Evaluation du rein du donneur

Actualités néphrologiques Jean Hamburger

23 Avril 2018

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ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Inserm

FONDATION BETTENCOURT SCHUELLER

Liens d'intérêts

aucun

What do we know about kidney donation ?

1952 | 1978 | 1992 | 1997 | 2009

Gilberte Renard
85 ans - 1992

Living related kidney donors: complications and long-term renal function

Transplantation

20 years or more of follow-up of living kidney donors

Lancet

Kidney donors live longer

Transplantation

Long term consequences of LKD

NEJM

« The most important limitation of our study is the lack of an ideal control group... »

Increased ESRD risk: 2014

ESRD: x 11,4

Table 1 | Baseline characteristics of kidney donors and controls

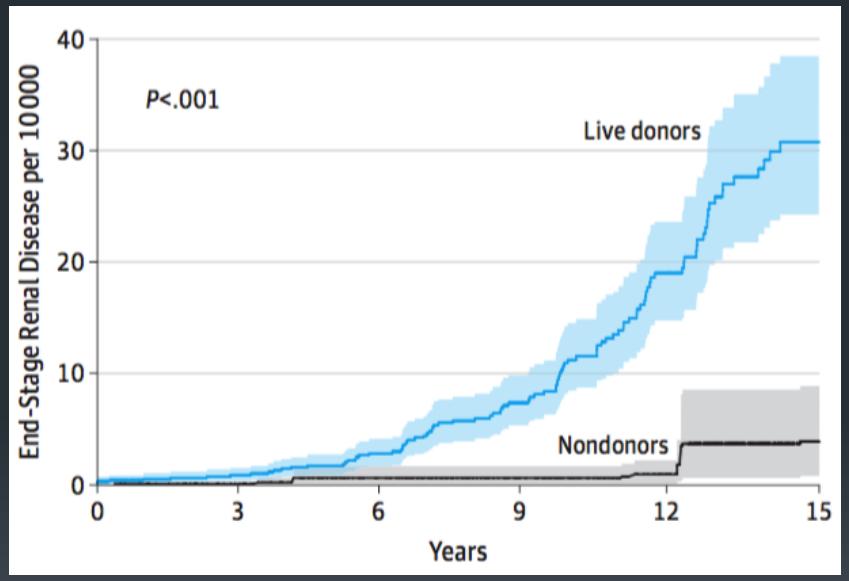
	Kidney donors	Controls
Age, years	46.0 ± 11.5 $n = 1901$	37.6 ± 11.7 $n = 32{,}621$
Male gender, %	41.0 $n = 1901$	46.9 $n = 32{,}621$
Current smoking, %	41.5 $n = 1375$	39.5 $n = 25{,}993$
Systolic BP, mm Hg	123.3 ± 10.0 $n = 1768$	121.4 ± 10.4 $n = 31{,}398$
Diastolic BP, mm Hg	77.4 ± 7.2 $n = 1768$	77.2 ± 7.9 $n = 31{,}394$
BMI, kg/m^2	24.2 ± 2.8 $n = 1558$	23.5 ± 2.6 $n = 31{,}421$

Abbreviations: BMI, body mass index; BP, blood pressure.

1901 donors

Mjoen et al. Kidney Int. 2014

ESRD: x 7,4

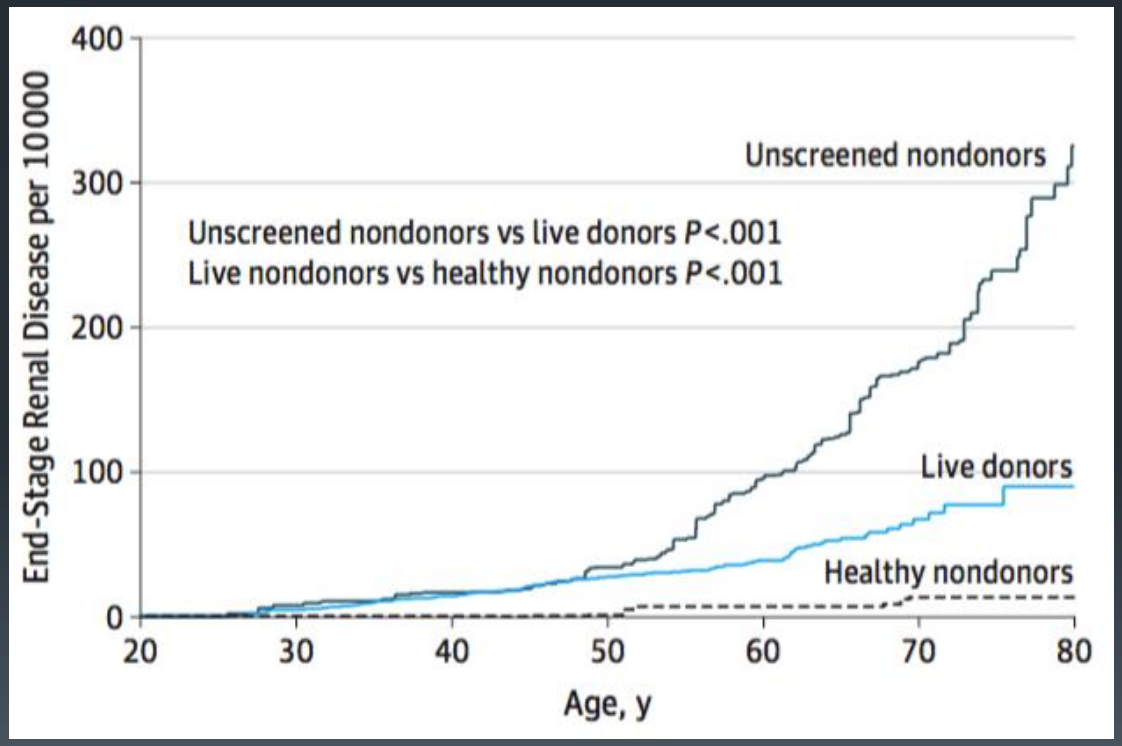


96 000 donors

Muzaale et al. JAMA. 2014

Increased ESRD risk

« The most important limitation of our study is the lack of an ideal control group... »



Muzaale et al. JAMA. 2014

ESRD among donors

	Mjoen *et al.*	Ibrahim *et al.*	Kido *et al.*
% ESRD	0,47%	0,32%	0,53%
Glomerulonephritis	3	1	
Lupus	1		
ANCA	2		1
BBS	1		
DM	2		
UHS		1	
HTA		3	
RCC		1	
Sclerodermie		1	
Cardiac failure			4
Unknown		4	

Relation to the recipient

Mjoen : 9/9

Muzaale : 83/99

Ibrahim : 11/11

Kido : 8/8

ESRD among donors

TABLE 3 Known causes of donor ESRD (n = 25)

Cause of ESRD	n
HTN	6
Essential	4
Atherosclerotic renal disease	2
DM plus HTN	4
DM	2
Renal cancer	2
Alport syndrome	2
Hemolytic uremic syndrome	2
Glomerular disease	4
Scleroderma	1
Other	2
Sepsis	
Interstitial nephritis	

DM, diabetes mellitus; HTN, hypertension.

Matas *et al.* AJT, 2018

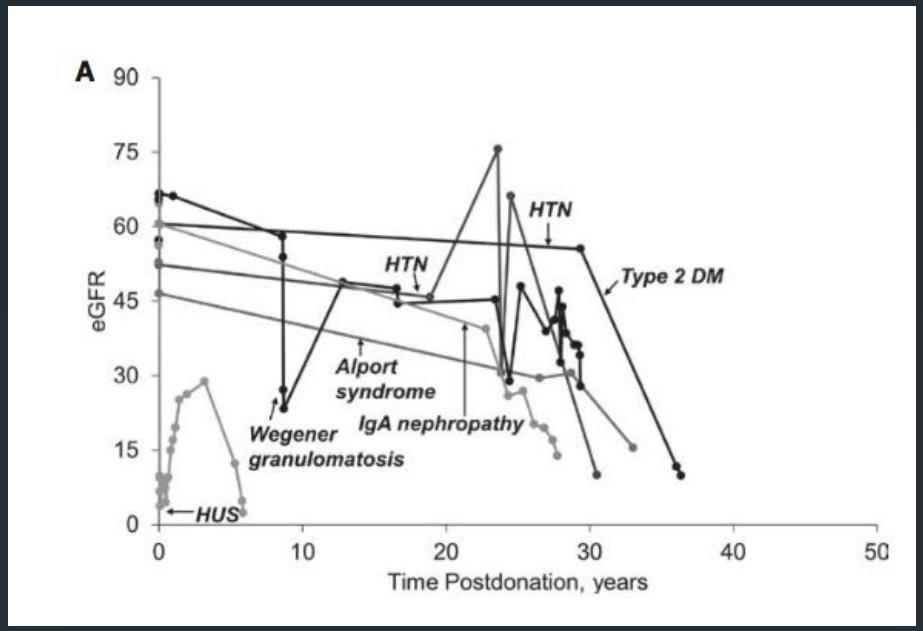
ESRD among donors

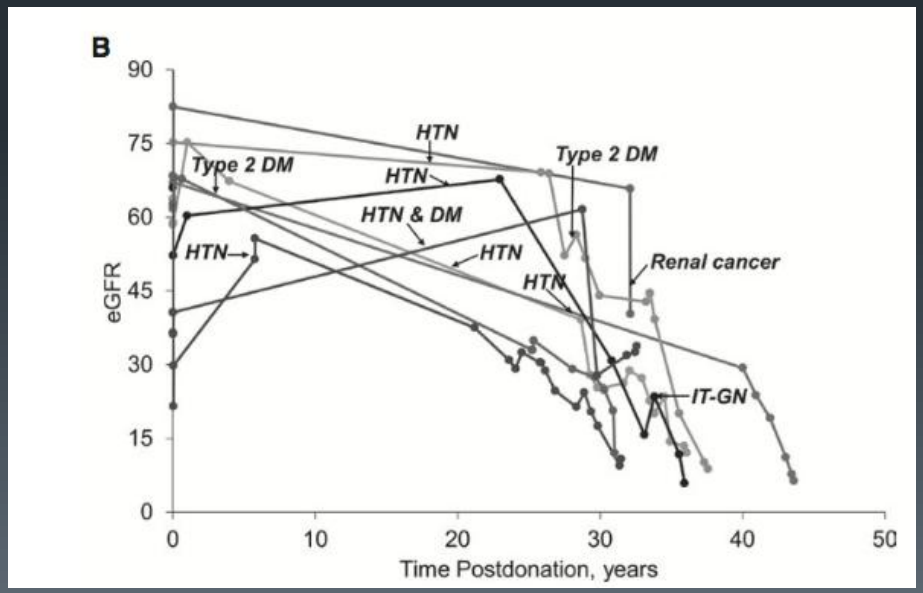
eGFR « decline » after donoation is similar in related and unrelated donors

		Family History ESRD		No Family History ESRD	
	Time Since Donation	Estimated Slope	SE	Estimated Slope	SE
Current Age < 70 years	6 wks -5 yrs post-donation	1.12	0.10	1.32	0.11
	5-10 years post-donation	0.24	0.12	0.44	0.13
	10-20 years post-donation	0.07	0.09	0.27	0.11
	>20 years post-donation	-0.19	0.28	0.01	0.29
Current Age > 70 years	6 wks -5 yrs post-donation	0.74	0.18	0.94	0.18
	5-10 years post-donation	-0.14	0.19	0.06	0.19
	10-20 years post-donation	-0.31	0.16	-0.11	0.17
	>20 years post-donation	-0.57	0.31	-0.37	0.31

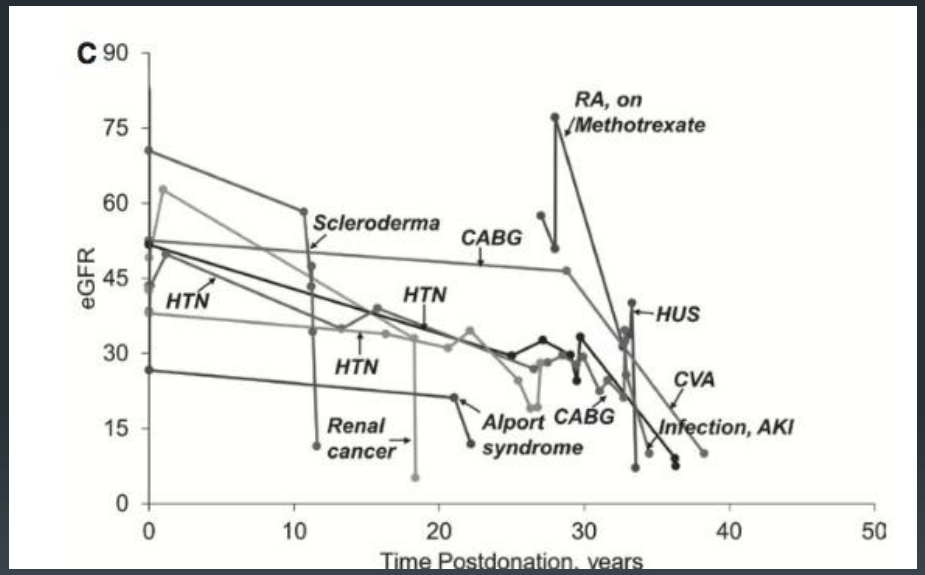
Matas *et al.* AJT, 2018

ESRD among donors





Sudden ESRD onset



Matas *et al.* AJT, 2018

Can ESRD risk be predicted ?

Risk calculators

Can ESRD risk be modified?

Before donation – After donation

Can ESRD risk be predicted?

Risk calculators

Can ESRD risk be modified?

Before donation – After donation

Can ESRD risk be predicted?

	Grams *et al.*	Ibrahim *et al.*	Massie *et al.*
Sample	4 933 414	3956	133 824
Donors	No	Yes	Yes
Population	International	Monocentric	USA
Variables	**Age**	**Age**	**Age**
	BMI	**BMI**	**BMI**
	Sex		**Sex**
	Origin		**Origin**
	SBP	**SBP**	
	DM		
	Medications		
	eGFR		
	Albuminuria		
	Smoking		Relation to recipient
Lien	http://www.transplantmodels.com/esrdrisk/	http://jasn.asnjournals.org/content/27/9/2885/suppl/DCSupplemental	www.transplantmodels.com/donesrd/

Can ESRD risk be predicted?

