9° WORKSHOP NAZIONALE CISAI

PREVENZIONE
E GESTIONE
DELLE CO-MORBIDITÀ
ASSOCIATE
ALL'INFEZIONE DA HIV

Paolo Maggi
Università degli Studi
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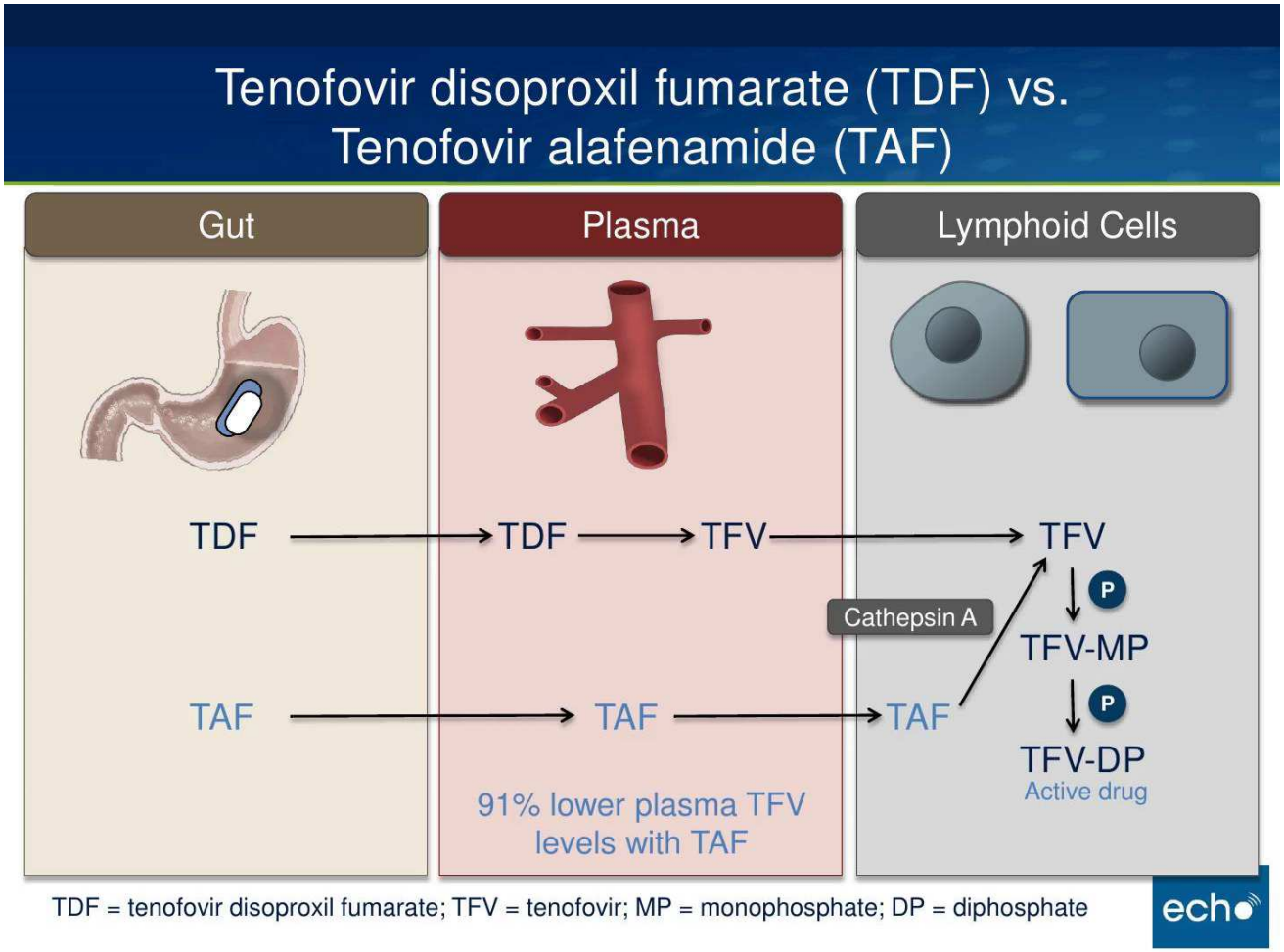
Il Danno Renale

FONDAZIONE ASIA

CISAI
Coordinamento
Italiano
Studio
Allergie e
Infezione da HIV

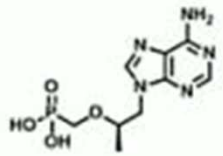
BARI | 21-22 MARZO 2019
CENTRO CONGRESSI PALACE HOTEL BARI

Il rene nell'era TAF: tempo di bilanci

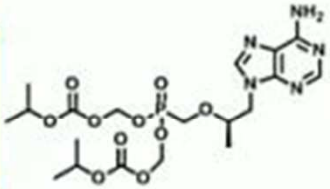


Tenofovir Alafenamide (TAF, GS-7340)
Novel Prodrug of Tenofovir

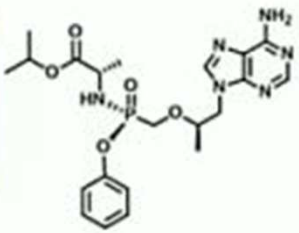
Tenofovir (TFV)

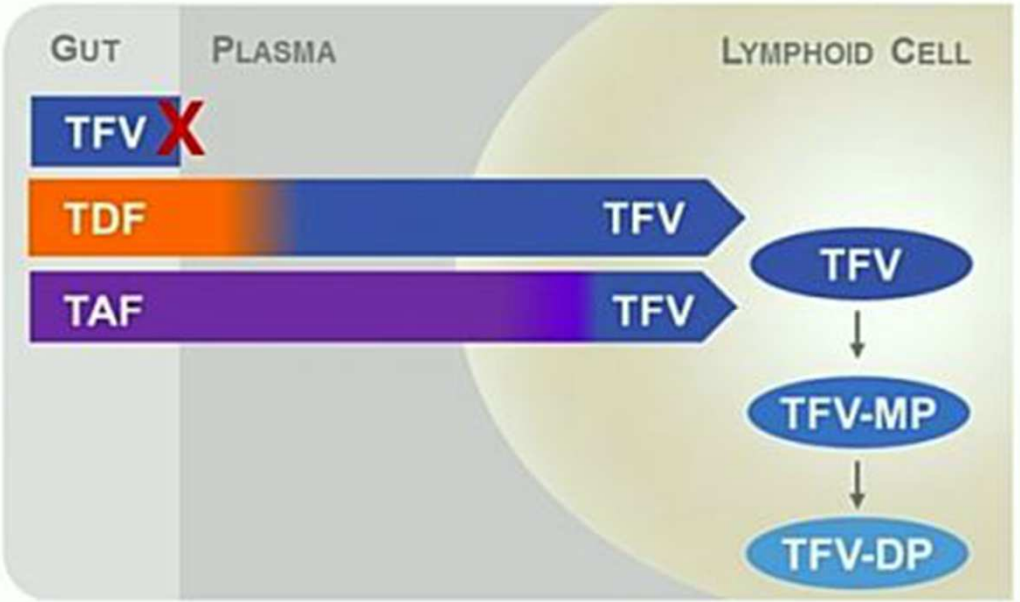


Tenofovir disoproxil fumarate (TDF)



Tenofovir alafenamide (TAF)



