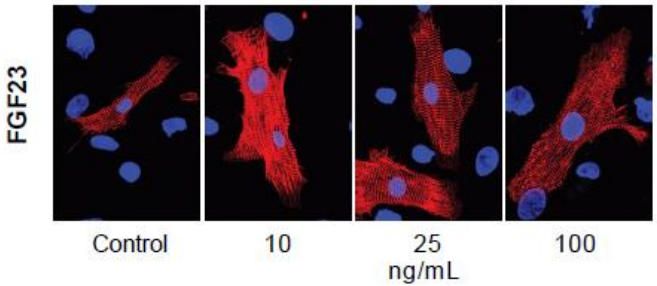
FGF-23 promotes left ventricular hypertrophy

Control CKD rat



rat

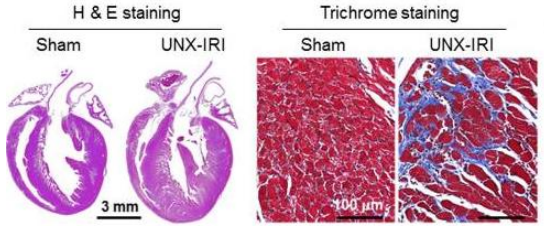
Neonatal rat ventricular cardiomyocytes



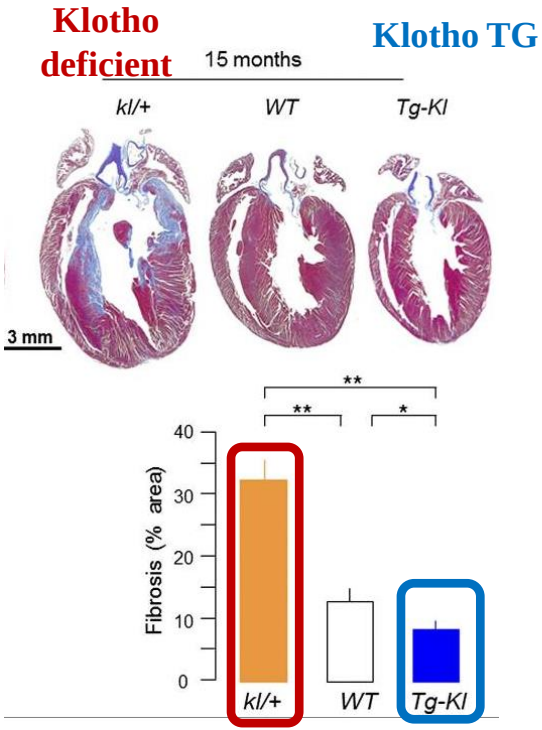
Faul C, et al. *J Clin Invest.* 2011;121(11):4393-4408.