Donor		5-Year	10-Year	15-Year	20-Year
Black Male	20-year-old	5 (1-8)	24 (7-40)	62 (20-103)	111 (35-186)
	40-year-old	3 (1-4)	13 (6-21)	35 (16-53)	63 (29-96)
	60-year-old	1 (0-3)	8 (1-14)	20 (3-36)	35 (5-65)
Black Female	20-year-old	3 (1-5)	14 (4-23)	35 (11-59)	63 (19-107)
	40-year-old	2 (1-2)	8 (3-12)	20 (9-30)	36 (17-55)
	60-year-old	1 (0-2)	4 (1-8)	11 (2-21)	20 (3-37)
White Male	20-year-old	1 (0-1)	3 (1-5)	7 (3-12)	13 (5-22)
	40-year-old	1 (0-1)	5 (2-7)	12 (6-17)	21 (11-31)
	60-year-old	1 (0-2)	7 (3-11)	19 (8-30)	34 (14-54)
White Female	20-year-old	0 (0-1)	2 (1-3)	4 (2-7)	8 (3-13)
	40-year-old	1 (0-1)	3 (1-4)	7 (4-10)	12 (7-18)
	60-year-old	1 (0-1)	4 (2-6)	11 (5-17)	20 (9-30)

Time Since Donation

Wainright *et al.* , AJT 2018

A paradigm shift

Age	**OK**
GFR	**OK**
Blood pressure	**OK**
BMI	**OK**
Albuminuria	**OK**
Smoking	**OK**
DM	**OK**
Relation to recipient	**OK**

→

Age
+ GFR
+ Blood pressure
+ BMI
+ Albuminuria
+ Smoking
+ DM
+ Others …..

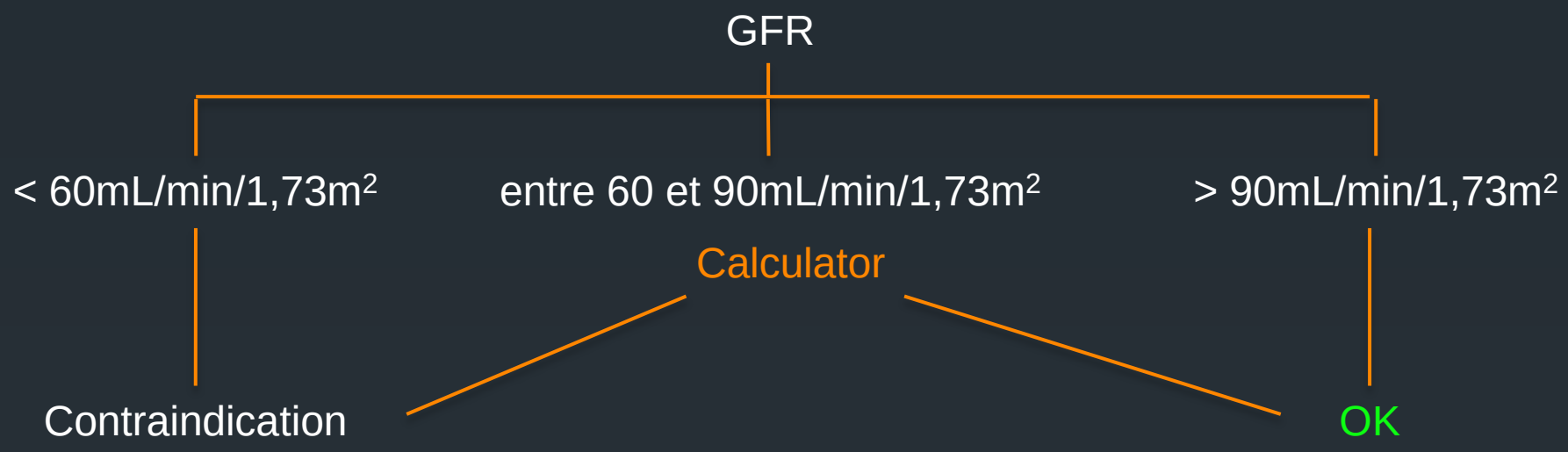
= OK

KDIGO LKD

Lipids	**Calculator**
GFR	**Calculator**
Blood pressure	**Calculator**
BMI	**Calculator**
Albuminuria	**Calculator**
Smoking	**Calculator**
DM	**Calculator**

Lentine *et al.* Transplantation 2017

KDIGO LKD



Lentine *et al.* Transplantation 2017

Unanswered questions

1. Use of calculators in clinical practice ?
2. Why to evaluate GFR ?
3. Impact of age on acceptable GFR thresholds ?
4. How to evaluate GFR ?
5. How to evaluate renal asymetry ?

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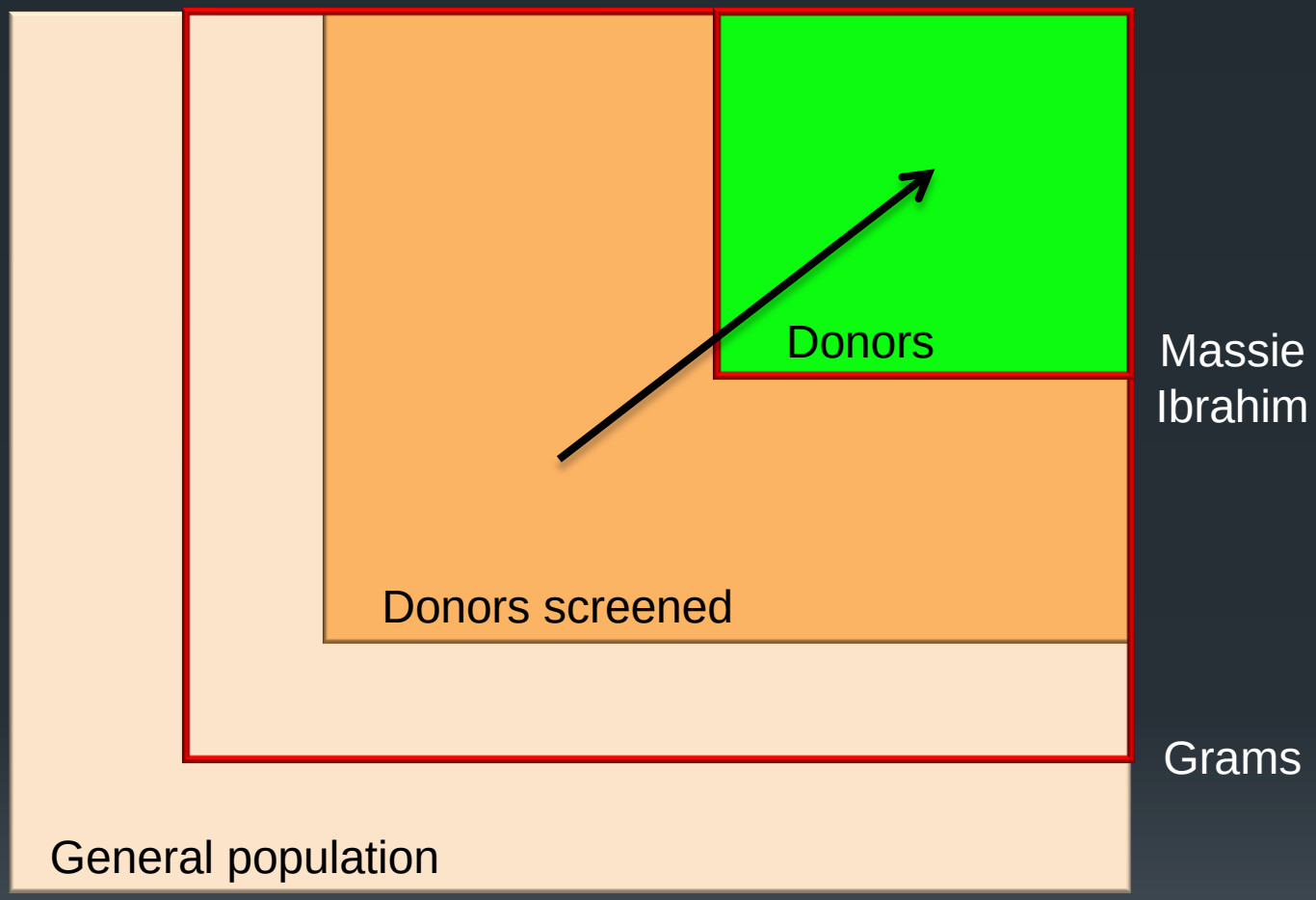
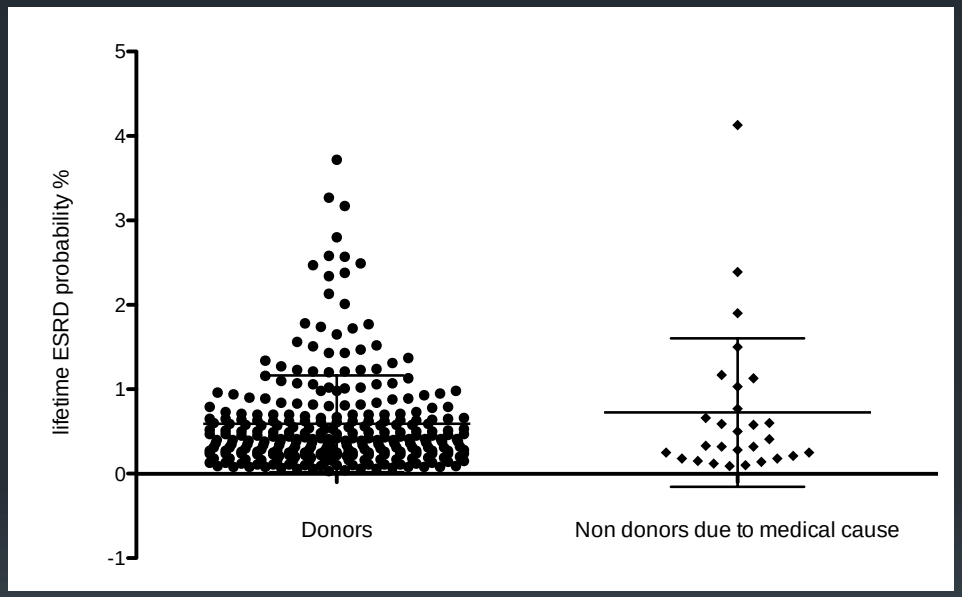
Use of calculators

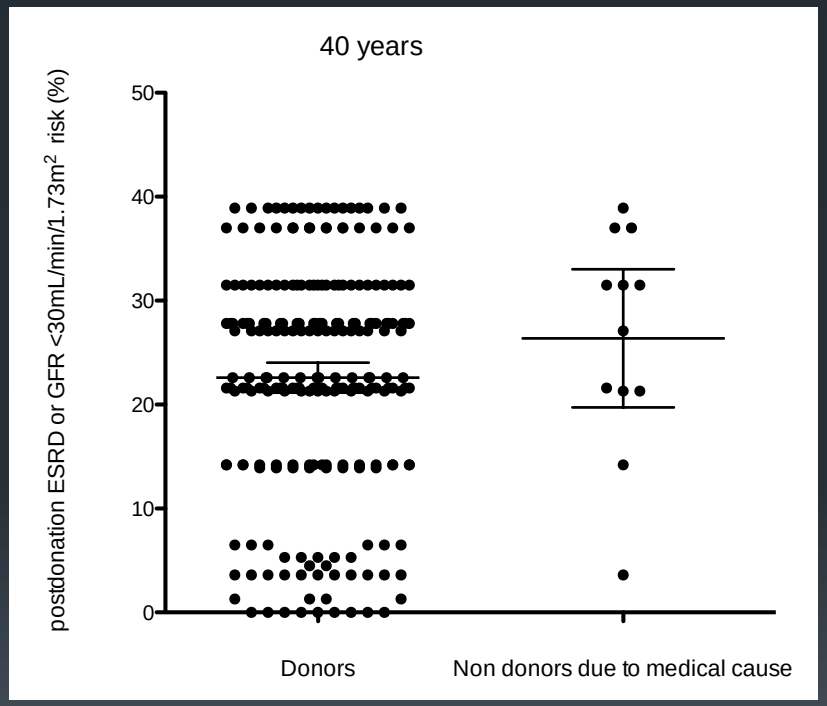


Use of calculators

ESRD risk predicted by calculators for non donors due to medical cause is not different from the one of donors



0,59 *p=0,97* 0,72



22,6 *p=0,32* 26,4

Gaillard *et al.* Transplant Int 2017.

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Why to evaluate GFR

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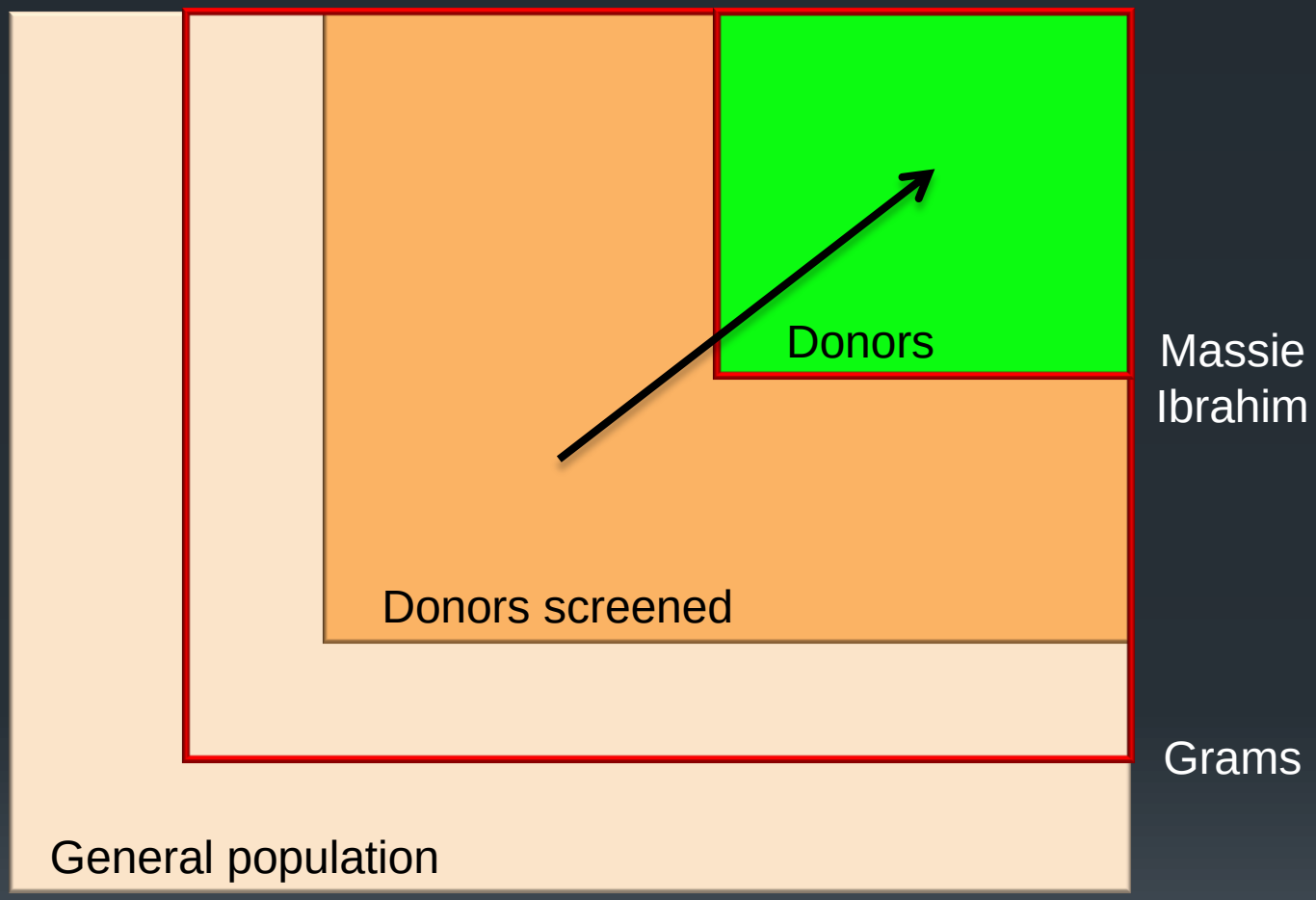
Why to evaluate GFR