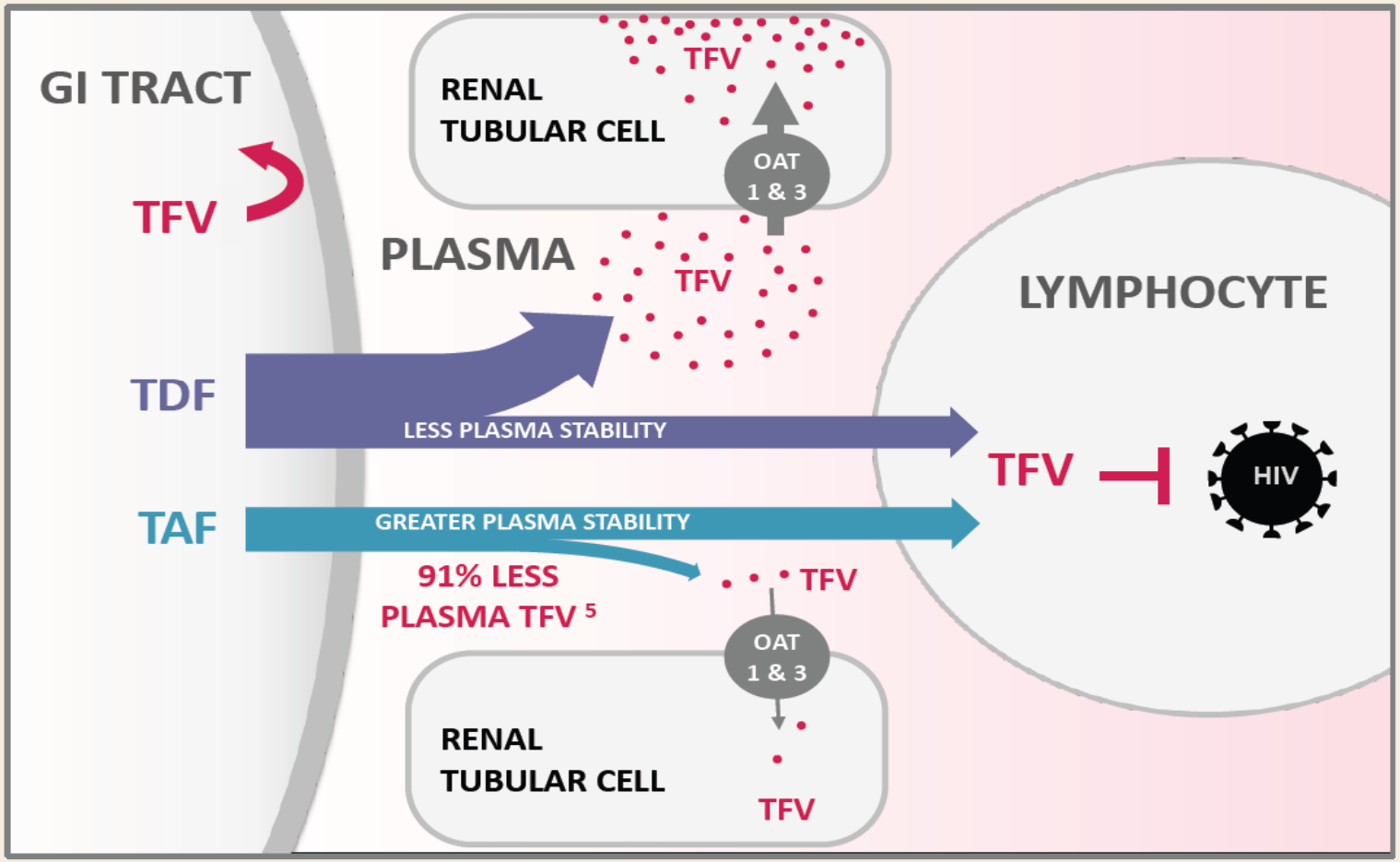


Renal Safety of Tenofovir Alafenamide in Patients at High Risk of Kidney Disease

David Wohl[1], Anders Thalme[2], Robert Finlayson[3], Shinichi Oka[4], Thai Nguyen[5], Susan Guo[5], Andrew Cheng[5], Moupali Das[5], Marshall Fordyce[5]

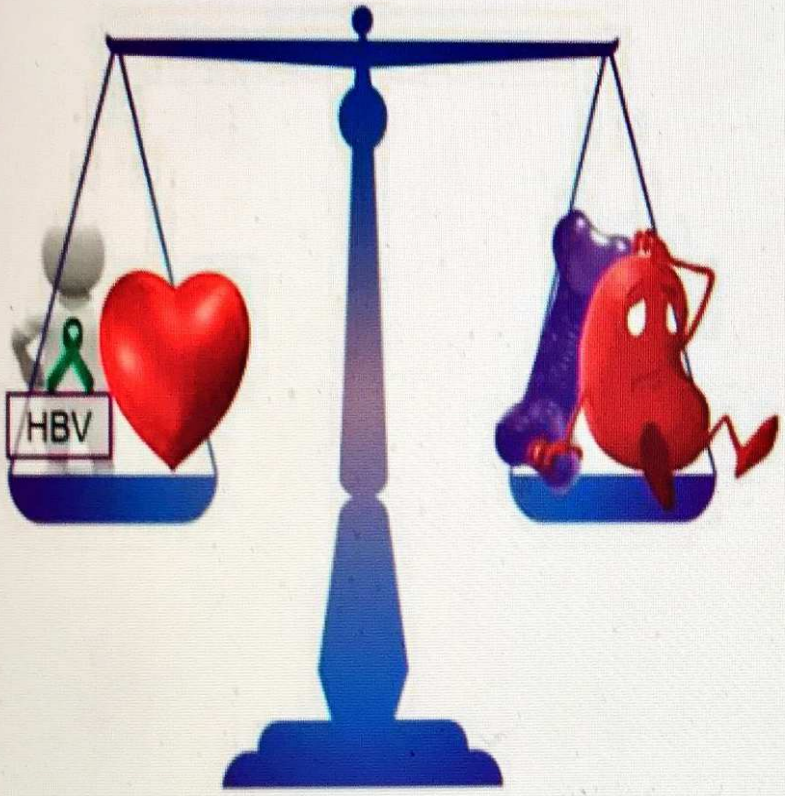
[1]University of North Carolina at Chapel Hill, USA; [2]Karolinska University Hospital, Stockholm, Sweden; [3]Taylor Square Private Clinic, NSW, Australia; [4]National Center for Global Health and Medicine Hospital, Tokyo, Japan; [5]Gilead Sciences, Inc., Foster City, CA, USA

Mechanism of Action
Tenofovir Disoproxil Fumarate and Tenofovir Alafenamide



OAT, organic anion transporter; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir.

Ways to avoid the safety concerns of the NRTI 'backbone'

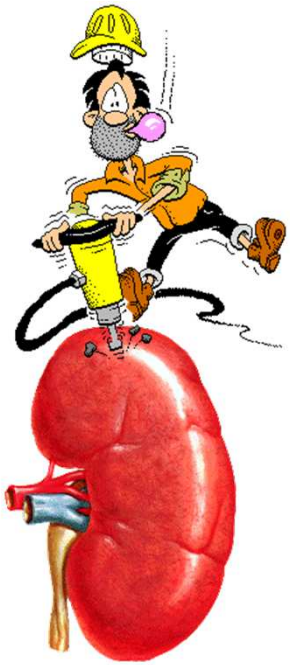


Options:

- TAF backbone in triple ART
- Two-drug regimens (2DR)

2DR, two-drug regimen; ART, antiretroviral therapy; HBV, hepatitis B; NRTI, nucleoside reverse transcriptase inhibitor; TAF, tenofovir alafenamide fumarate

Quali sono gli strascichi dell'era TDF?