Klotho deficiency promotes cardiac fibrosis

CKD and heart hypertrophy and fibrosis

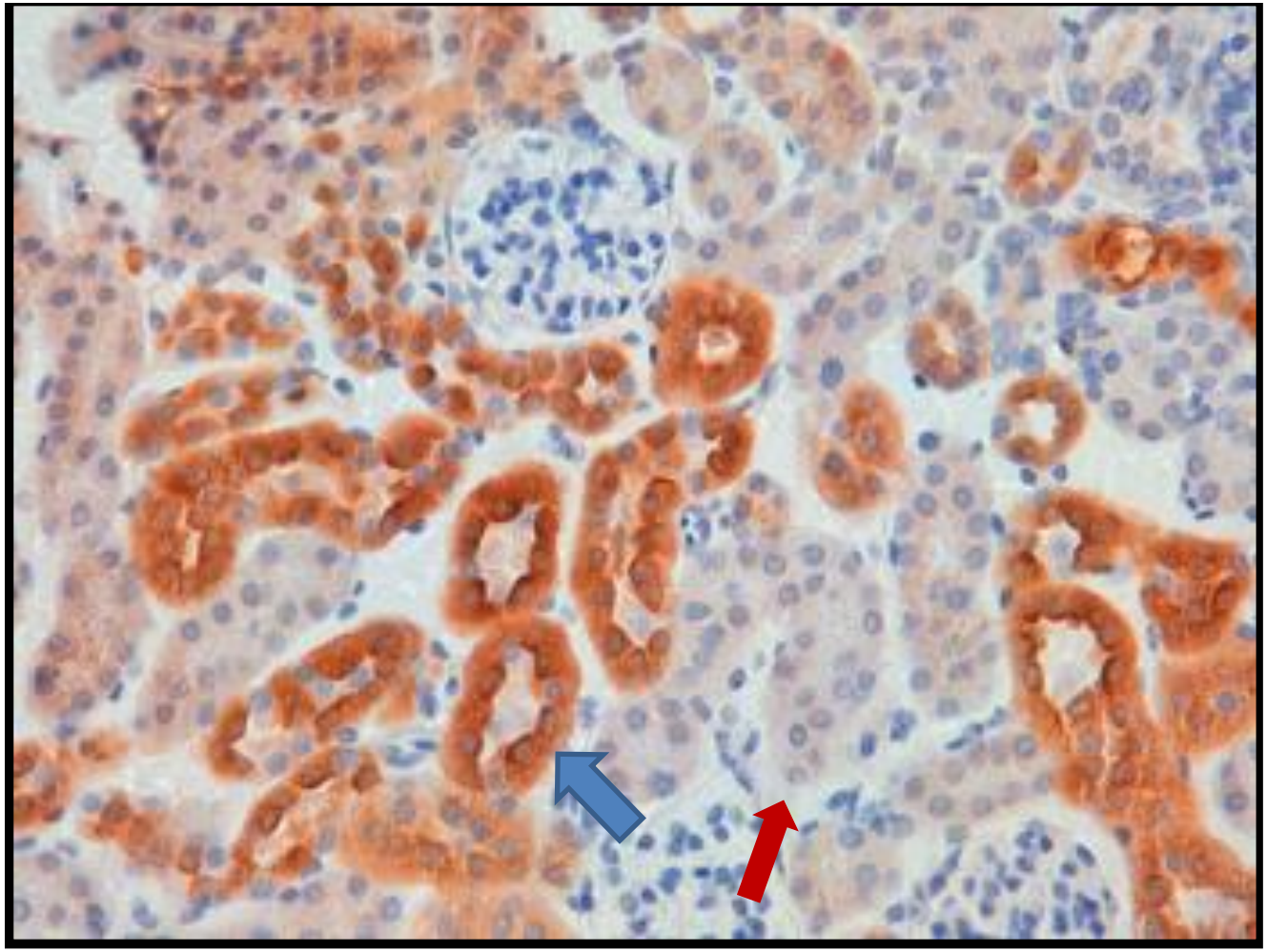


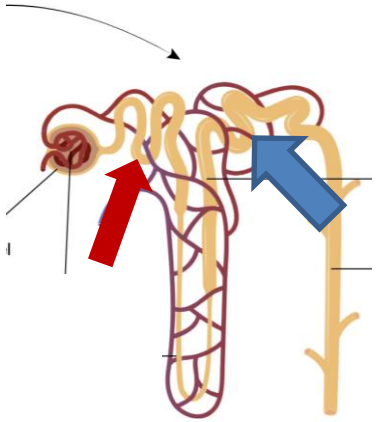
CKD **CKD**



Hu MC, et al. J Am Soc Nephrol. 2015 Jun;26(6):1290-302

Wy does **Klotho decrease** so **early** in the course of CKD?





Nephrol Dial Transplant (2018) 1–11
doi: 10.1093/ndt/gfx376

ndt
Nephrology Dialysis Transplantation

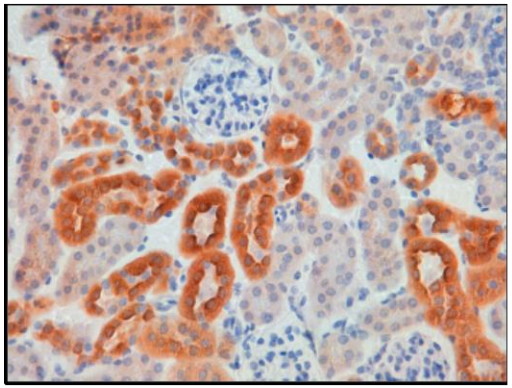
2018

Albumin downregulates Klotho in tubular cells

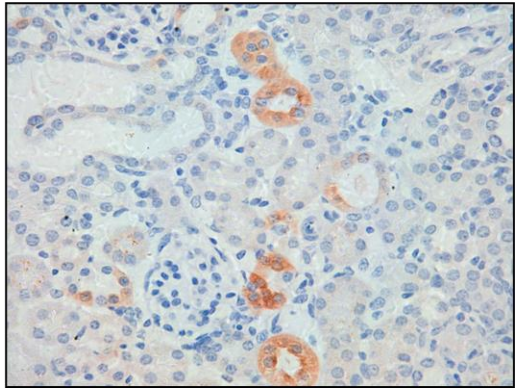
Beatriz Fernandez-Fernandez[1,2,3,a], M. Concepcion Izquierdo[1,2,3,5,a], Lara Valiño-Rivas[1,2,3], Dimitra Nastou[4], Ana B. Sanz[1,2,3], Alberto Ortiz[1,3,b] and Maria D. Sanchez-Niño[1,2,3,b]

Cited by 69

Control



Albuminuria



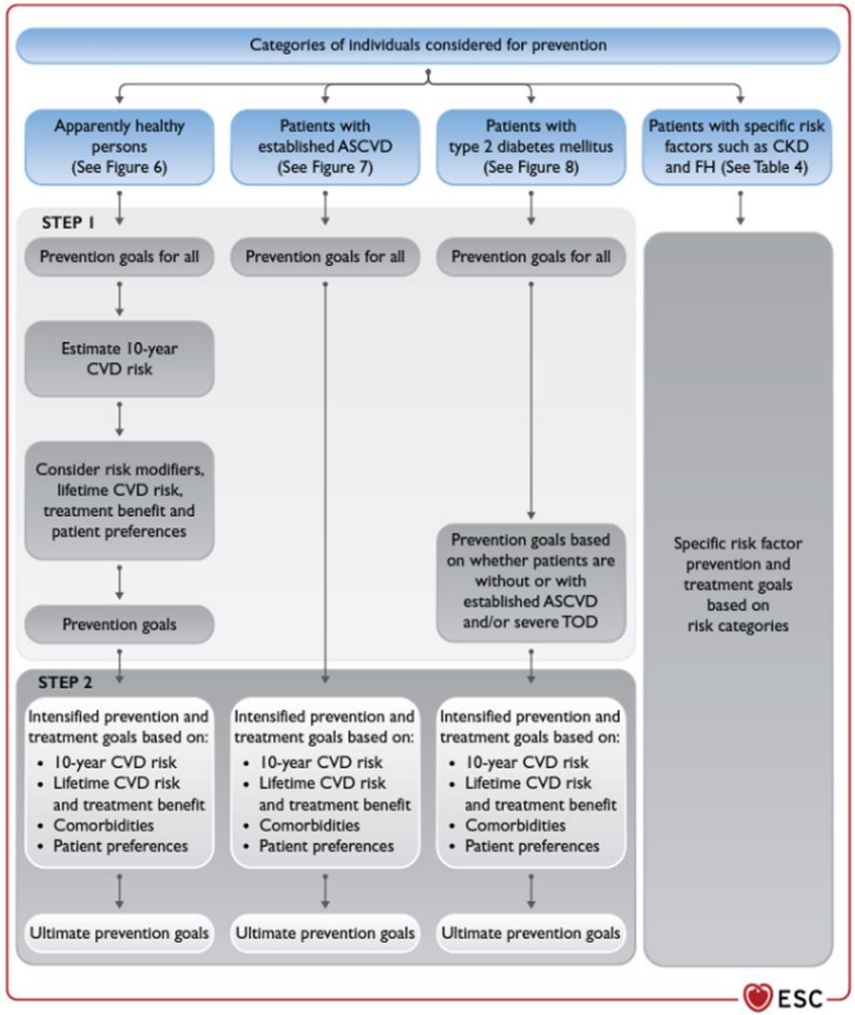
ESC
European Society of Cardiology
European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