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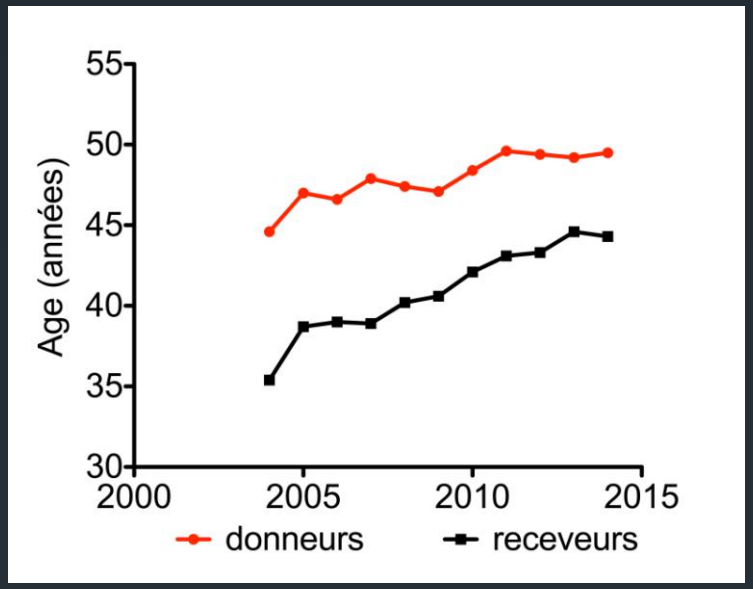
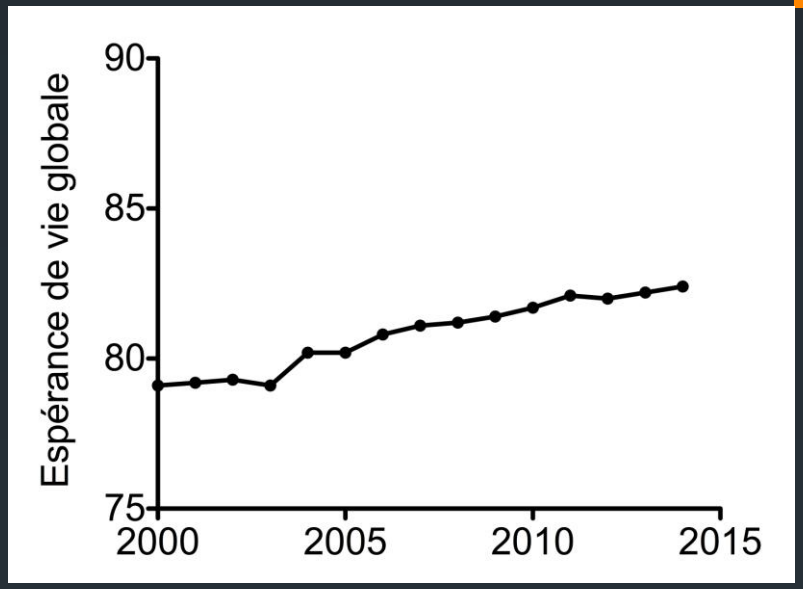




Soit 33 ans après le don → Prédire l'évolution du DFG

Why to evaluate GFR

Effets cardiovasculaires mesurables à 1an

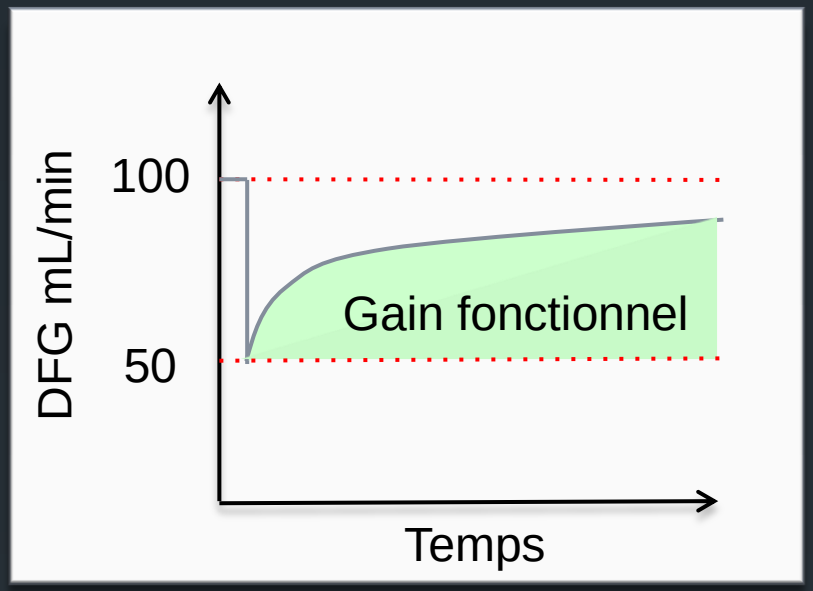
- Troponine US detectable
- CRP US
- FGF 23
- Acide urique
- Masse VG
- Epaisseur septum
- Distensibilité aortique

→ Directement proportionel à la baisse du DFG mesuré

D'après Moody *et al.* Hypertension, 2016

Why to evaluate GFR

For renal function follow up



Van Londen *et al.* NDT, 2018

	Baisse	Stable	Hausse
DFGm (mL/min/an)	-0,82	0,93	3,25
CKD-EPI	0,59	0,95	2,18
MDRD	0,69	1,04	2,16
CG	0,38	0,70	2,04

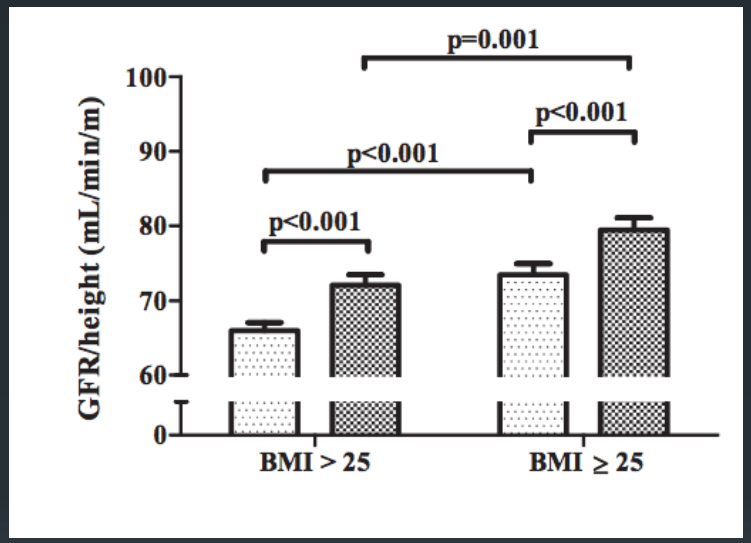
Why to evaluate GFR

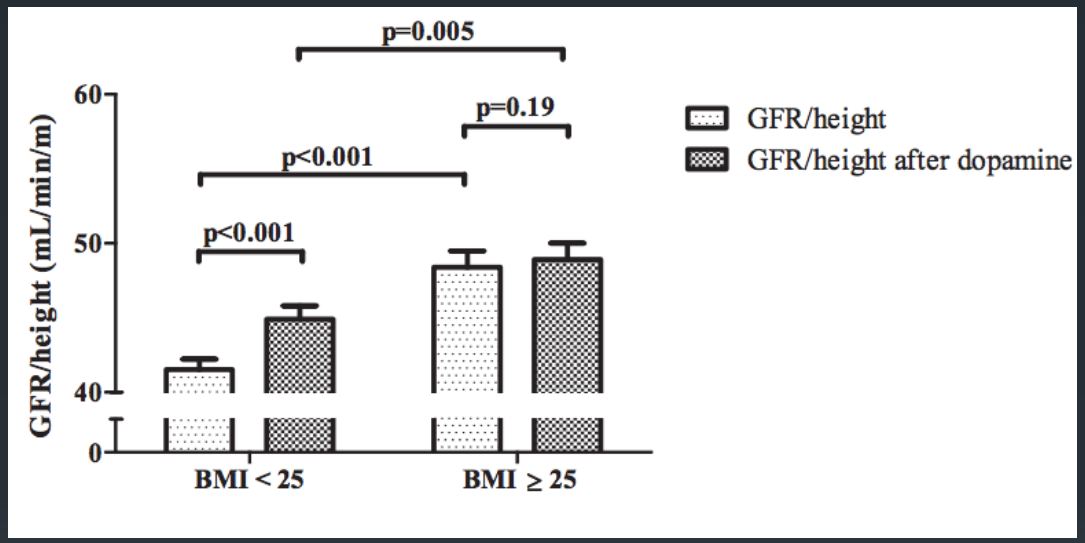
Renal reserve = increase of remaining kidney GFR after donation

Stimulated by dopamine Infusion

Why to evaluate GFR

Loss of renal reserve after donation in young women with BMI≥25





Van Londen *et al.* , AJPRP 2018

Why to evaluate GFR

1. Associated with ESRD risk
2. Associated with cardiovascular remodeling
3. Mandatory for follow up of kidney function
4. Insights into uninephrectomy pathophysiology

Unanswered questions

1. Use of calculators in clinical practice ?
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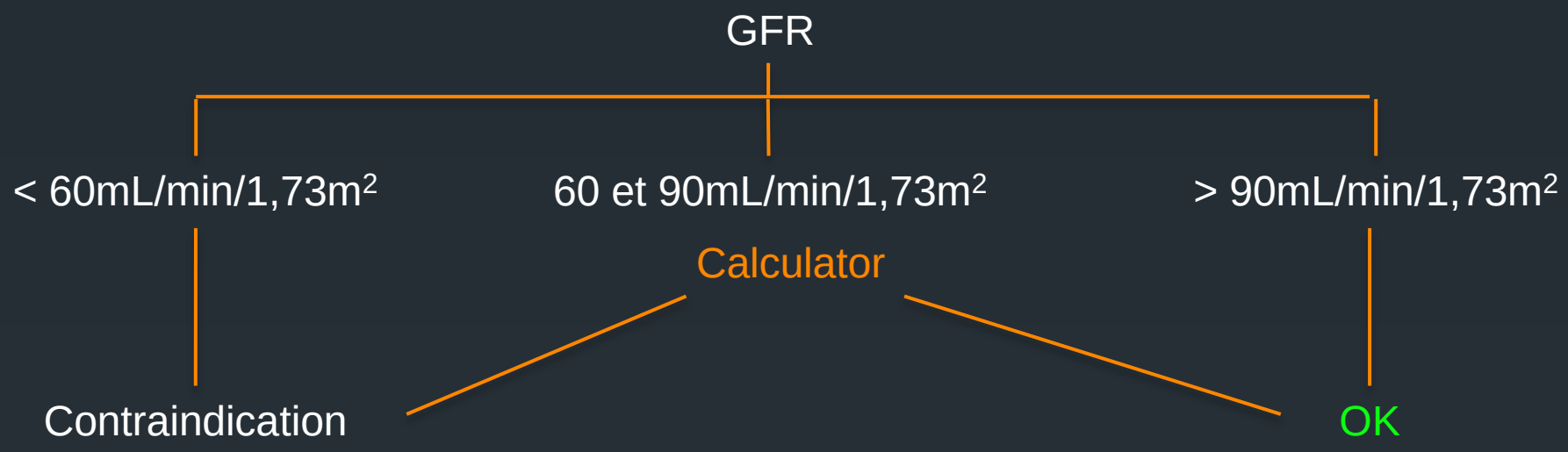
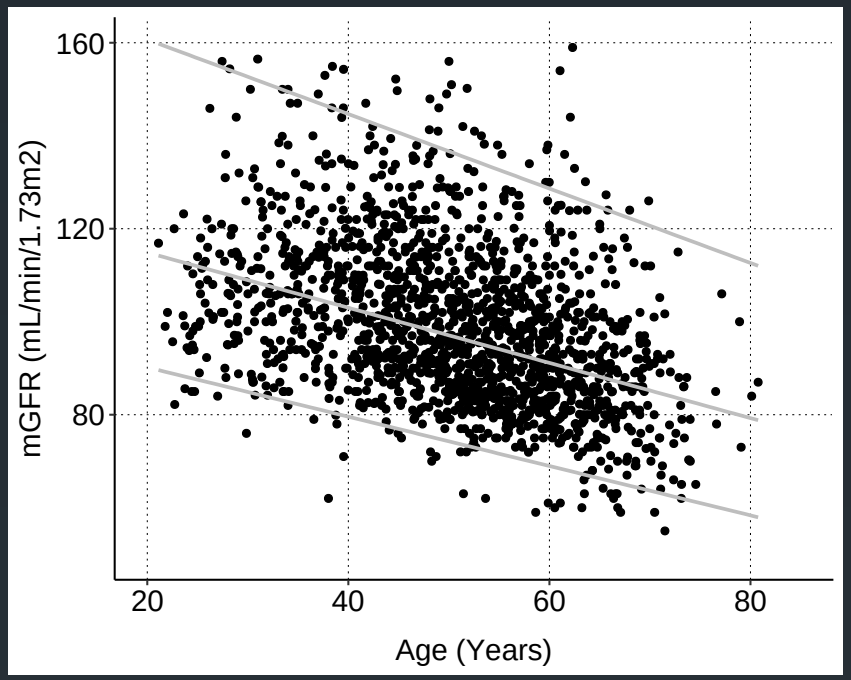
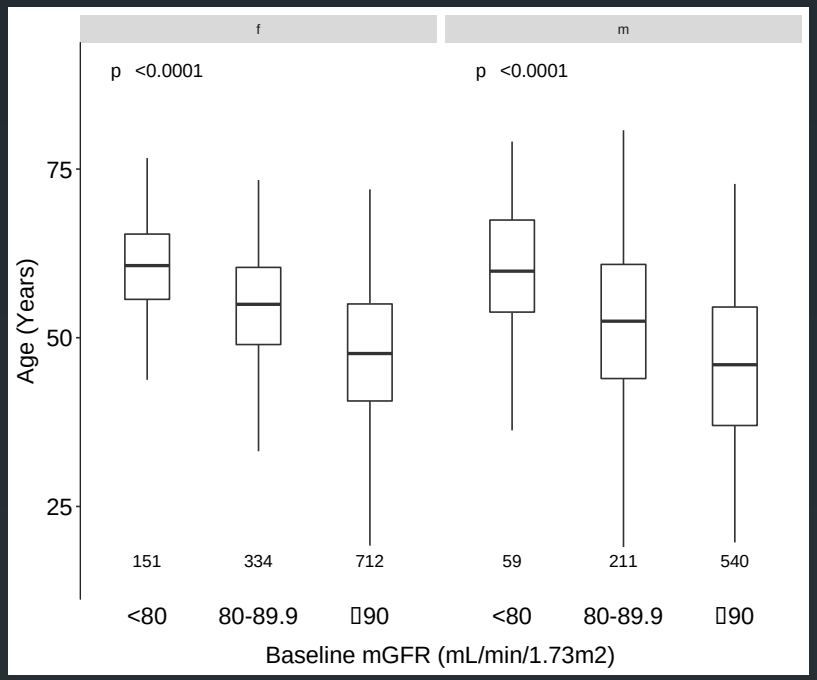
KDIGO LKD