#693

EVOLUTION AND REVERSIBILITY OF RENAL FUNCTION AFTER SWITCH FROM TDF TO TAF REGIMENS

Roberta Gagliardini for the Icona Foundation Study Group

After switching from TDF to TAF, only a small even statistically significant improvement in eGFR was observed a complete recovery of renal filtrate or a transition to normal CKD category occurred in less than half of cases over a median of 1 year of observation.

Unboosted regimens seem to be associated with a higher probability of regaining renal filtrate.

These data may be useful for selecting in which patients to maintain TDF without jeopardizing renal function.

Table 1. Adjusted IRR (Incidence rate ratio) from Poisson regression analysis of eGFR recovery to pre-TDF values (model A) and of change from G2 to G1 eGFR category in CKD (model B). *eGFR in model A was calculated at baseline pre-TDF and in model B at switch; n.e.=variable not entered in the model. Significant values are reported in bold.

	Model A			**Model B**		
	aIRR	**95%CI**		**aIRR**	**95%CI**	
Age, (10 yrs older)	n.e.			0.80	0.65	0.99
Years of HIV infection, (per 1 yr more)	1.01	0.98	1.03	n.e.		
CDC stage C va A/B	1.17	0.80	1.70	n.e.		
Nadir CD4<=200 cell/mmc vs >200	0.85	0.62	1.17	n.e.		
CD4 at BL>=350 cell/mmc vs <350	1.29	0.82	2.02	n.e.		
CD8 at BL>=800 cell/mmc vs <800	**1.50**	**1.19**	**1.90**	n.e.		
Number of previous regimen (per 1 more)	0.97	0.90	1.06	n.e.		
eGFR*, (per 10 mL/min higher)	**0.87**	**0.82**	**0.93**	**2.41**	**1.73**	**3.37**
Years of TDF exposure (per 1 yr more)	0.99	0.94	1.04	1.03	0.95	1.11
Unboosted third drug vs boosted	**1.35**	**1.07**	**1.71**	1.29	0.86	1.93

#694
GLOMERULAR FILTRATION RATE RECOVERY AFTER A SWITCH FROM TDF TO TAF OR ABC

Rosanne Verwijs

Although a modest improvement in eGFR was observed after TDF discontinuation, few patients recovered >50% of their eGFR.

The recovery rate in patients that switched to TAF and ABC was comparable

#689

IMPACT OF RENAL TUBULE FUNCTION ON BONE MINERAL DENSITY IN OLDER PEOPLE WITH HIV

Patrick W. Malllon, Frank Post

In this cohort of older PWH with a high prevalence of osteoporosis, **RBPCR** was the only marker of RTD associated with BMD, but the association lessened with demographic adjustment and was fully abrogated after adjustment for TDF exposure.

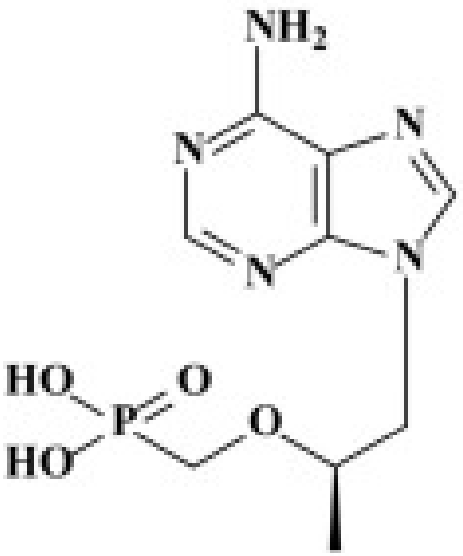
Continuous TDF exposure was associated with significantly lower BMD at the femoral neck.

Table: Factors associated with BMD lumbar spine and BMD femoral neck

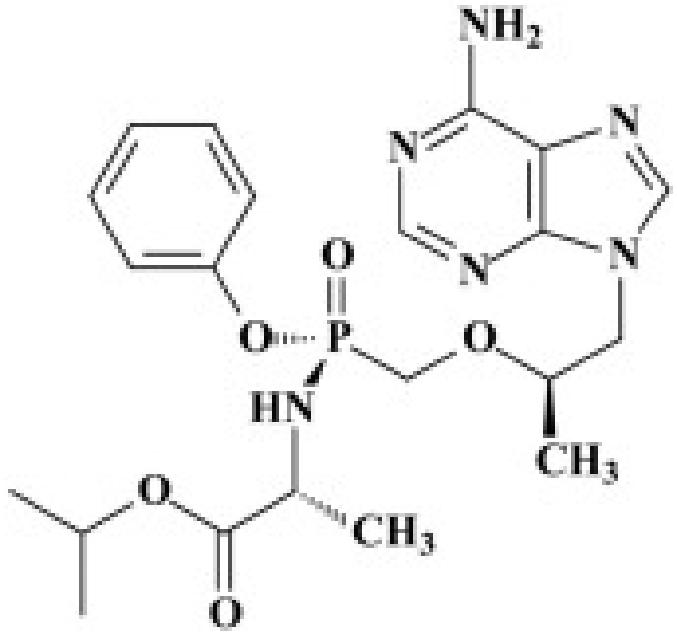
	LS-BMD: Model 1		LS-BMD: Model 2		FN-BMD: Model 1		FN-BMD: Model 2	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
Age per year	-		-		-0.003 (-0.006, -0.001)	0.011	-0.004 (-0.006, -0.001)	0.005
Female sex	-0.073 (-0.124, -0.022)	0.005	-0.085 (-0.137, -0.032)	0.002	-0.053 (-0.091, -0.016)	0.005	-0.053 (-0.091, -0.014)	0.007
BMI (per 1 unit)	0.008 (0.002, 0.014)	0.009	0.009 (0.003, 0.016)	0.003	0.011 (0.007, 0.015)	<0.0001	0.010 (0.006, 0.142)	<0.0001
RBPCR (log transformed)	0.003 (-0.012, 0.019)	0.662	0.007 (-0.009, 0.023)	0.409	-0.005 (-0.016, 0.006)	0.359	-0.001 (-0.012, 0.011)	0.932
ART: No TDF/No PI	-		1		-		1	
ART: No TDF/PI	-		-0.084 (-0.016, -0.012)	0.022	-		-0.046 (-0.097, 0.006)	0.083
ART: TDF/No PI	-		-0.078 (-0.015, -0.010)	0.025	-		-0.074 (-0.012, -0.026)	0.003
ART: TDF/PI	-		-0.057 (-0.013, 0.017)	0.131	-		-0.062 (-0.114, -0.011)	0.019