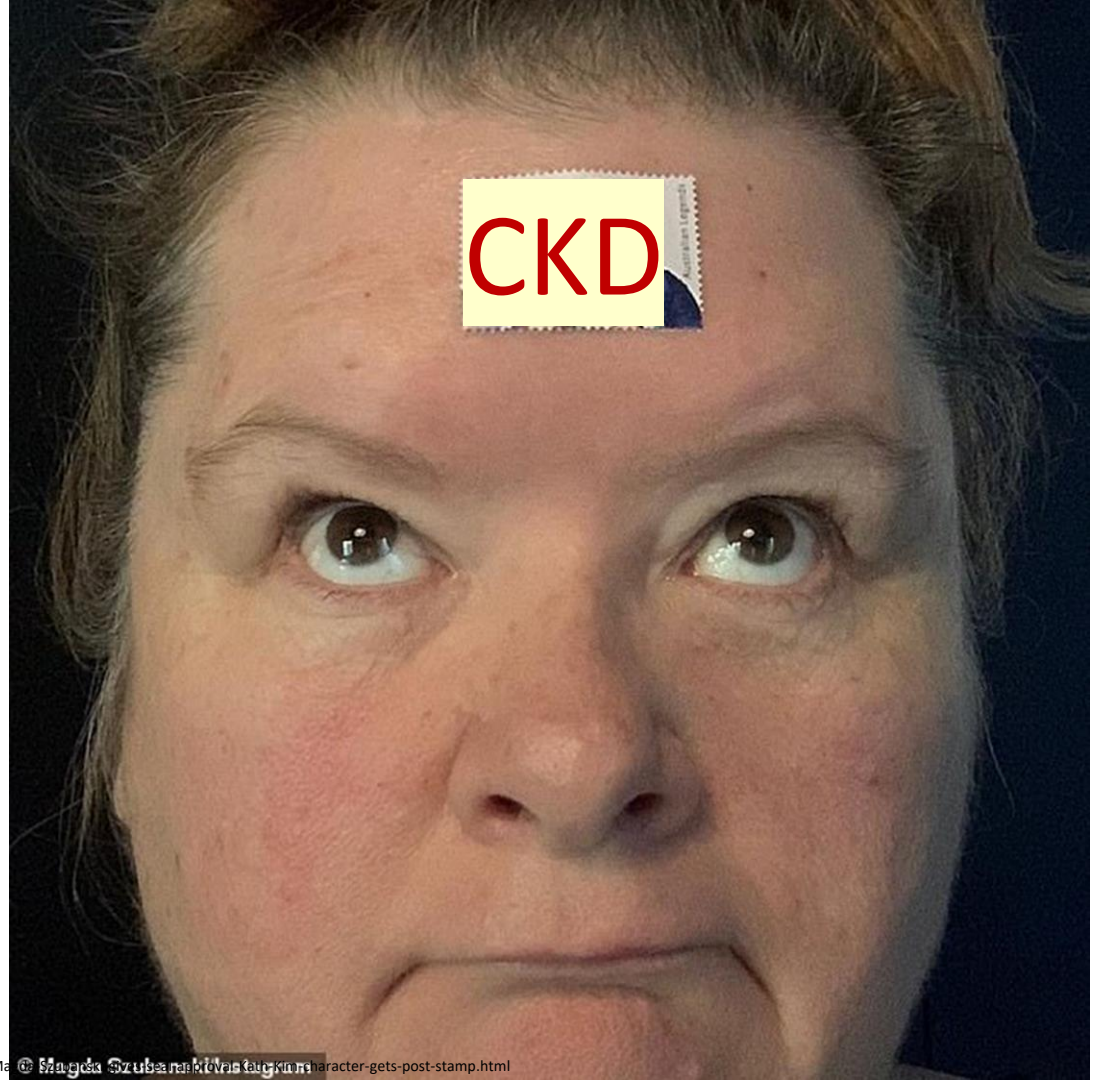
Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

Considerar la evaluación oportunista o sistemática
del riesgo cardiovascular
en **varones de más de 40** años
o **mujeres de más de 50 años** o post menopaúsicas


Categories of individuals considered for prevention
Apparently healthy persons (See Figure 6)
Patients with established ASCVD (See Figure 7)
Patients with type 2 diabetes mellitus (See Figure 8)
Patients with specific risk factors such as CKD and FH (See Table 4)
STEP 1
Prevention goals for all
Prevention goals for all
Prevention goals for all
Estimate 10-year CVD risk
Consider risk modifiers, lifetime CVD risk, treatment benefit and patient preferences
Prevention goals based on whether patients are without or with established ASCVD and/or severe TOD
Prevention goals
Specific risk factor prevention and treatment goals based on risk categories
STEP 2
Intensified prevention and treatment goals based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit
• Comorbidities
• Patient preferences
Intensified prevention and treatment goals based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit
• Comorbidities
• Patient preferences
Intensified prevention and treatment goals based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit
• Comorbidities
• Patient preferences
Ultimate prevention goals
Ultimate prevention goals
Ultimate prevention goals
ESC


Categorize individuals considered for prevention



https://www.dailymail.co.uk/tvshowbiz/article-8220581/Ma[illegible]character-gets-post-stamp.html