Lentine *et al.* Transplantation 2017

Impact of age on GFR



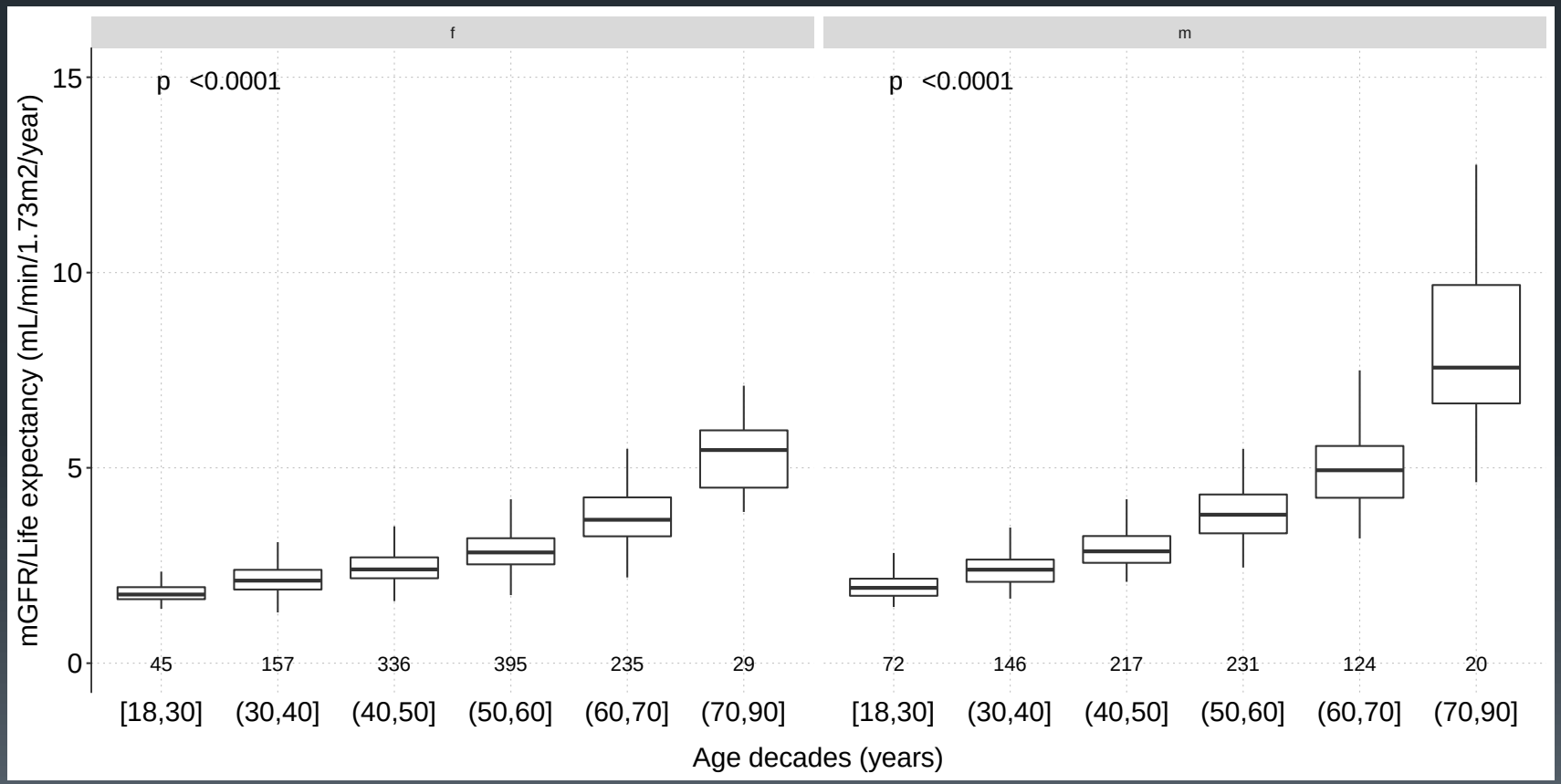


	mGFR		
Age decade (n)	**Mean** (SD)	**95%CI**	**2.5th – 97.5th** percentile
18-30 *(117)*	106.3 (15.5)	103.5 – 109.1	84.9 – 146.8
30-40 *(303)*	107.6 (18.1)	105.5 – 109.6	78.5 – 150.0
40-50 *(553)*	103.4 (16.7)	102.0 – 104.8	79.0 – 140.0
50-60 *(626)*	95.4 (15.4)	94.2 – 96.7	72.0 – 130.0
60-70 *(359)*	89.7 (16.4)	88.0 – 91.4	63.0 – 125.1
70-90 *(49)*	81.7 (13.9)	77.7 – 85.7	59.6 – 110.8

Under review

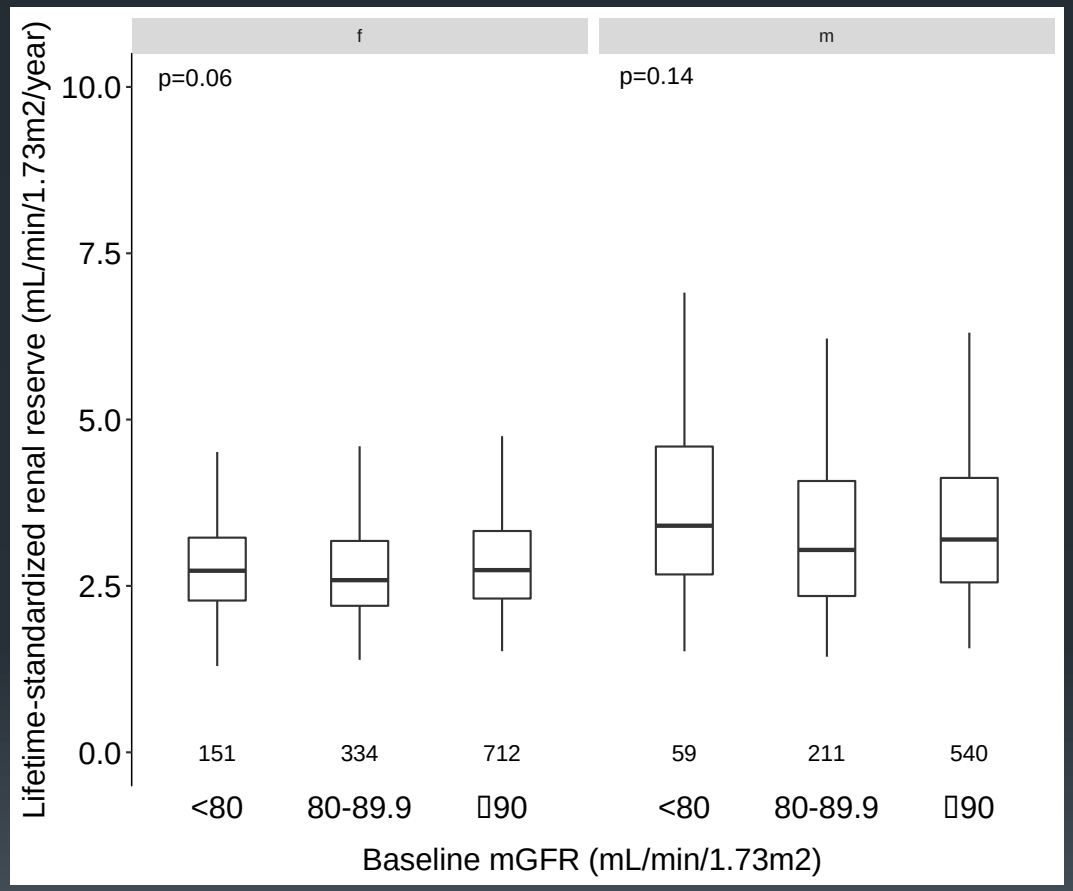
Impact of age on GFR

$$\text{Réserve rénale ajustée} = \frac{\text{DFGm}}{\text{Années de vie restantes}}$$



En révision

Impact of age on GFR



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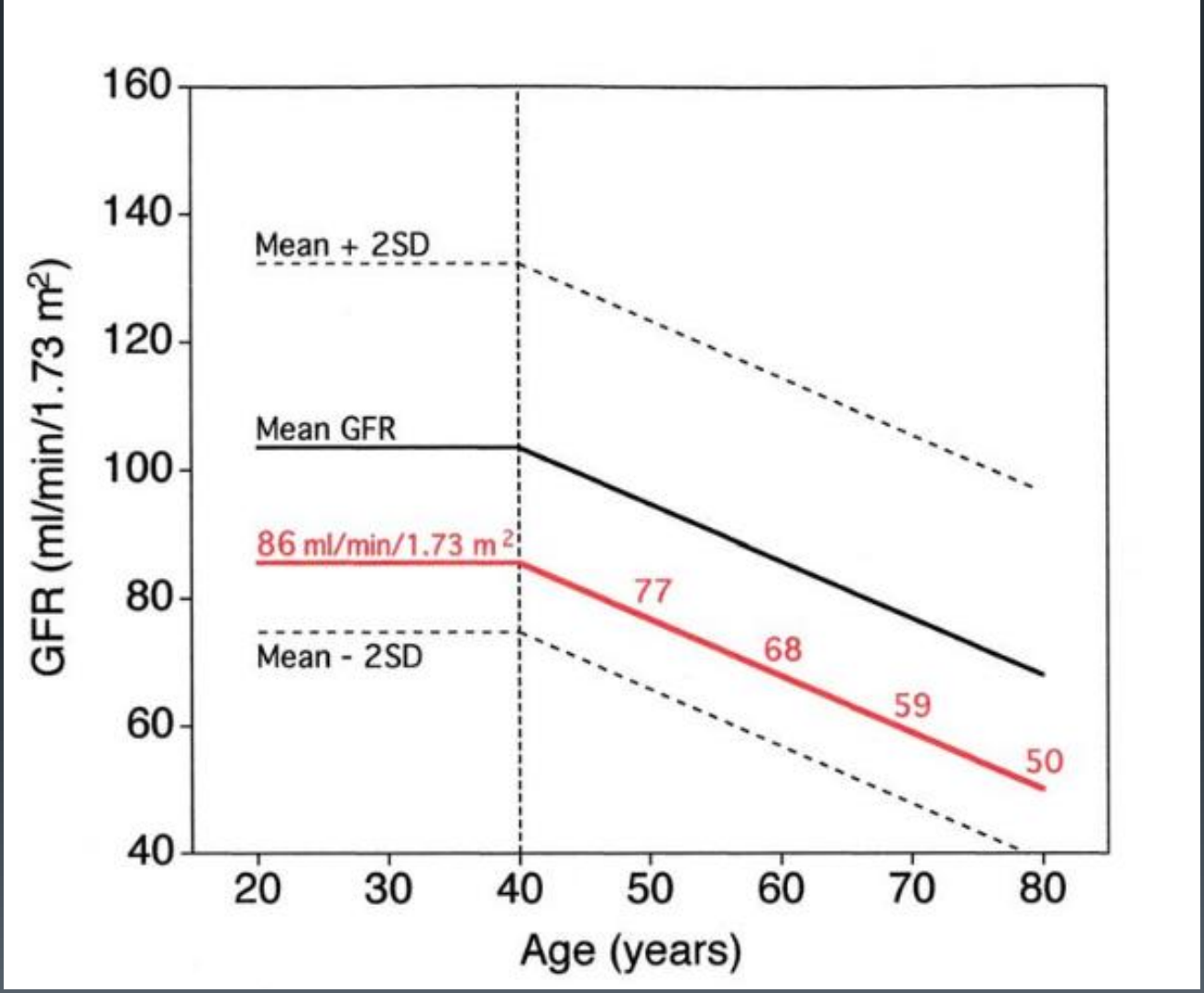
Impact of age on GFR