Cosa abbiamo imparato dal TDF

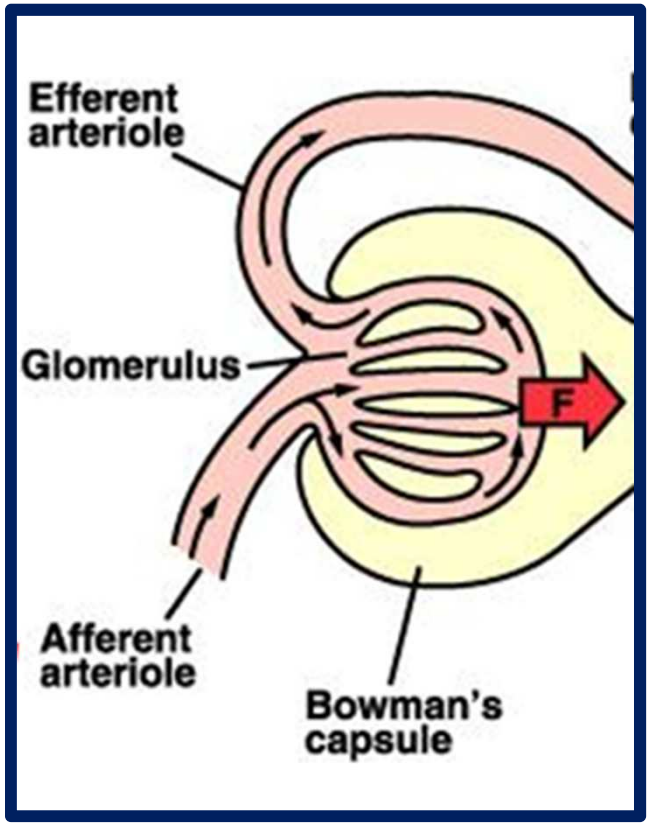
Tenofovir



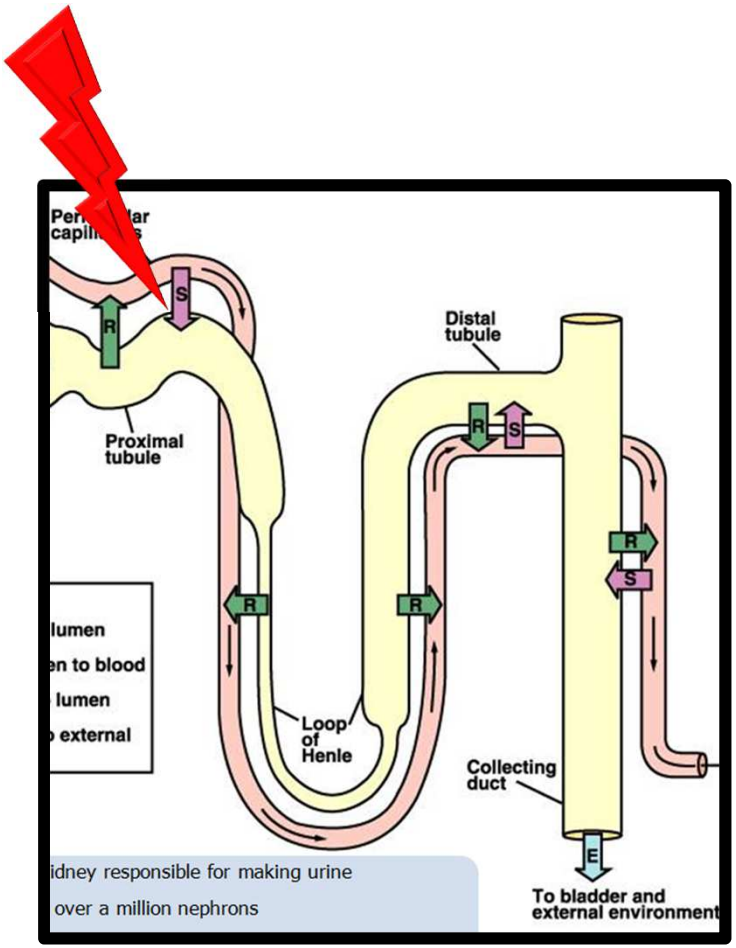
Tenofovir alafenamide



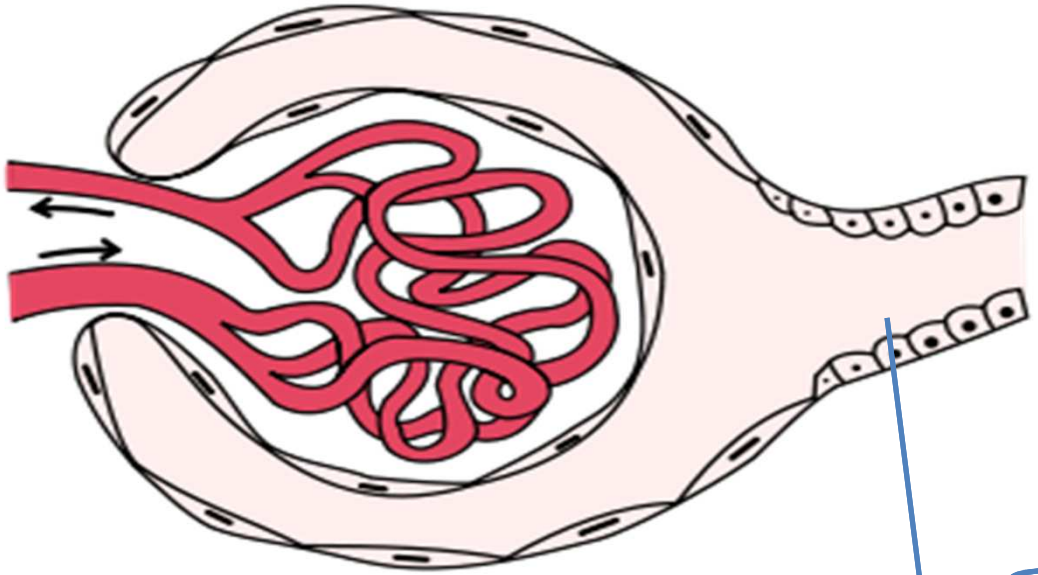
Farmaci



glomerulo



tubulo



proteine a basso pm

fosforo

glucosio

acido urico

Valutazione qualitativa della proteinuria

- Proteinuria glomerulare
  - Danno della MBG (strutturale, funzionale)
  - **Prevalentemente Albumina**
  - Albumina/Proteine urinarie > 0,4
- Proteinuria tubulare
  - **Polipeptidi a basso peso molecolare** (< 25 kD)
  - Scarsa quantità di Albumina
  - Albumina/Proteine urinarie < 0,4
  - Dosaggio immunometrico di proteine a basso peso molecolare [Retinol-binding protein, b2-microglobulina, a1-microglobulina,
  - Cistatina C, NGAL]

Valutazione della proteinuria

- Dipstick (Screening) [0 – 4 +; 0 – 300 mg/dl]
- Proteinuria quantitativa su raccolta urine 24 h [0 – 0,3 g/24h]
- Rapporto Proteine/Creatinina (PCR) [0 – 0,2 g/g]⌘
- Rapporto Albumina/Creatinina (ACR) [0 – 30 mg/g] ⌘

⌘ Esame su campioni spot della mattina

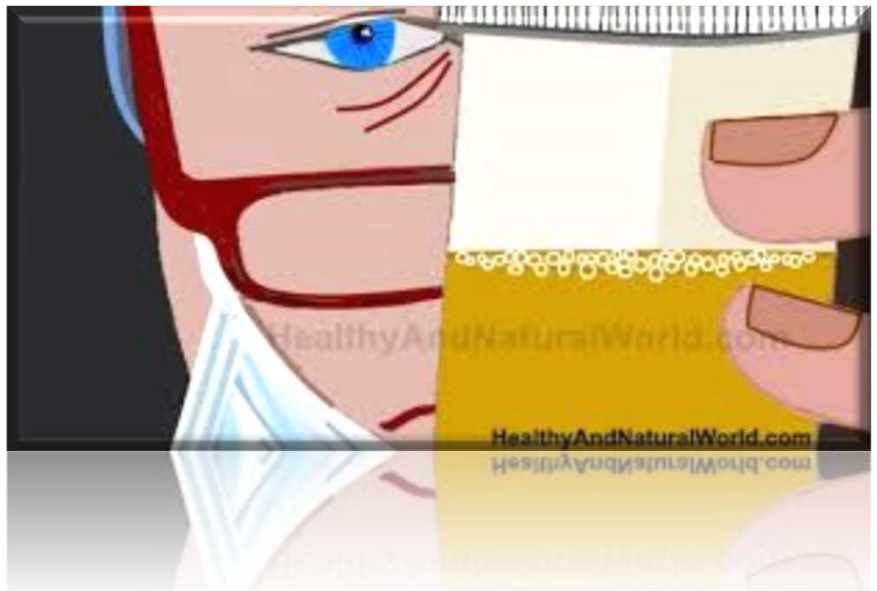
Dosaggio immunometrico di proteine a basso peso molecolare