Categorize individuals considered for prevention

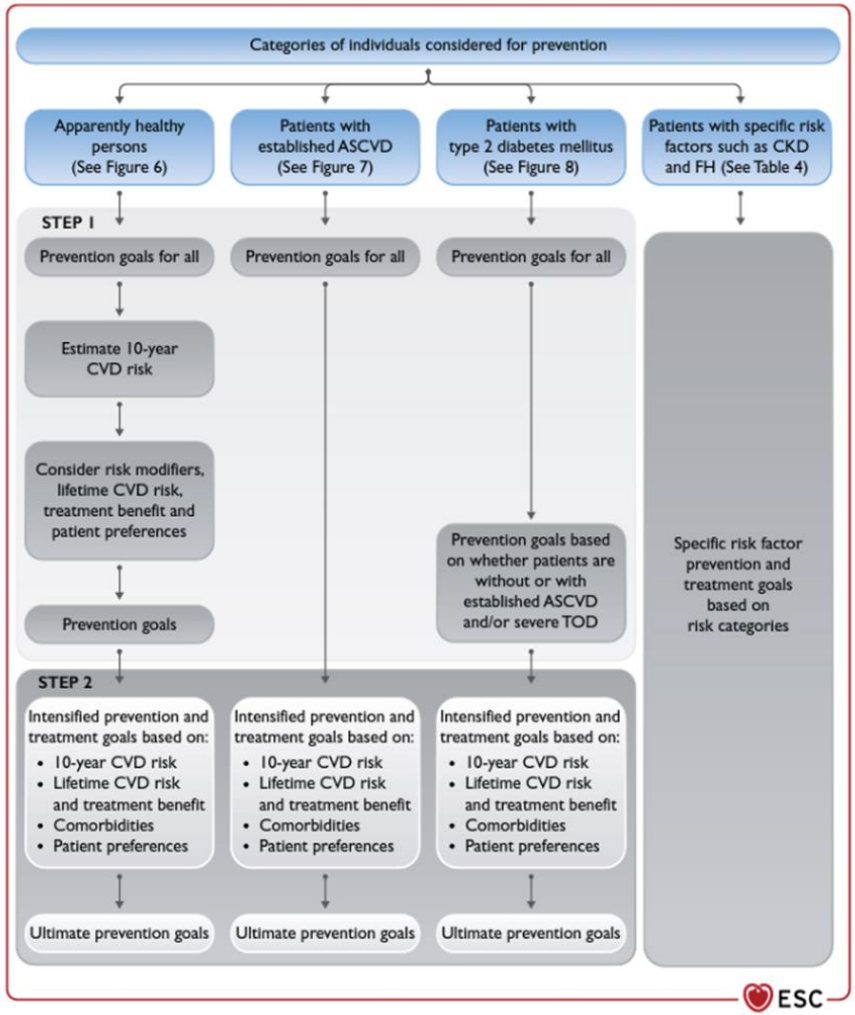
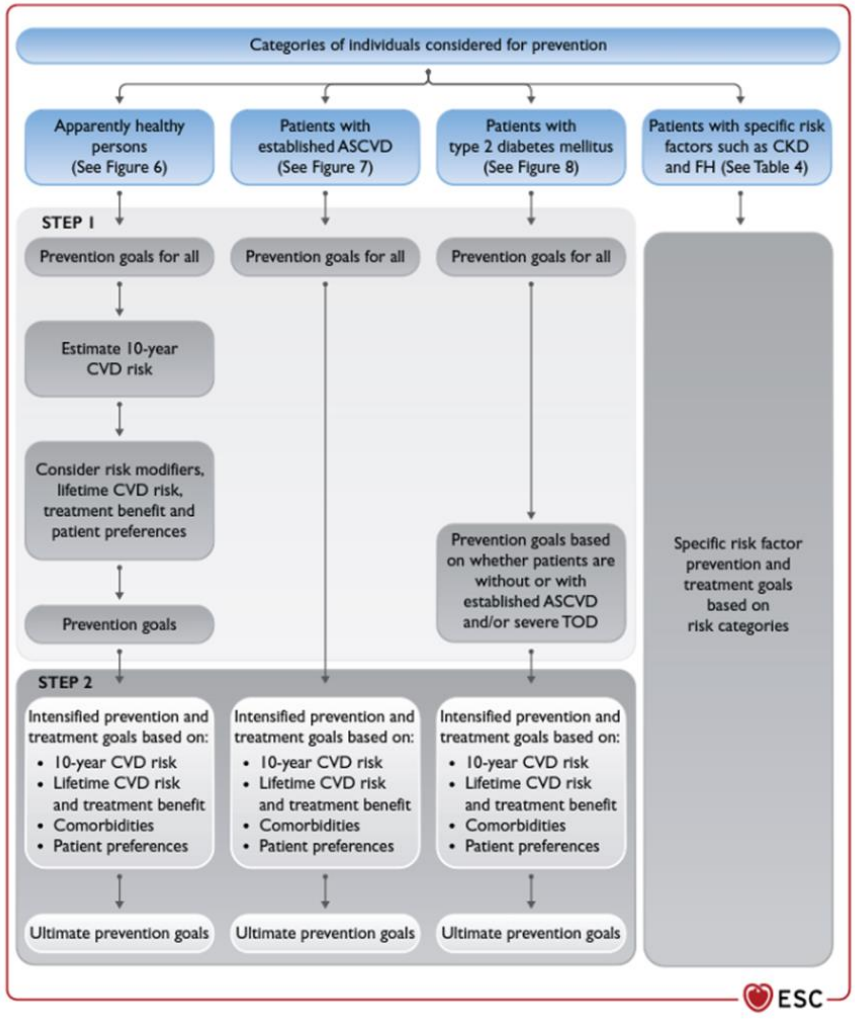


Figure 2. Examples of a stepwise approach to risk stratification and treatment options. ASCVD=atherosclerotic cardiovascular disease; CKD=chronic kidney disease; DM=diabetes mellitus; FH=familial hypercholesterolaemia; TOD=target organ damage



Categorize individuals considered for prevention

Past medical history:

ASCVD

DM* ← Serum glucose

FH* ← Serum cholesterol

CKD* ← Serum creatinine: eGFR

← Urinary albumin:creatinine ratio

Labs:

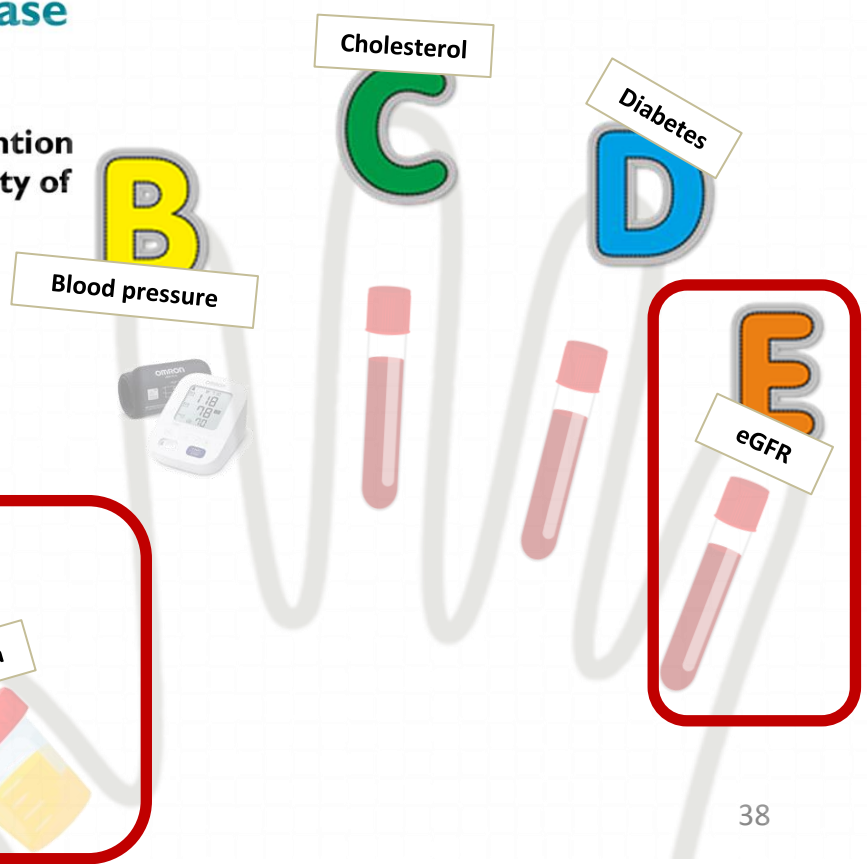
* Implies that serum glucose, cholesterol and creatinine, and urinary albumin:creatinine ratio have already been assessed

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)



Considerar la evaluación oportunista o sistemática
del riesgo cardiovascular
en **varones de más de 40** años
o **mujeres de más de 50 años** o post menopaúsicas

We have diagnosed CKD….

What now?

Treatment of hyperglycaemia and ASCVD/cardiorenal risks		
Metformin is recommended as first-line therapy, following evaluation of renal function, in the majority of patients without previous ASCVD, CKD, or HF.[589]	I	B
In persons with type 2 DM with ASCVD, metformin should be considered, unless contraindications are present.[5,590–592]	IIa	B
Avoidance of hypoglycaemia and excessive weight gain should be considered.[559,588,593]	IIa	B
In persons with type 2 DM and ASCVD, the use of a GLP-1RA or SGLT2 inhibitor with proven outcome benefits is recommended to reduce CV and/or cardiorenal outcomes.[590–592]	I	A
In patients with type 2 DM and TOD,[c] the use of an SGLT2 inhibitor or GLP-1RA with proven outcome benefits may be considered to reduce future CV and total mortality.[594–597]	IIb	B
In patients with type 2 DM and CKD, the use of an SGLT2 inhibitor is recommended to improve ASCVD and/or cardiorenal outcomes.[598,599]	I	A
In patients with type 2 DM and HFrEF, use of an SGLT2 inhibitor with proven outcome benefits is recommended to lessen HF hospitalizations and CV death.[600,601]	I	A
In patients with type 2 DM but without ASCVD, HF, or CKD, use of an SGLT2 inhibitor or GLP-1RA should be considered based on estimated future risks (e.g. with the ADVANCE risk score or DIAL model) for adverse CVD or cardiorenal outcomes from risk factor profiles.[602]	IIa	B

Recommendations in patients with chronic kidney disease: best medical therapy

ESC

Recommendations	Class	Level
Treatment with an ACE inhibitor or an ARB is recommended in patients with DM, hypertension, and albuminuria. These medications should be titrated to the highest approved dose that is tolerated.	I	B
An SGLT2 inhibitor with proven outcome benefits should be considered for the prevention of renal deterioration and mortality in patients with CKD.	IIa	B
Combination treatment with ACE inhibitors and ARBs is not recommended.	III	C

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

Treatment goals for different patient categories (1)