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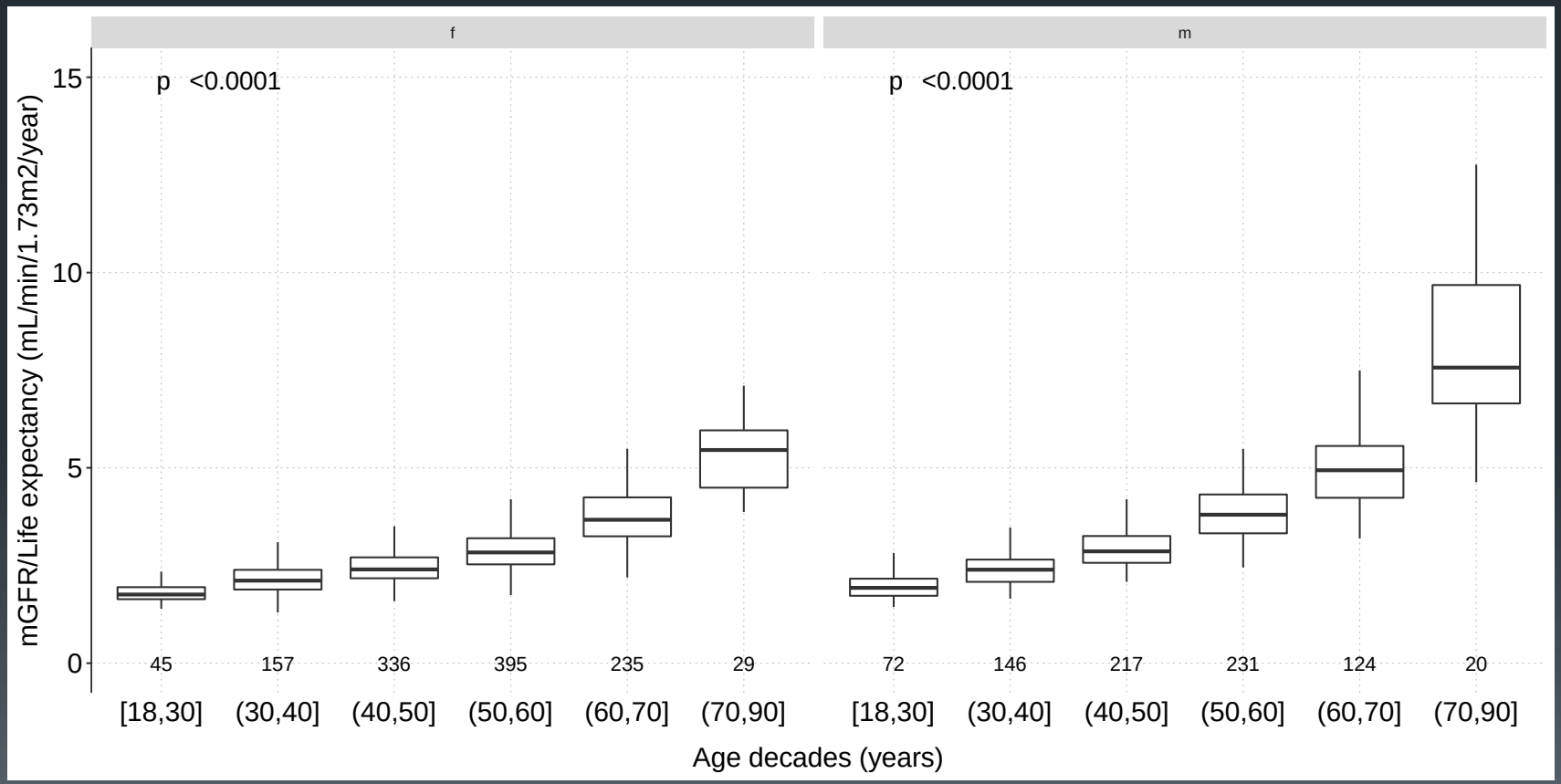

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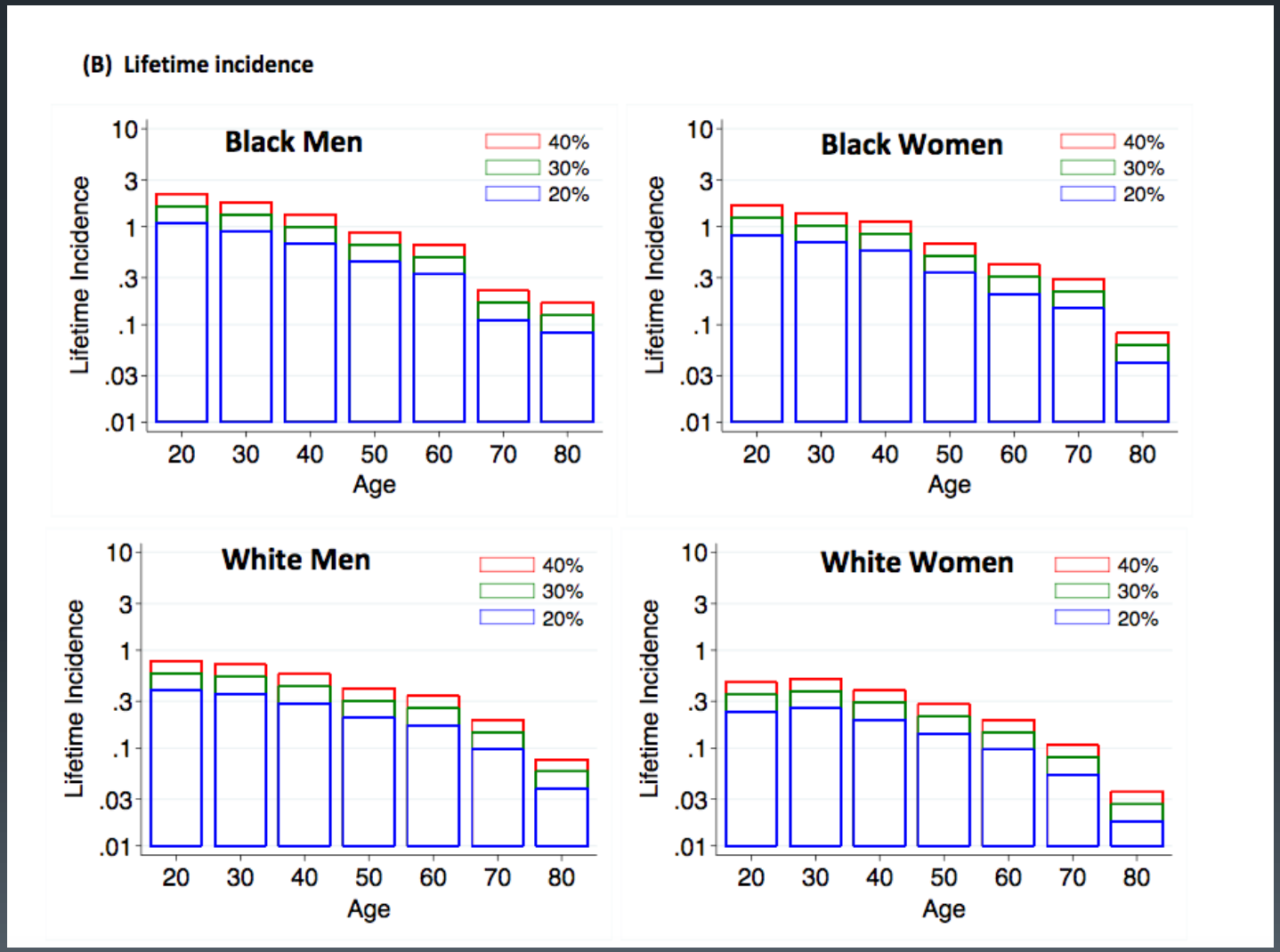
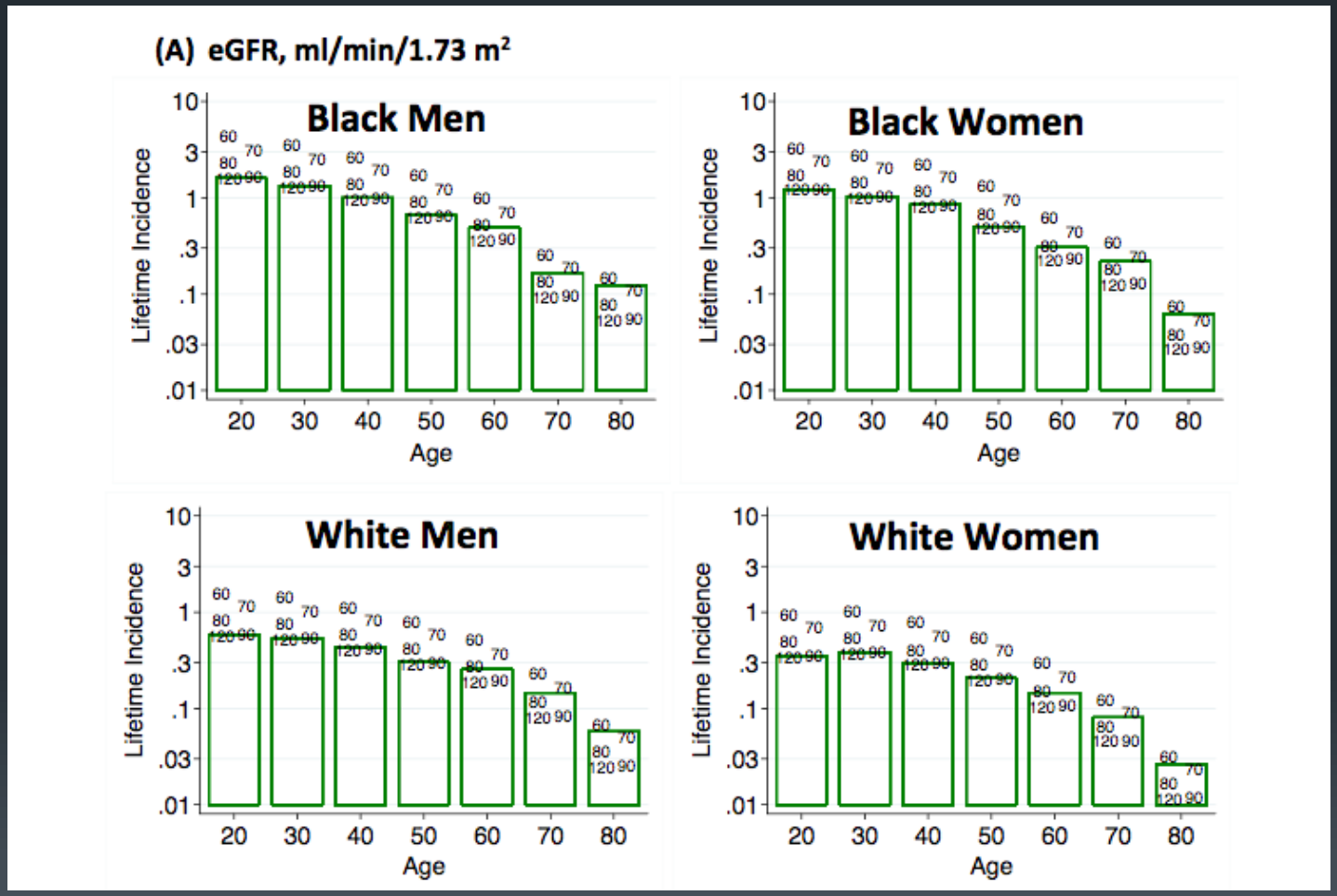


Grams et al. NEJM 2016

Impact of age on GFR



Grams et al. NEJM 2016

Impact of age on GFR

1. GFR physiologically declines with age after 40
2. Age is already taken into account to evaluate LKD in France
3. A GFR threshold independant from age may be deleterious for younger donors or unreasonably restrictive for older donors

Unanswered questions

1. Use of calculators in clinical practice ?
2. Why to evaluate GFR ?
3. Impact of age on acceptable GFR thresholds ?
4. How to evaluate GFR ?
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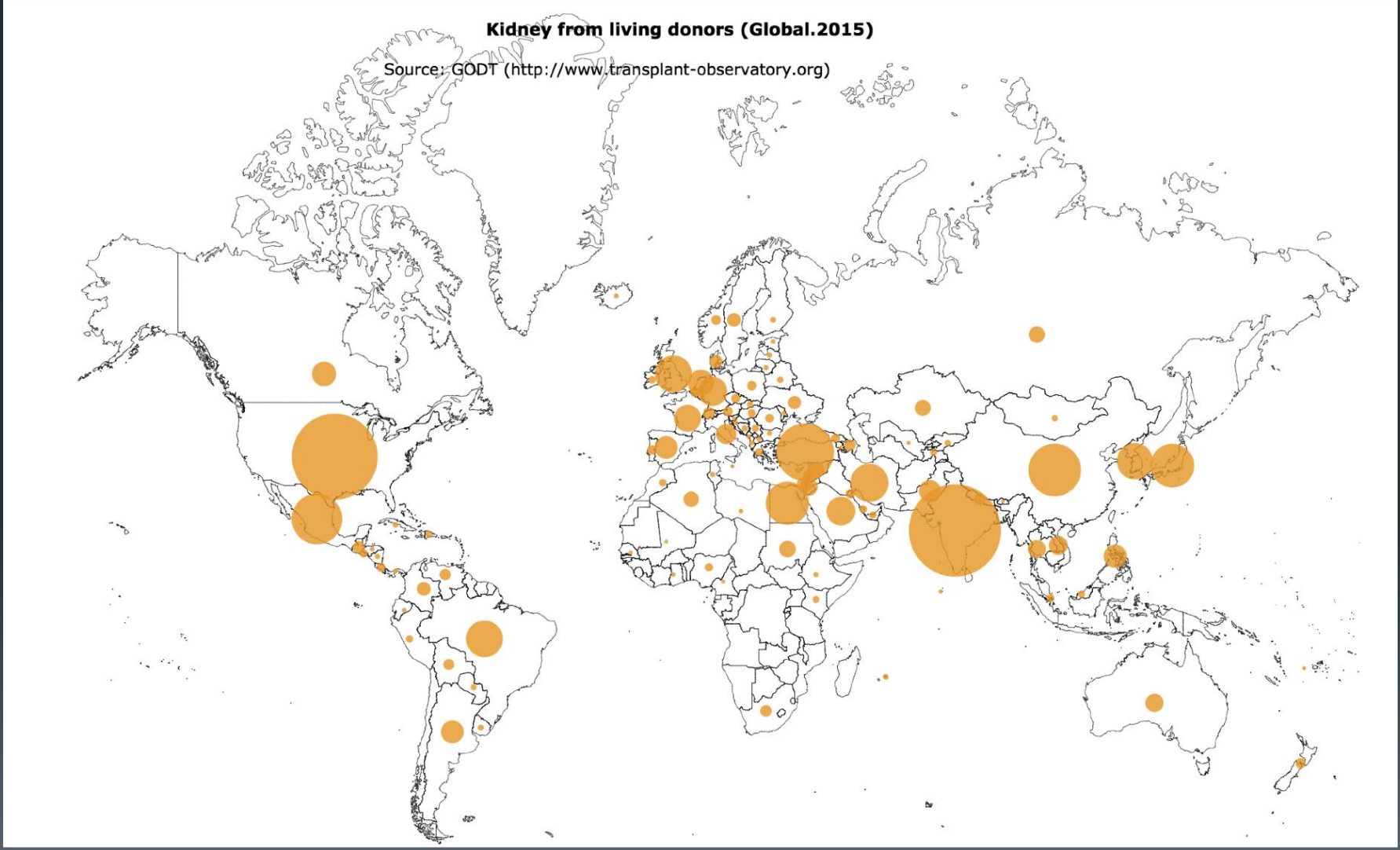
KDIGO LKD