-Retinol-binding protein

-b2-microglobulina

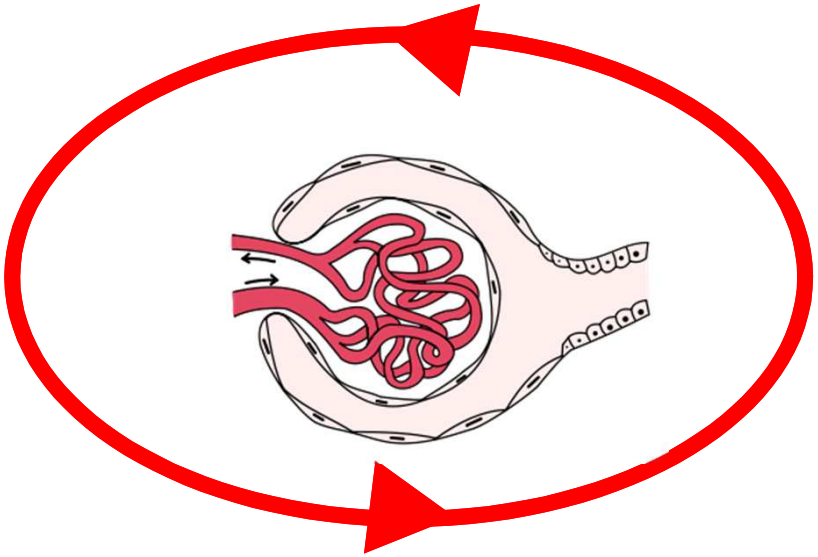
- a1-microglobulina

- NGAL



Glomerulosclerosi

Tubulo



Glomerulo

Sovraccarico tubulare

Fattori che influenzano la Creatininemia

- Massa muscolare
- Età
- Sesso
- Etnia
- Amputazione
- Uso di steroidi
- Alimentazione iperproteica (dieta carnea)

Formule per la stima del GFR
III. CKD-EPI

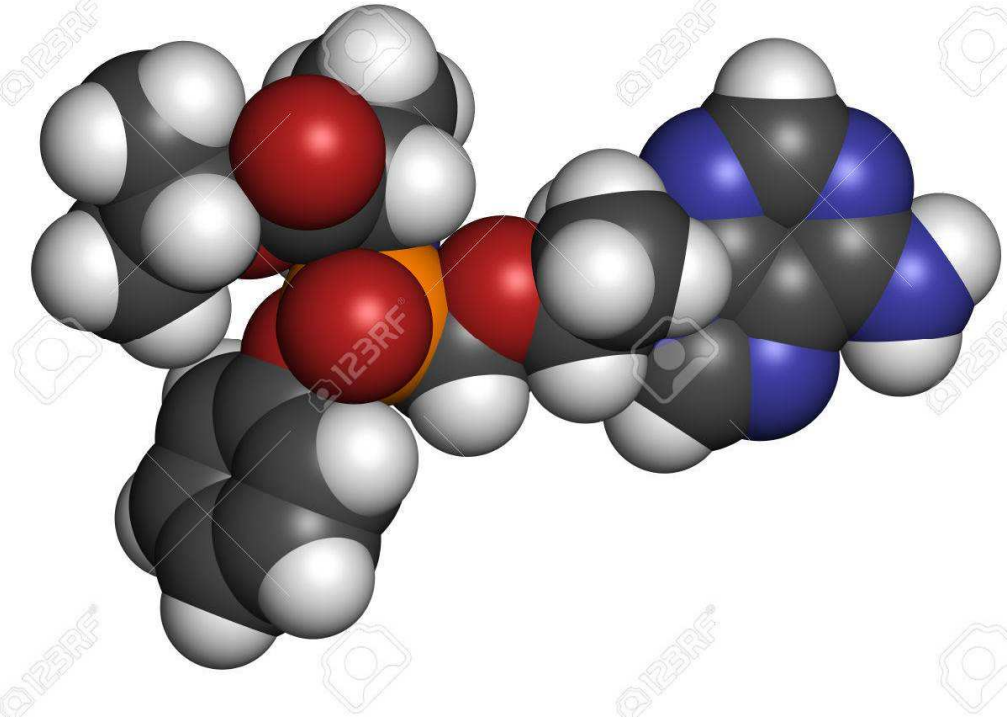
$eGFR = 141 * \min(SCr/k, 1)^{\alpha} * \max(SCr/k, 1)^{-1,209} * 0,993^{Età} * 1,018\ (F) * 1,159\ (B)$

k = 0,7 (F), 0,9 (M)

α -0,329 (F), -0,411 (M)

- Valutazione del GFR con metodo di riferimento
- Inclusi soggetti con valori normali di GFR
- Calcolo basato su creatininemia
- Non validata in altre razze
- Non accuratezza della misurazione della creatinina a bassa concentrazione (< 1 mg/dl)

Possiamo dimenticarci di tutto questo nell'era TAF?



I nuovi farmaci:

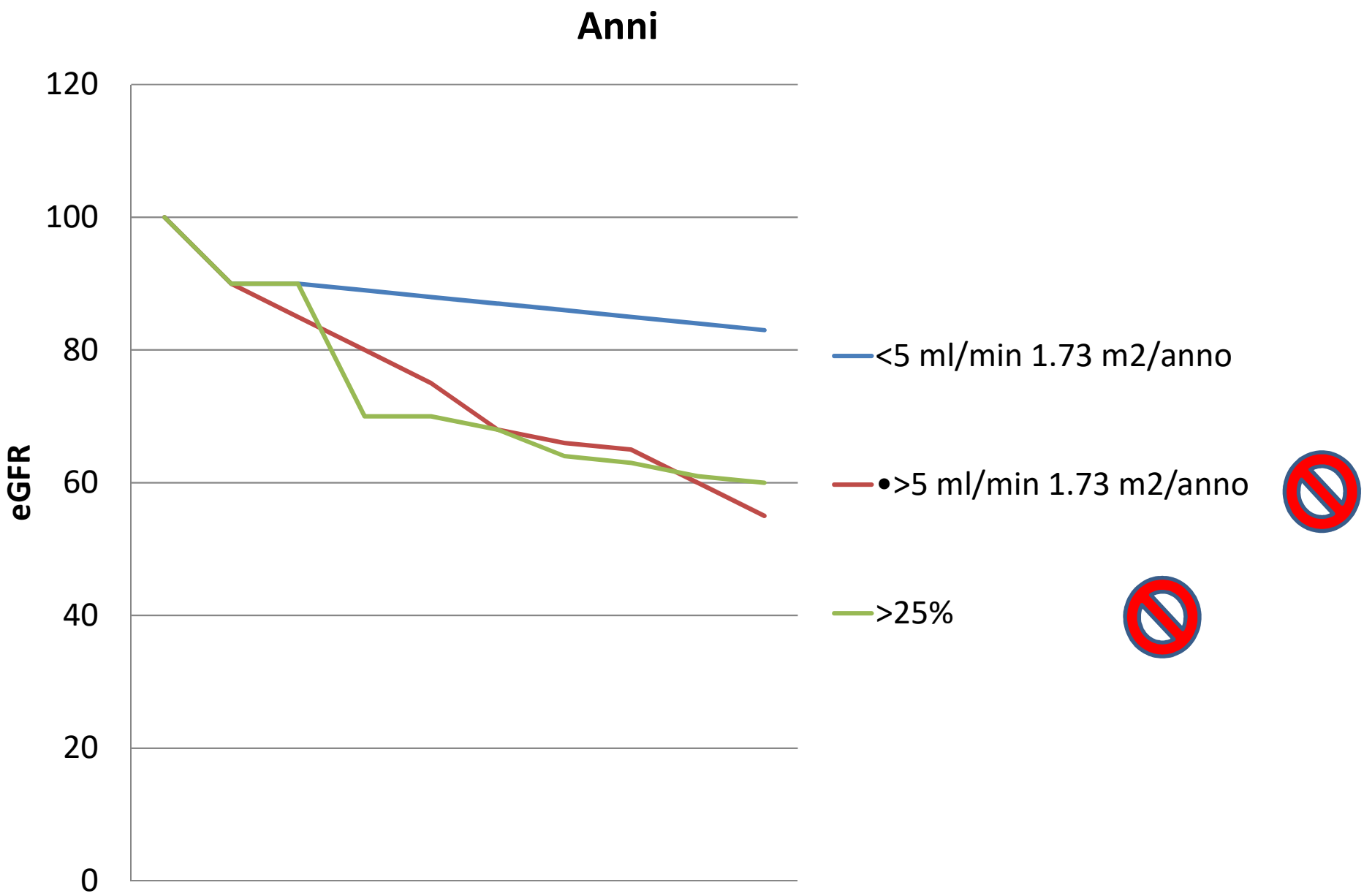
- Cobicistat
- Dolutegravir
  - (rilpivirina e **bictegravir**)