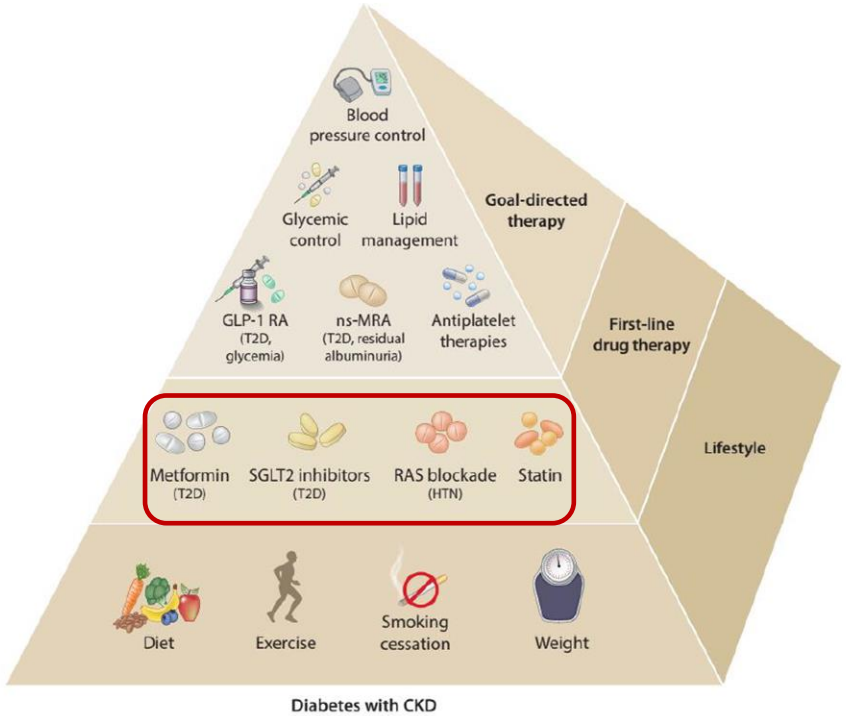
Patient category	Prevention goals (STEP 1)	Intensified/additional prevention goals[a] (STEP 2)
Patients with CKD	Stop smoking and lifestyle optimization SBP <140 down to 130 mmHg if tolerated[b] LDL-C <2.6 mmol/L (100 mg/dL) and ≥50% LDL-C reduction	LDL-C <1.8 mmol/L (70 mg/dL) in high-risk patients and <1.4 mmol/L (55 mg/dL) in very-high-risk patients (see *Table 4*)

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

Diabetes tipo 2

KDIGO 2022 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE (Public review version)

Figure 1. Kidney-heart risk factor management



Glycemic control is based on insulin for type 1 diabetes and a combination of metformin and SGLT2 inhibitors (SGLT2i) for type 2 diabetes. Metformin may be given when eGFR ≥30 ml/min per 1.73 m^2 and SGLT2i should be used when eGFR is ≥20 ml/min per 1.73 m^2. SGLT2i are recommended for patients with type 2 diabetes and chronic kidney disease (CKD). Renin–angiotensin system (RAS) inhibition is recommended for patients with albuminuria and hypertension. Aspirin generally should be used lifelong for secondary prevention among those with established cardiovascular disease and may be considered for

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dapagliflozin in Patients with Chronic Kidney Disease

Hiddo J.L. Heerspink, Ph.D., Bergur V. Stefánsson, M.D., Ricardo Correa-Rotter, M.D., Glenn M. Chertow, M.D., Tom Greene, Ph.D., Fan-Fan Hou, M.D., Johannes F.E. Mann, M.D., John J.V. McMurray, M.D., Magnus Lindberg, M.Sc., Peter Rossing, M.D., C. David Sjöström, M.D., Roberto D. Toto, M.D., Anna-Maria Langkilde, M.D., and David C. Wheeler, M.D., for the DAPA-CKD Trial Committees and Investigators*

Fabry Disease: Renal Involvement Limited to Podocyte Pathology and Proteinuria in a Septuagenarian Cardiac Variant. Pathologic and Therapeutic Implications

Shane M. Meehan, MD, Tipsuda Junsanto, MD, James J. Rydel, MD, and Robert J. Desnick, PhD, MD

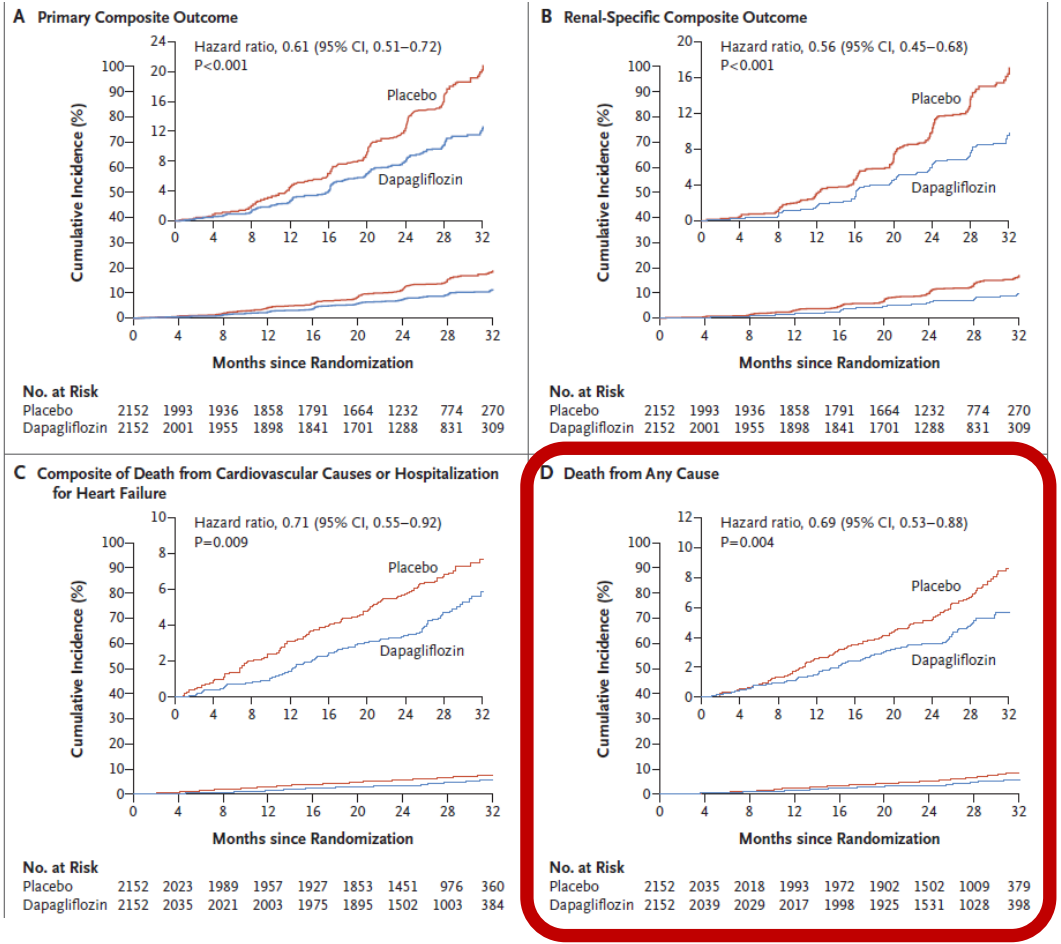
Am J Kidney Dis. **2004** Jan;43(1):164-71.