…. The best technique locally available…..

eGFR with CKD-EPI

- mGFR with exogenous tracer
- Creatinine clearance
- eGFR with CKD-EPI $_{\text{creat+ cystatine}}$
- eGFR with CKD-EPI $_{\text{creat}}$

How to evaluate GFR

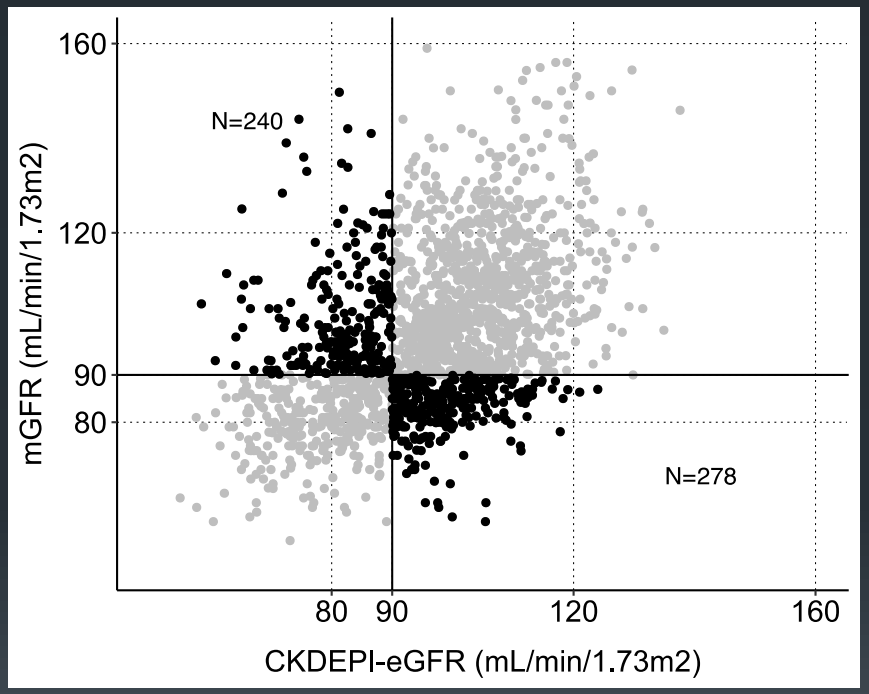


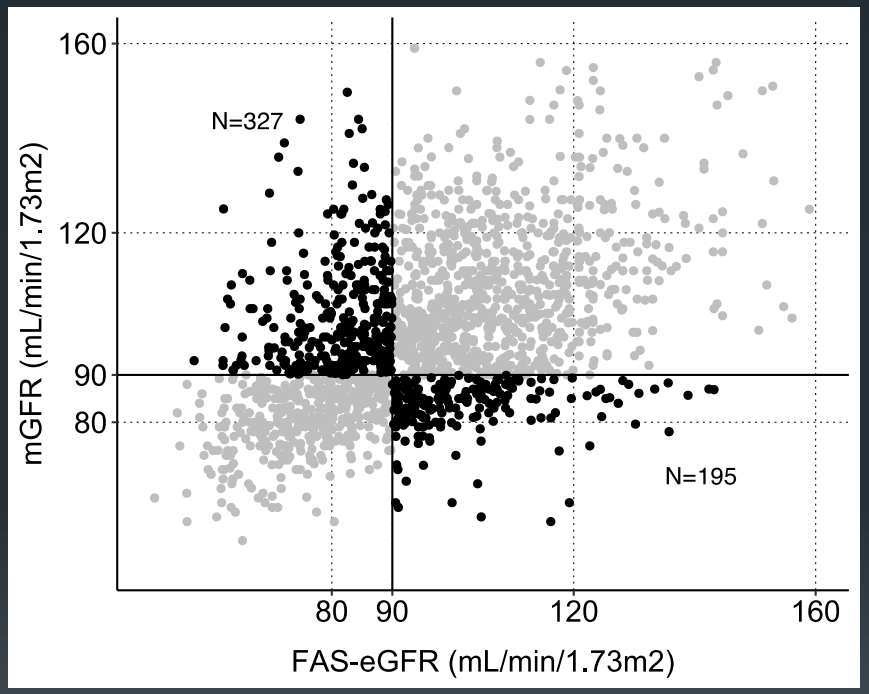
How to evaluate GFR

Full mGFR range (55 – 187 mL/min/1.73m²)	MDRD 51-167	CKDEPI 55-138	LM 53-127	FAS 51-173
RMSE	19.9 *(19.1, 20.7)*	16.4 *(15.6, 17.1)*	19.5 *(18.8, 20.2)*	18.1 *(17.3, 19.2)*
P10	40.8 *(40.8, 40.8)*	48.5 *(48.5, 48.5)*	40.1 *(40.1, 40.1)*	44.6 *(44.6, 44.6)*
P30	89.9 *(89.9, 89.9)*	94.7 *(94.7, 94.7)*	92.0 *(92.0, 92.0)*	92.6 *(92.6, 92.6)*
Relative Bias	0.94 *(0.93, 0.94)*	0.99 *(0.98, 0.99)*	0.89 *(0.88, 0.90)*	0.98 *(0.97, 0.98)*
Absolute Bias	-7.7 *(-8.6,-6.7)*	-2.7 *(-3.4,-1.9)*	-11.9 *(-12.6,-11.2)*	-3.3 *(-4.1, -2.5)*
Lin's CCC	0.385 (0.349, 0.420)	0.462 (0.427, 0.495)	0.346 (0.317, 0.375)	0.492 (0.458, 0.525)