COBI Inhibits Active Tubular Secretion of Creatinine, Resulting in Increased SCr[1,2]

- Preclinical studies indicate that COBI blocks a transport pathway used for creatinine secretion from the proximal tubule by inhibiting a transport protein called MATE1 that is responsible for transporting creatinine into the proximal tubule[1-3]
- Other drugs have been reported to block tubular secretion of creatinine, such as ritonavir, cimetidine, and trimethoprim[4-6]

For illustrative purposes only.

[1] Lepist EI, et al. ICAAC 2011. Abstract A1-1724; [2] German P, et al. J Acquir Immune Defic Syndr. 2012;61:32-40; [3] Lepist EI, Ray AS. Expert Opin Drug Metab Toxicol. 2012;8:433-448; [4] Cohen C, et al. CROI 2010. San Francisco, CA. 58LB; [5] Andreev E, et al. J Intern Med. 1999;246:247-252; [6] Naderer O, et al. Antimicrob Agents Chemother. 1997;41:2466-2470.


Anni
120
100
80
60
40
20
0
eGFR
<5 ml/min 1.73 m2/anno
>5 ml/min 1.73 m2/anno
>25%

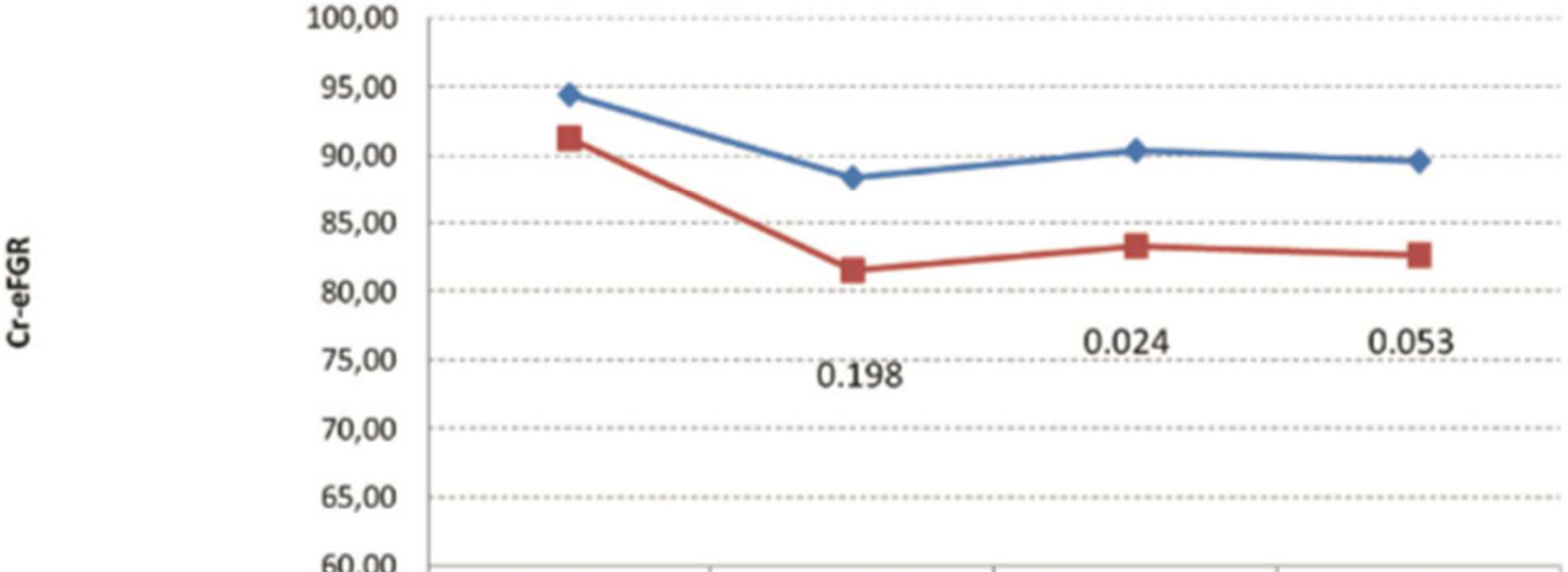
#692

DYNAMICS OF E-FGR WITH ONE OR MORE ANTIRETROVIRALS THAT INHIBIT CR TUBULAR SECRETION

Maria Jesus P . Elias

The concomitant use of **Darunavir/cobicistat** plus other known inhibitors of tubular creatinine secretion (dolutegravir, rilpivirine or both) produced an additive effect in the expected Cr-eGFR decrease.