4304 participants, **diabetic** (67%) and **non-diabetic**

- eGFR 25-75 mL/min/1.73m2
- UACR 200-5000 mg/g
- randomized to dapagliflozin 10mg or placebo,

All the participants were required to be receiving a stable dose of an **ACE inhibitor or ARB** for at least 4 weeks before screening. However, participants who were documented to be unable to take ACE inhibitors or ARBs were allowed to participate.

sustained **decline in the eGFR** >=50%, **end-stage kidney disease**, or **death** from renal or cardiovascular causes.



Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med*. 2020;383(15):1436-1446.

A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy

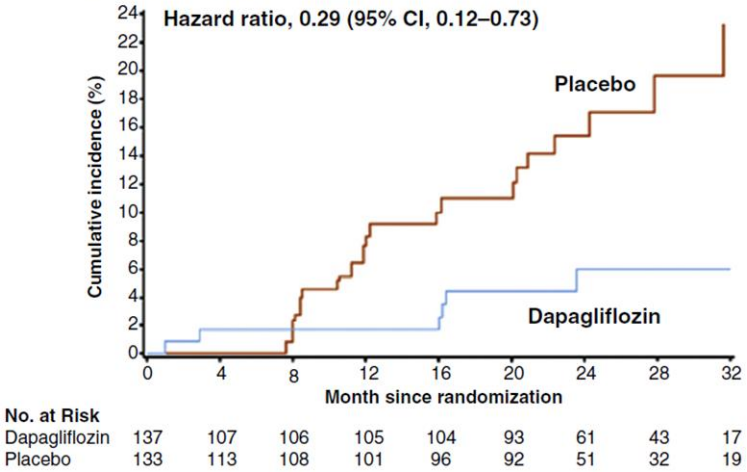
see commentary on page 24

OPEN

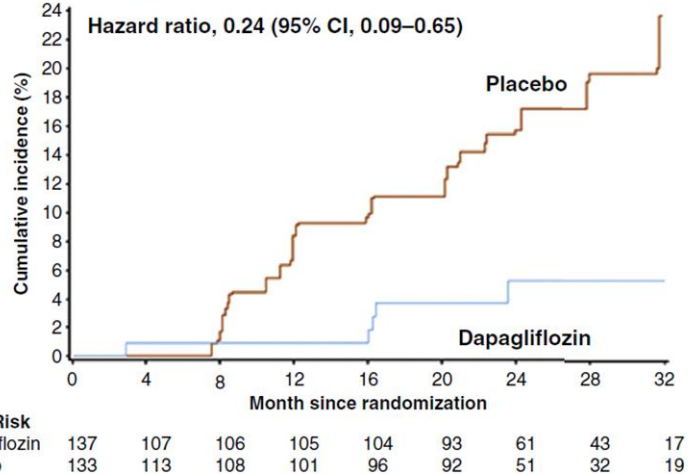
David C. Wheeler[1,2], Robert D. Toto[3], Bergur V. Stefánsson[4], Niels Jongs[5], Glenn M. Chertow[6,7], Tom Greene[8], Fan Fan Hou[9], John J.V. McMurray[10], Roberto Pecoits-Filho[11,12], Ricardo Correa-Rotter[13], Peter Rossing[14,15], C. David Sjöström[4], Kausik Umanath[16,17], Anna Maria Langkilde[4] and Hiddo J.L. Heerspink[5]; for the DAPA-CKD Trial Committees and Investigators

- N=270
- eGFR 25-75 mL/min/1.73m2
- UACR 200-5000 mg/g
- randomized to dapagliflozin 10mg or placebo,

Primary endpoint (IgA FAS)



Renal endpoint (IgA FAS)



Waijer SW, Vart P, Cherney DZI, et al. Effect of dapagliflozin on kidney and cardiovascular outcomes by baseline KDIGO risk categories: a post hoc analysis of the DAPA-CKD trial [published online ahead of print, **2022 Apr 21**]. *Diabetologia*. 2022;10.1007/s00125-022-05694-6. doi:10.1007/s00125-022-05694-6

Appendix A. Renal involvement

- Assessment: eGFR + albuminuria (UACR) ± renal biopsy
- Therapy
  - **Initiate** therapy for Fabry disease as **early** as possible
    - All classical males

    - Others with eGFR, UACR (**>30** mg/g) or kidney biopsy evidence of kidney injury
  - **Adjunctive** therapies
    - Aggressive management of albuminuria: **RAS blockade**: initiated with the lowest possible dose administered at nighttime with subsequent titration according to therapeutic response

      Consider **SGLT2 inhibition**
    - It is reasonable to monitor **25OH-vitamin D** levels and to correct any observed nutritional vitamin D deficiency
    - Specific management **recommendations for CKD** patients regarding blood pressure targets and statin therapy apply

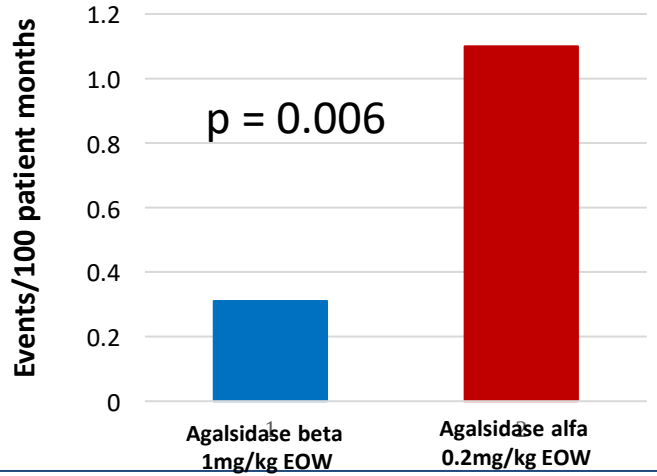
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; RAS, renin–angiotensin system; UACR, urinary albumin:creatinine ratio; EOW every other week.