How to evaluate GFR

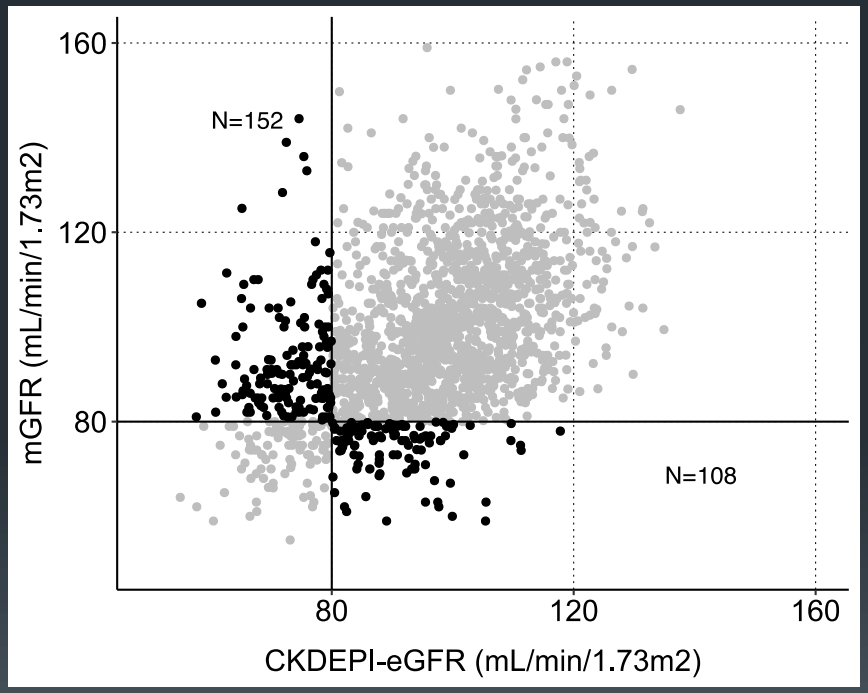
90 mL/min/1,73m^2

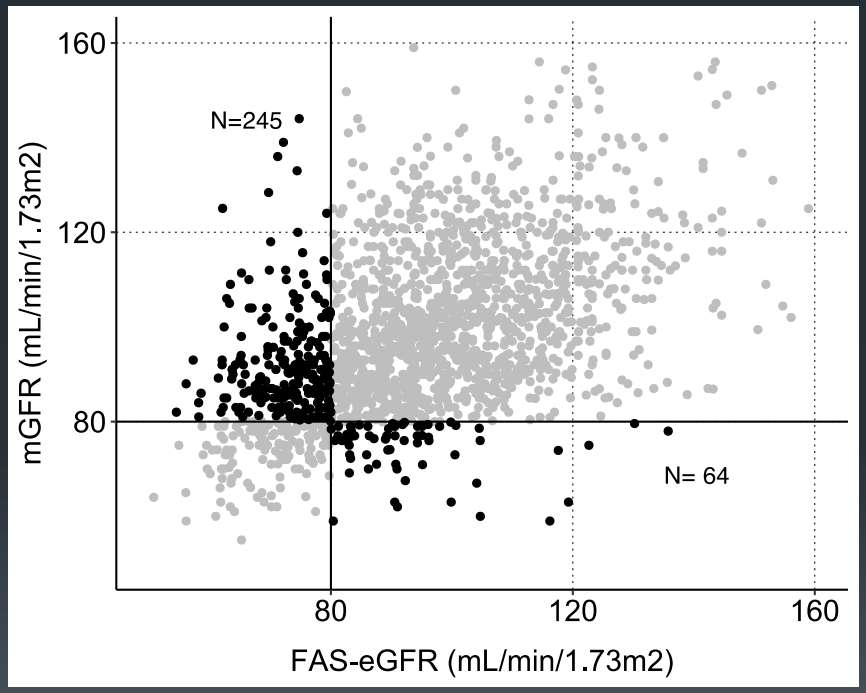




How to evaluate GFR

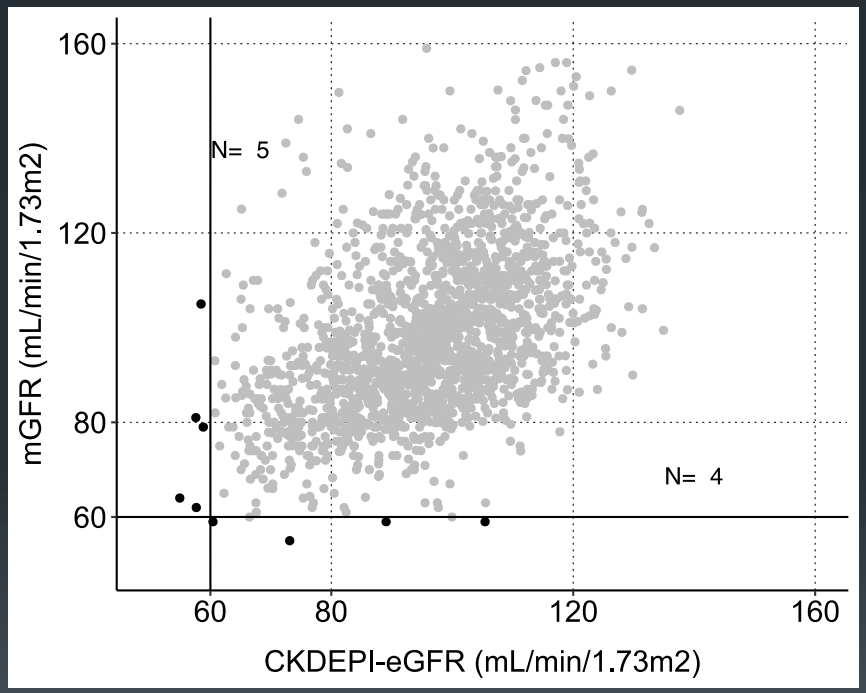
80 mL/min/1,73m^2

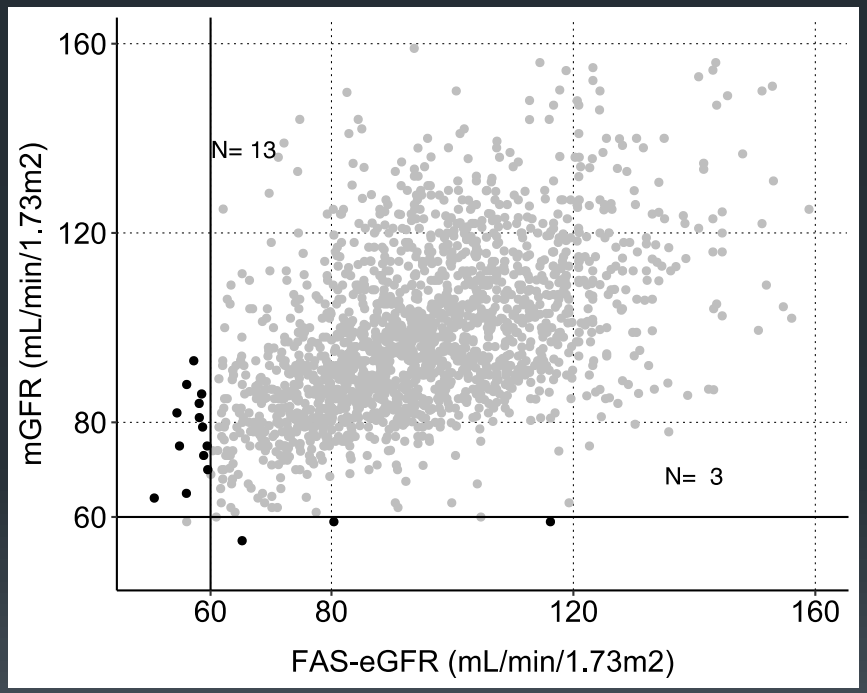




How to evaluate GFR

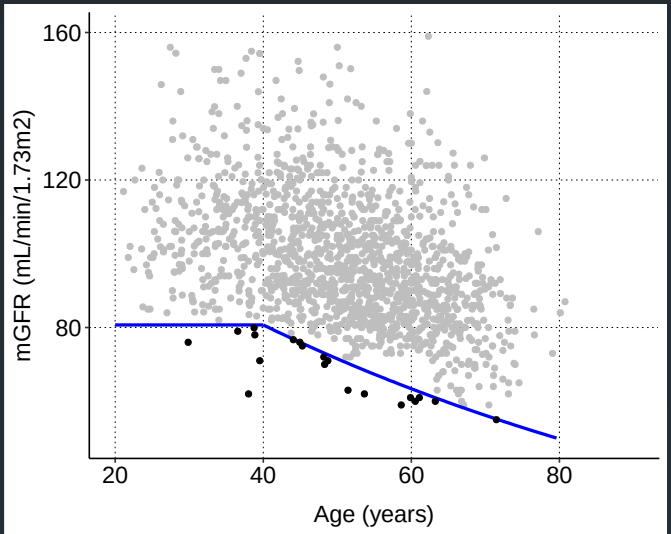
60 mL/min/1,73m^2

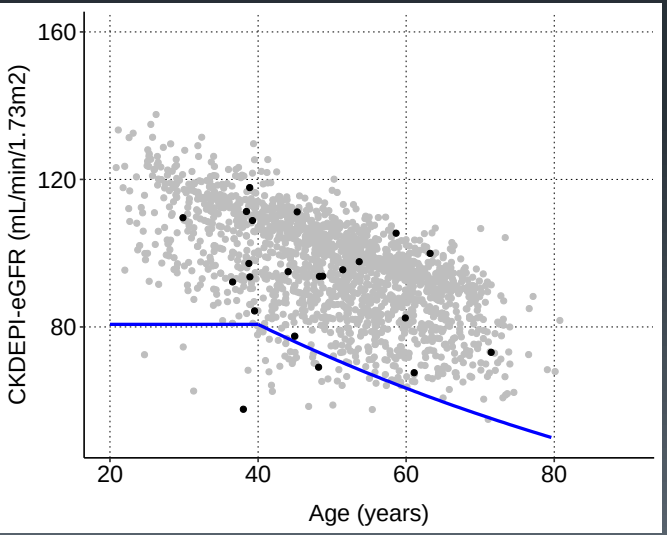


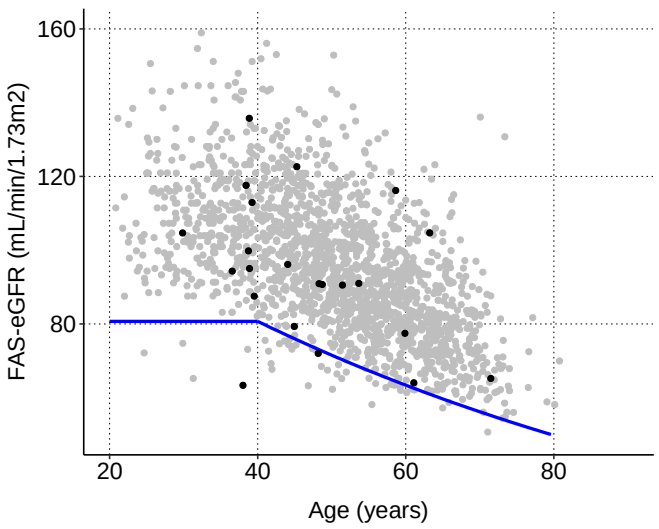


How to evaluate GFR

Age dependent thresholds

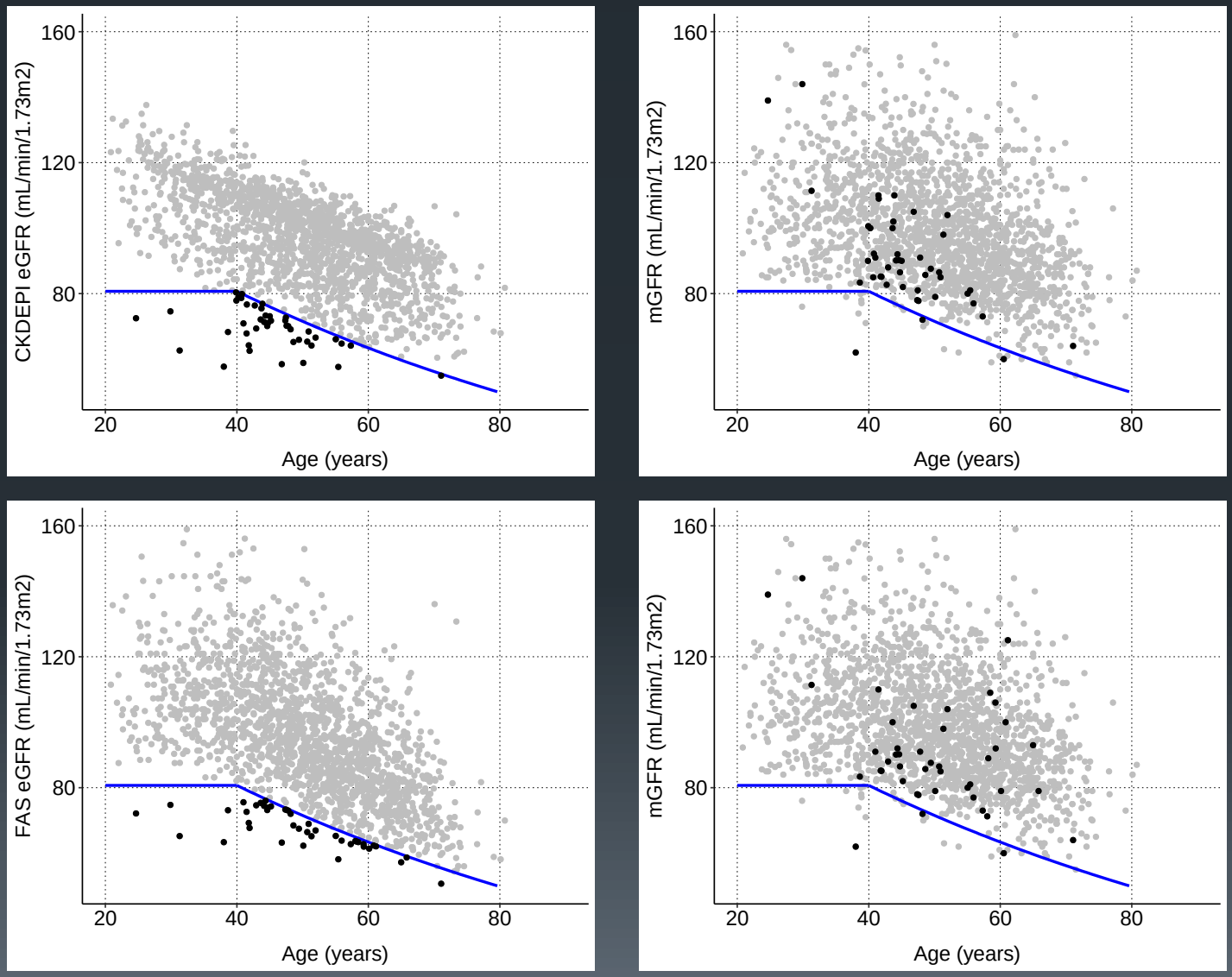




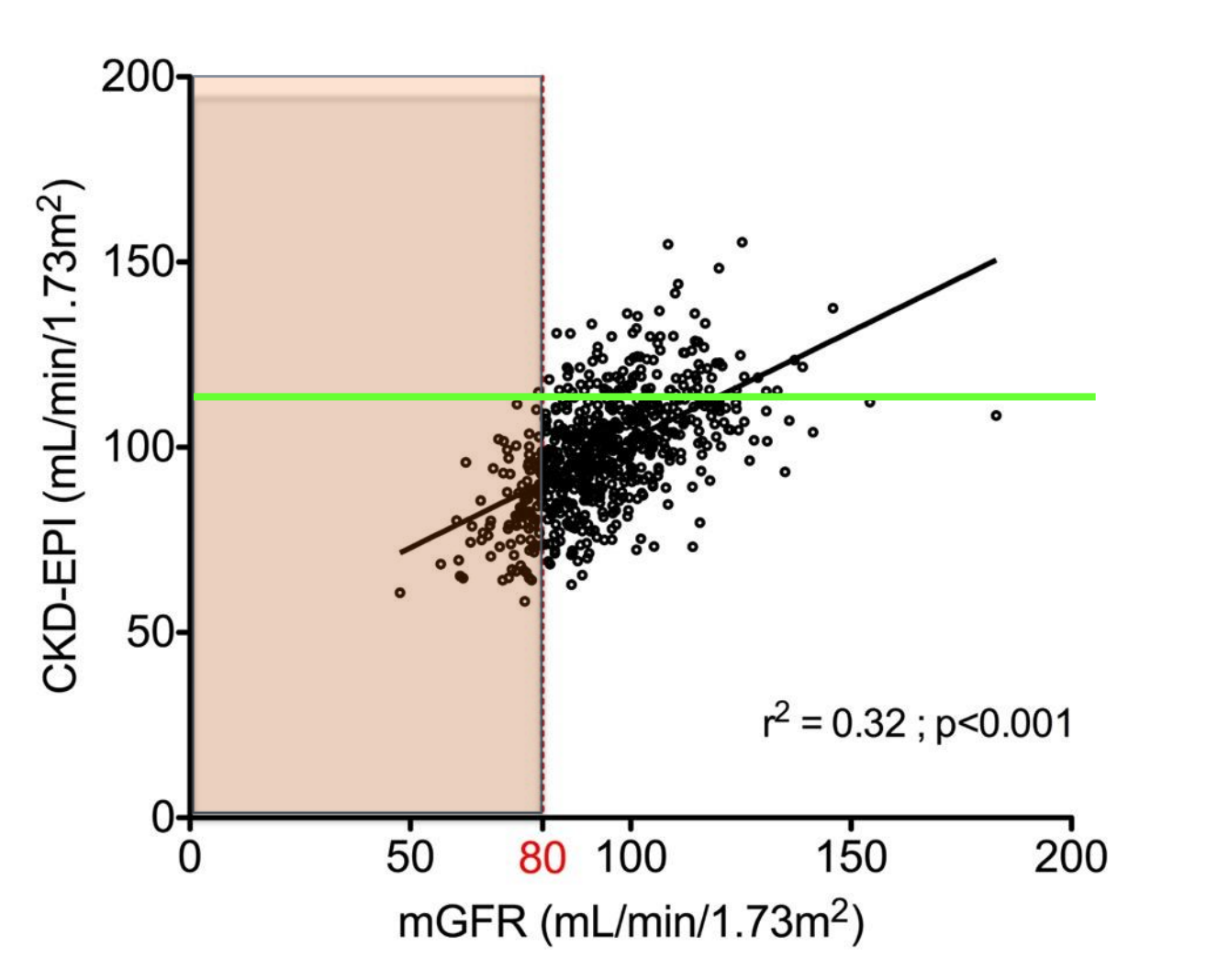


How to evaluate GFR

Age dependent thresholds



How to evaluate GFR

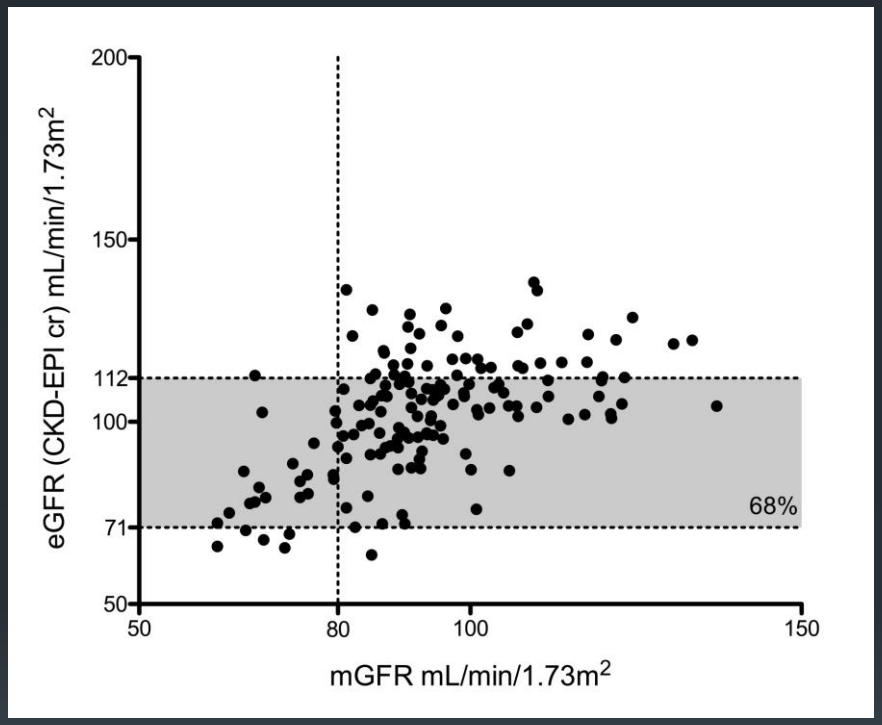


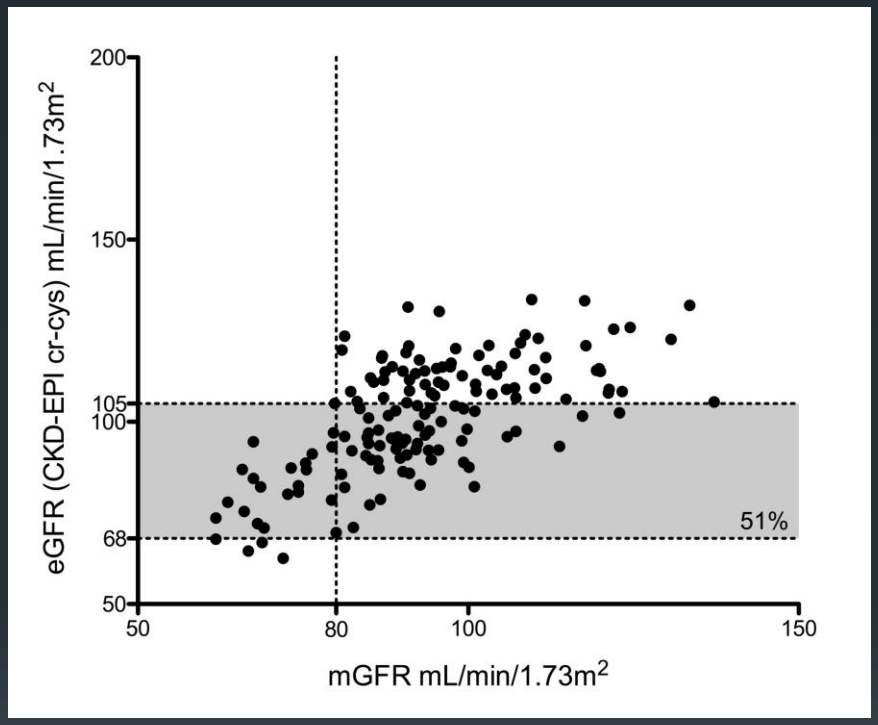
How to evaluate GFR

	CKD-EPI	MDRD	Post-test 90
Seuil	104 mL/min/1.73m^2	100 mL/min/1.73m^2	2%
Sensibilité (IC95)	0.95 (0.86 – 0.99)	0.92 (0.81 – 0.97)	0.95 (0.86 – 0.99)
Spécificité (IC95)	0.51 (0.45 – 0.56)	0.54 (0.48 – 0.60)	0.47 (0.42 – 0.53)
AUC (IC95)	0.85 (0.80 – 0.91)	0.85 (0.79 – 0.90)	0.84 (0.79 – 0.89)
% de mesures de DFG evités	43%	45%	40%

Thresholds are necessarily different between techniques !!