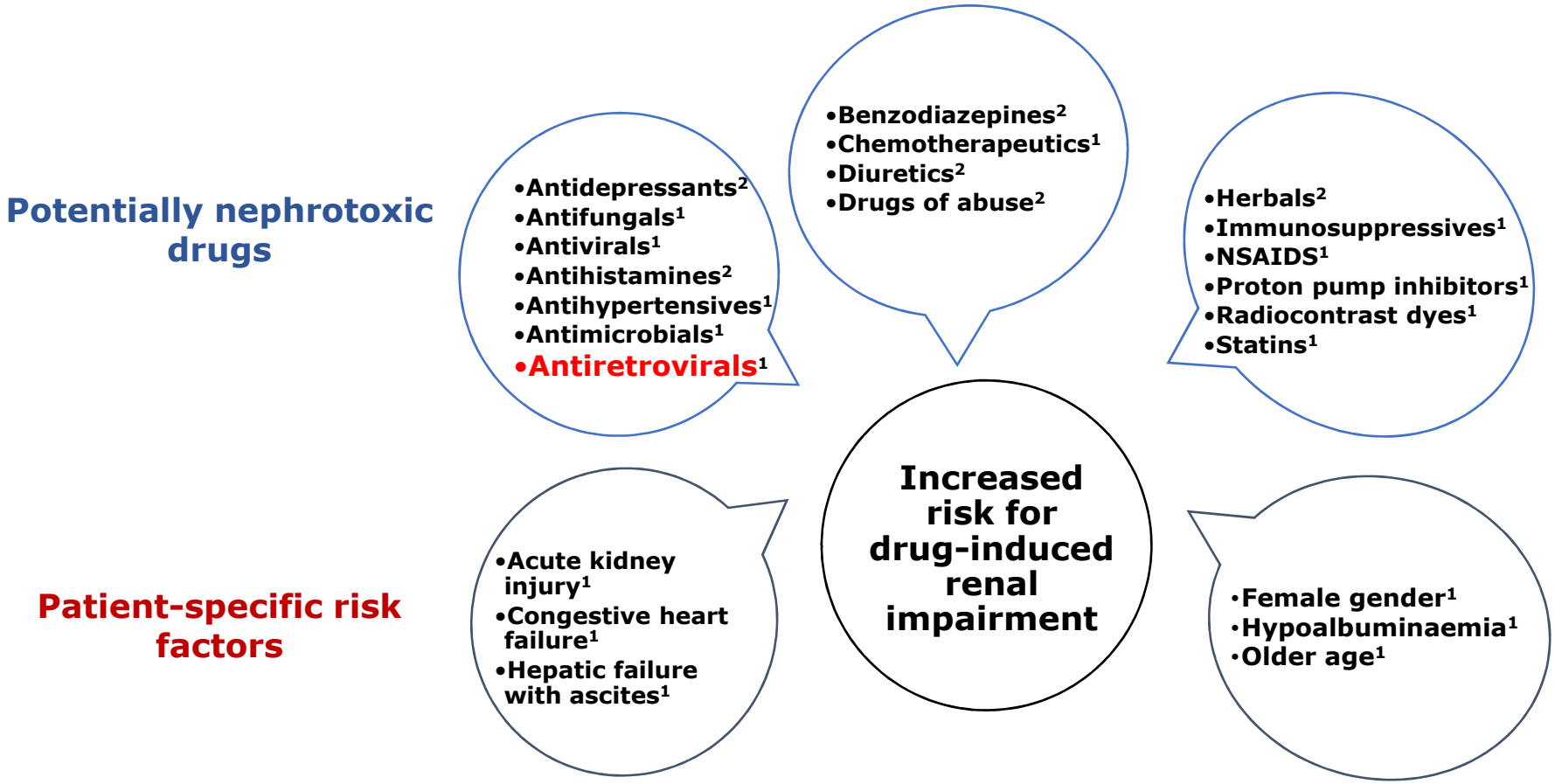
Cr-eFGR at 12, 24 and 48 Weeks, DRV/c vs. DRV/c plus DTG and/or RPV



	Baseline	W12	W24	W48
DRV/c alone	94,49	88,36	90,42	89,61
DRV/c + DTG and/or RPV	91,28	81,55	83,31	82,68
	N= 623	256	514	463
	N= 102	56	86	69

Factors for drug-induced renal impairment

- Several classes of drugs can impair renal function at any of its composite steps, including changing renal arterial blood flow, reducing glomerular filtration, altering tubule function, or obstructing urine flow



NSAID, non-steroidal anti-inflammatory drugs

1. Pazhayattil GS and Shirali AC. Int J Nephrol Renovasc Dis 2014;7:457–468; 2. Naughton CA. Am Fam Physician 2008;78(6):743–750

Classic Risk Factors:

Age

High blood pressure

Diabetes

Genetic

Viruses (HIV, HCV, HBV)

Chronic inflammation

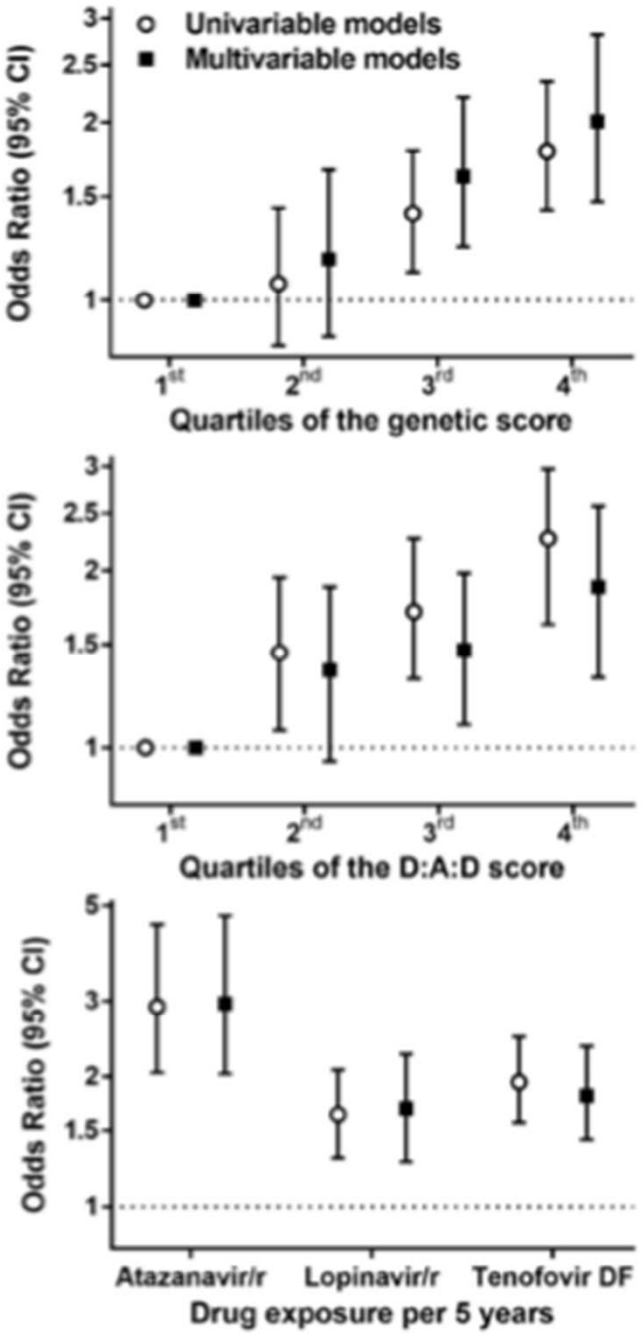
Drugs

#690
GENETIC AND CLINICAL RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN HIV

Léna G . Dietrich

The effect of an unfavorable genetic background on CKD risk in HIV-positive persons was similar to the effect of the established D:A:D clinical risk score, and similar to 5-year exposure to nephrotoxic antiretrovirals.

Genetic testing may provide prognostic CKD information complementary to clinical and antiretroviral risk factors.


Univariable models
Multivariable models
Odds Ratio (95% CI)
3
2.5
2
1.5
1
1st
2nd
3rd
4th
Quartiles of the genetic score
Odds Ratio (95% CI)
3
2.5
2
1.5
1
1st
2nd
3rd
4th
Quartiles of the D:A:D score
Odds Ratio (95% CI)
5
3
2
1.5
1
Atazanavir/r
Lopinavir/r
Tenofovir DF
Drug exposure per 5 years

AIDS October 23, 2014 - Volume 28 - Issue 16

Renal epithelial cells produce and spread HIV-1 via T-cell contact

Blasi M et al.