Ortiz A et al. *Mol Genet Metab* 2018;123:416–27

CFDI: the Canadian Fabry Disease Initiative

10-year outcomes of an RCT of ERT[1]

Events: (renal replacement therapy, doubling of serum creatinine, proteinuria > 3.5 g/day)



More renal events in males receiving agalsidase alfa than in males receiving agalsidase beta
(1.1 vs 0.31 events/100 patient months **IRR 0.24** p = 0.006)

Estimated sample size: **600**
Enrolled: **132** patients
n = 56 agalsidase beta 1mg/kg/EOW
n = 76 agalsidase alfa 0.2mg/kg/EOW
Median follow-up: 99 mos
(range 5–123)

- **Rates of cardiac or neurological events or death did not differ**
- **No difference in renal events, or in the rate of decline in eGFR in females**

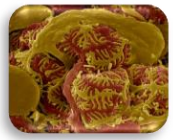
Statistical test, Safety outcomes were not reported in this abstract

IRR, incidence rate ratio.

Sirrs SM, et al. Differential effects of agalsidase alfa and beta in Faby outcomes: 10 year outcomes from the Canadian Fabry disease initiative. J Inherit Metab Dis. 2018;41(Suppl 1):abstract P-373.
Image available from:
https://upload.wikimedia.org/wikipedia/commons/4/48/201405_kidney.png.

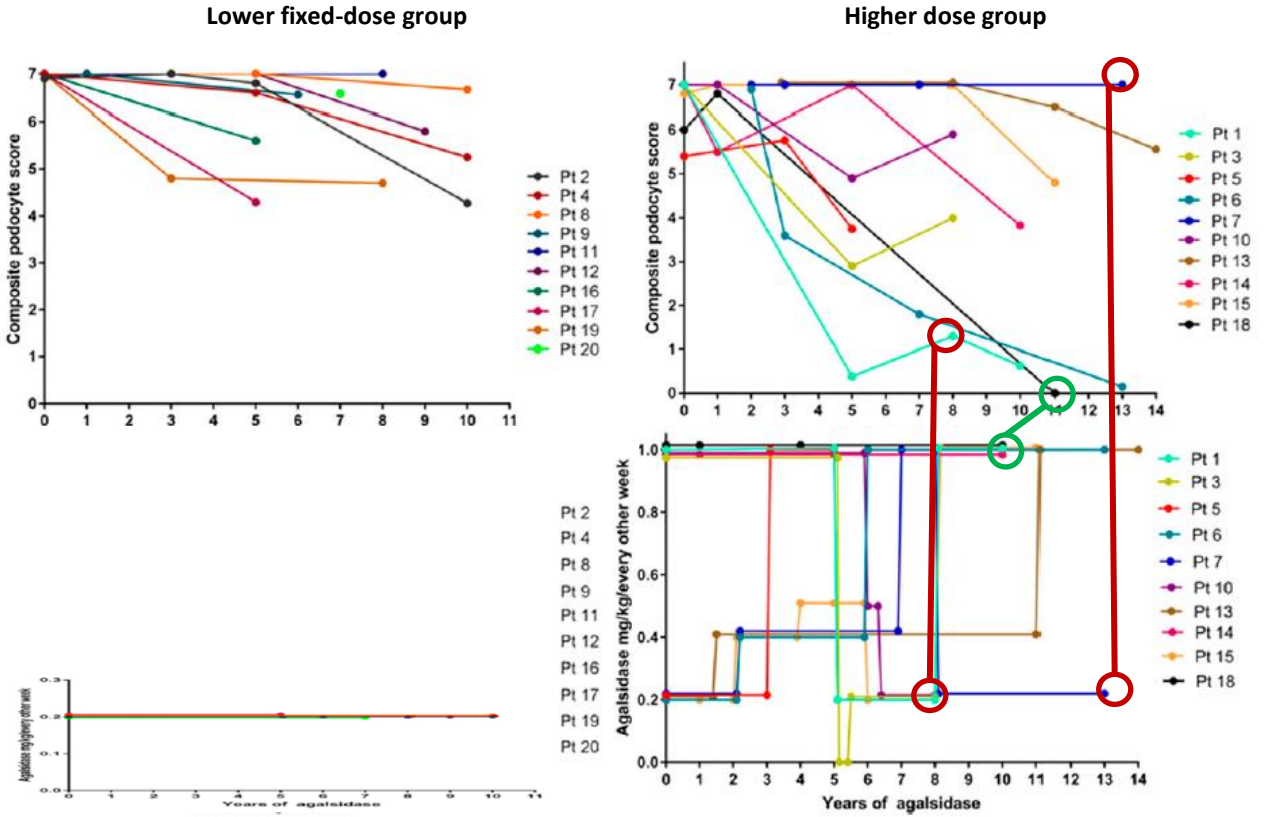
Observational: Long-term dose-dependent agalsidase effects on kidney histology in Fabry disease

- Reduction of **podocyte Gb3** correlated with **cumulative dose**



- Residual plasma **lyso-Gb3** correlated with **cumulative dose** in men

Endothelium cleared in all



Gb3, globotriaosylceramide.

Skrunes R, et al. Clin J Am Soc Nephrol. 2017;12:1470-9.

Take home message

Are you requesting **UACR** to all your patients?