How to evaluate GFR





Use of cystatin ?

How to evaluate GFR ?

1. Equations performances are limited
2. 99% of donors with normal mGFR for age have a normal eGFR for age.
3. At fixed GFR threshold roughly 25% of donors have different eGFR and mGFR.
4. Donors with low mGFR for age are not detected by eGFR (sensitivity 2%)
5. 99% of donors with low eGFR for age have a normal mGFR for age

Unanswered questions

1. Use of calculators in clinical practice ?
2. Why to evaluate GFR ?
3. Impact of age on acceptable GFR thresholds ?
4. How to evaluate GFR ?
5. How to evaluate renal asymetry ?

Why to evaluate GFR

$$\frac{\text{DFGm -RR}}{\text{Volume -RR}}$$

DFG mesuré de chaque rein

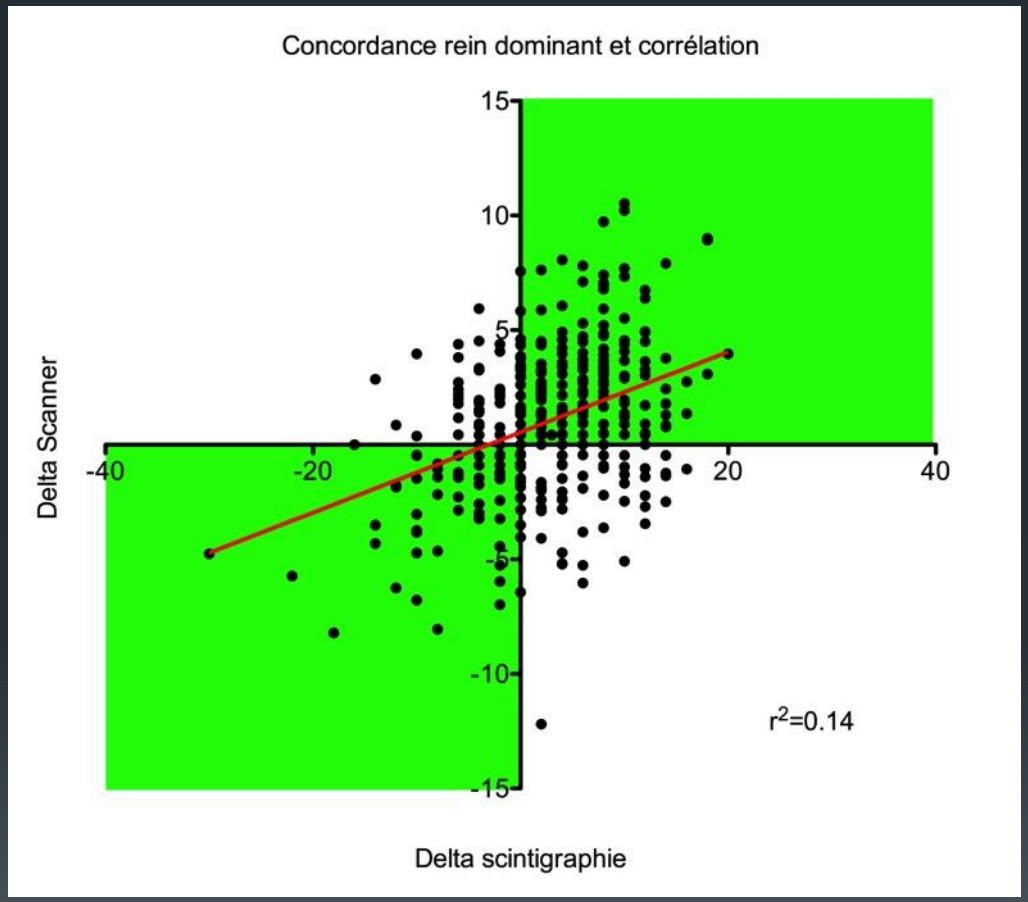
Scintigraphie

Volume rénal

Scanner

Courbebaisse et al. CJASN 2016

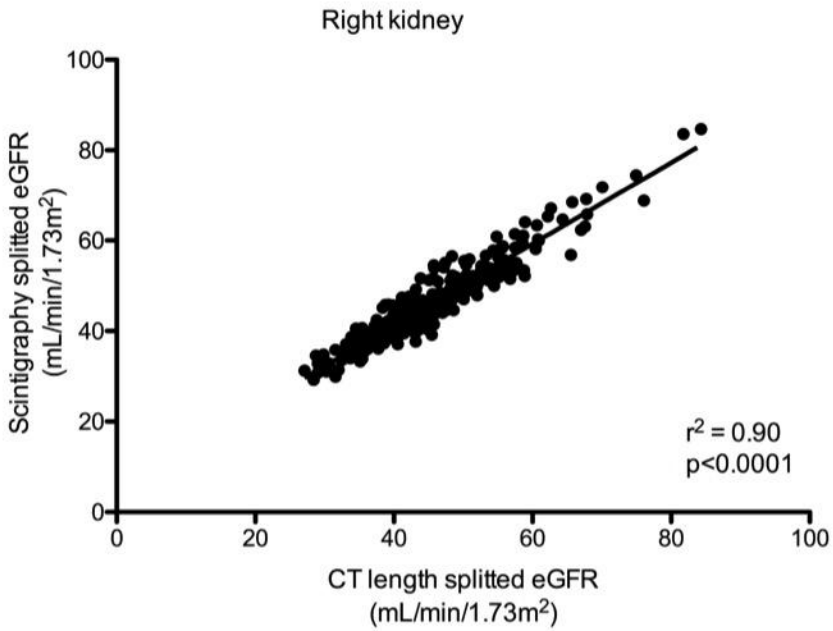
How to evaluate renal asymetry

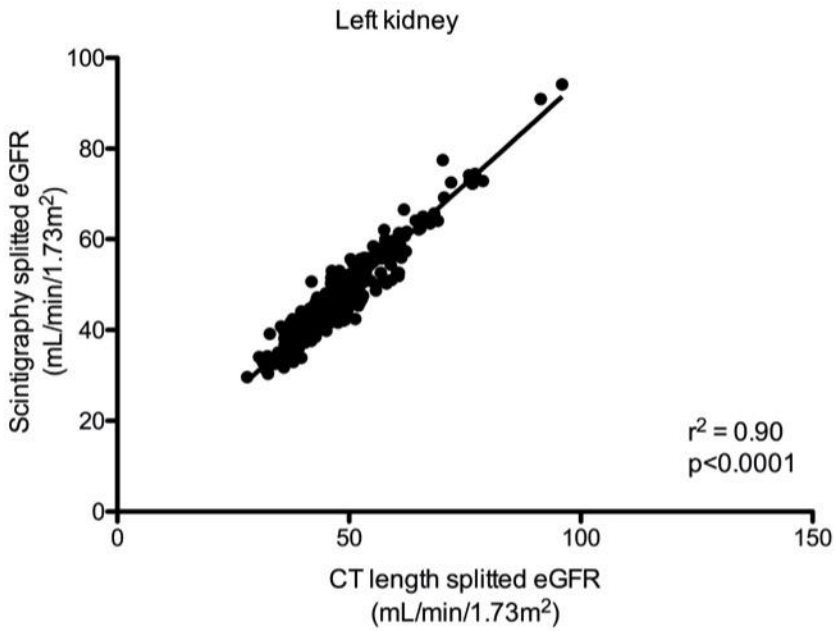


Halleck et al 2013,Transplant Int
Yanishi et al 2015, Transplant Proc
Summerlin et al 2008, Am J Roentgen

How to evaluate renal asymetry

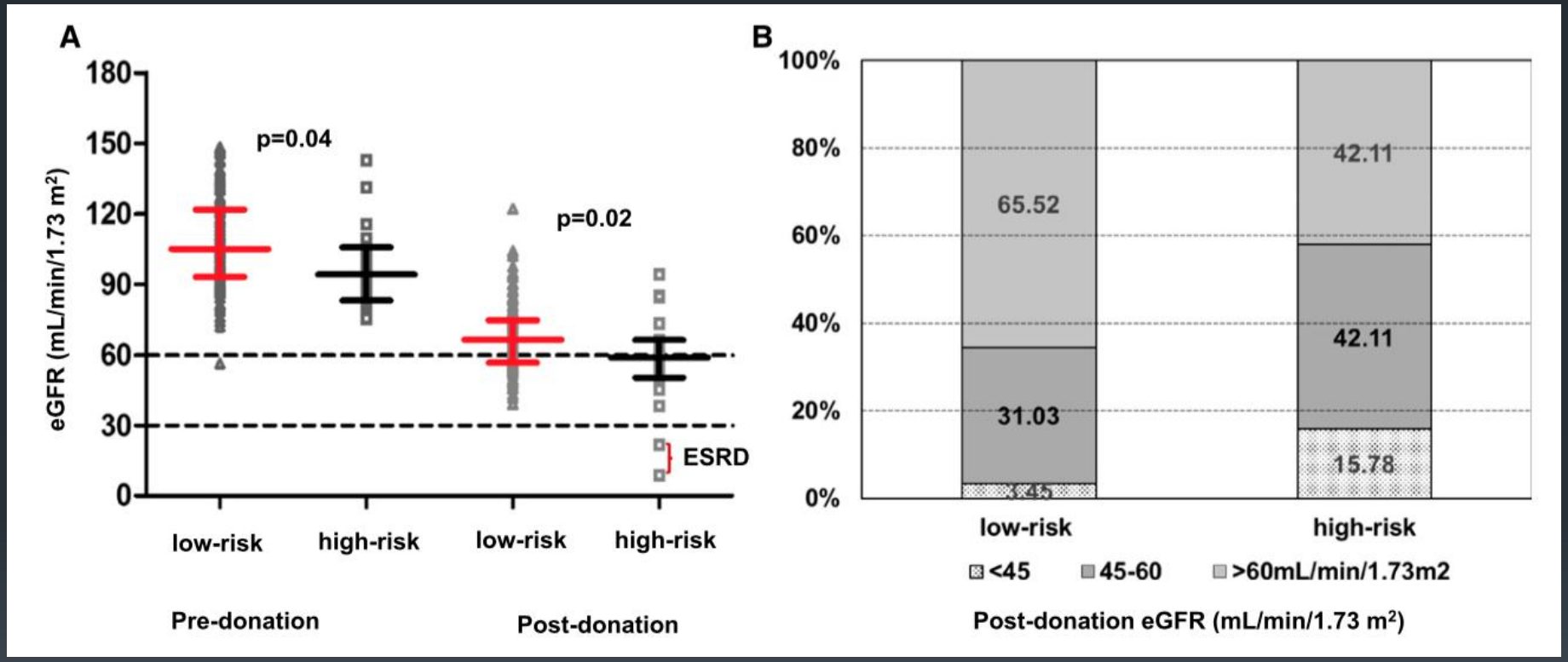
Asymetry 10%	LK	RK
GFR 80mL/min	44	36
GFR 120mL/min	66	54





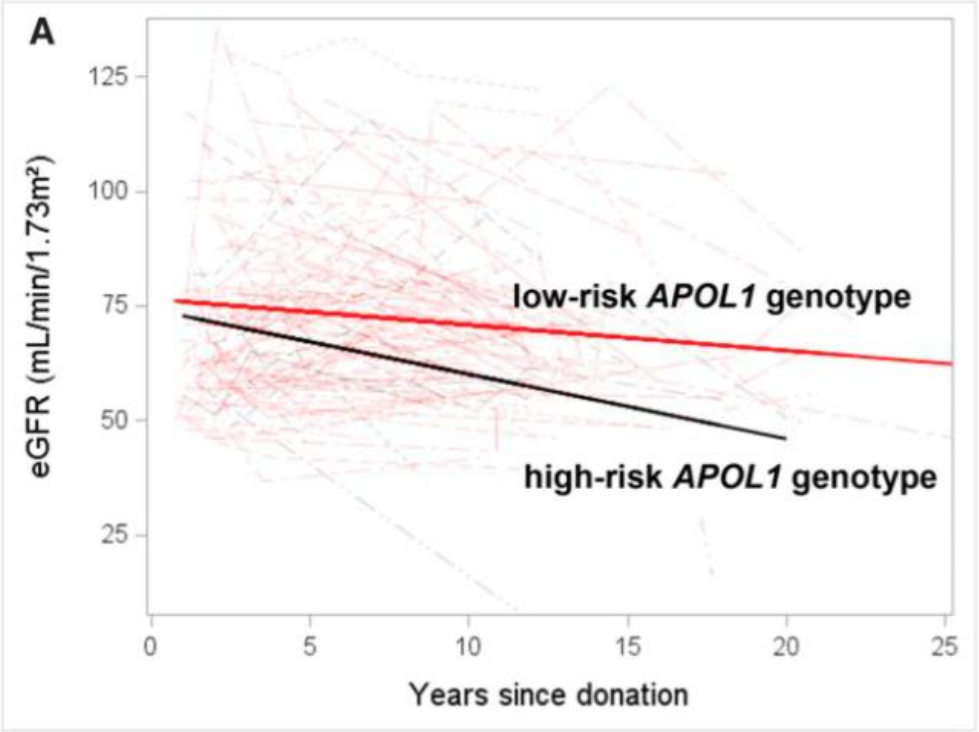
Gaillard et al. *Eur Radiol,* 2016

Génotypage apoL1



Doshi et al. *JASN*, 2018

apoL1 genotyping



apoL1 genotyping

	White donors	Donors of African Ancestry	P value
1 year eGFR ($mL/min/1.73m^2$)	66.1 (14.1)	62.4 (12.9)	0.22
Relative eGFR loss (%)	31.5 (9.6)	35.9 (10.2)	0.04
Relative FG (%)	39 (23)	29 (24)	0.05
Absolute FG ($mL/min/1.73m^2$)	18.3 (11.2)	13.2 (10.9)	0.03

ApoL1 is not sufficient

Can ESRD risk be predicted ?

Risk calculators

Can ESRD risk be modified?

Before donation – After donation

Can ESRD risk be modified ?

Account for **50% of the causes of ESRD**:

- Diabetes mellitus
- Hypertension
- Smoking

Follow up strongly recommended

- Cardiovascular risk factors
- Measured GFR

Special attention should be paid to youngest donors related to the recipient

Thank you