- Objectives: Increasing evidence supports the role of the kidney as a reservoir for HIV-1. In-vitro co-cultivation of HIV-infected T cells with renal tubule epithelial (RTE) cells results in virus transfer to the latter, whereas cell-free virus infection is inefficient. We further characterized the fate of HIV-1 after it is internalized in renal epithelial cells.
- Methods: Primary or immortalized CD4+ cells were infected with a green fluorescent protein (GFP)-expressing replication competent HIV-1. HIV-1 transfer from T cells to RTE cells was carried out in a co-culture system and evaluated by fluorescence-activated cell sorting analysis. HIV-1 integration in renal cells was evaluated by Alu-PCR and the production of infectious particles was assessed by p24-ELISA and TZM-bl assay. HIV-infected renal cells were used as donor cells in a co-culture system to evaluate their ability to transfer the virus back to T cells.
- Results: Renal cells become productively infected by HIV-1 and multiple copies of HIV-1 can be transferred from infected T cells to renal cells. Two separate cell populations were identified among infected renal cells based on reporter gene GFP expression level (low vs. high), only the high showing sensitivity to azidothymidine and ritonavir. Co-cultivation of HIV-1-infected renal cells with noninfected T cells resulted in HIV-1 transmission to T cells, supporting bidirectional exchange of virus between T cells and kidney-derived cells. Persistent expression and generation of infectious virus in renal cells required HIV integration.
- **Conclusion: These results support the kidney as a potential reservoir where virus is exchanged between interstitial T cells and RTE cells**

#793

Spectrum of HIV-Associated Kidney Disease in the Era of Combination Antiretroviral Therapy

John Booth

We reviewed consecutive renal biopsies (1998-2012) of HIV+ patients attending eight clinics in the UK.

This is the first study to demonstrate a relationship between HIV replication and ICKD (immune complex kidney disease) .

Compared to HIVAN, ICKD was associated with less advanced immunodeficiency and a lower rate of progression to ESKD.

The observed **association with HIV viraemia** for both 'core' ICKD and HIVAN may imply a pathogenetic role of HIV replication and its associated immune activation;

it also suggests that **suppressive ART may reduce the risk** of developing these types of kidney disease

797. Kidney Dysfunction and Markers of Inflammation in the Multicenter AIDS Cohort Study

Alison G. Abraham

- **Higher circulating levels of immune activation markers** among treated HIV+ individuals, despite virologic suppression, may partially explain their higher burden of kidney dysfunction compared to HIV- persons

Activation, senescenze and inflammation markers in HIV patients: association with renal function

Ozanne, Alexandra et al. for the CIADIS sub-study in the ANRS CO3 Aquitaine cohort study group

AIDS . 31(8):1119-1128, May 15, 2017.

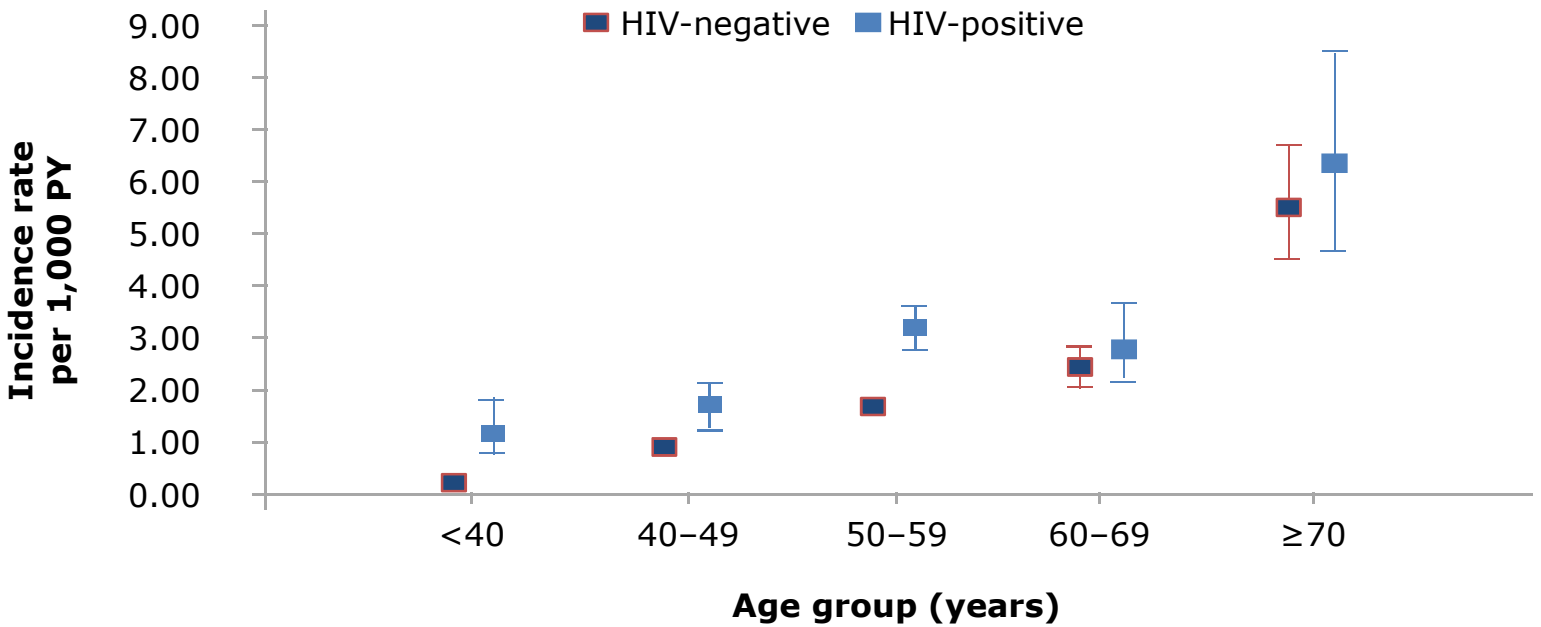
- Objectives: To assess the association among immune activation, immune senescence, inflammation biomarkers and renal function measured by estimated glomerular filtration rate (eGFR) at inclusion and its evolution over a 3-year follow-up in HIV-infected patients with undetectable viral load.
- Design: The **Chronic Immune Activation and Senescence (CIADIS**) substudy consecutively included patients between October 2011 and May 2013 enrolled in the ANRS CO3 Aquitaine observational cohort.
- Methods: Biomarkers of T-cell activation, differentiation and senescence were summarized in a cellular-CIADIS weighted score and inflammation biomarkers in a soluble-CIADIS weighted score using principal component analysis. Logistic regression and linear mixed models were used to determine the association between the CIADIS weighted scores and confirmed eGFR less than 60 ml/min per 1.73 m2, and evolution of eGFR, respectively.
- Results: Of 756 patients with an undetectable viral load, 76% were men, and median age was 51 years (Interquartile range: 45–57 years). In multivariable analysis, the soluble-CIADIS weighted score was independently associated with a confirmed eGFR less than 60 [odds ratio = 1.4; 95% confidence interval (CI) 1.1–1.8] but the cellular-CIADIS weighted score was not (odds ratio = 1.2; 95% CI 1.0–1.5). Only in patients with a confirmed eGFR less than 60 ml/min per 1.73 m2 at inclusion, a higher soluble-CIADIS weighted score (increased inflammation) was associated with a steeper decrease of renal function of −2.3 (ml/min per 1.73 m2) per year (95% CI −3.6 to −1.0).
- **Conclusion: At inclusion, soluble-CIADIS weighted score was independently associated with a confirmed eGFR less than 60 ml/min per 1.73 m2. The soluble-CIADIS weighted score was associated with a decrease of eGFR evolution during a 3-year follow-up only in patients with a confirmed eGFR less than 60 ml/min per 1.73 m2.**

VACS

Prevalence of end-stage renal disease (ESRD)

In a clinical prospective study, 98,687 HIV-positive and demographically matched HIV-negative veterans in the USA contributed 583,178 PYFU, 2003–2010

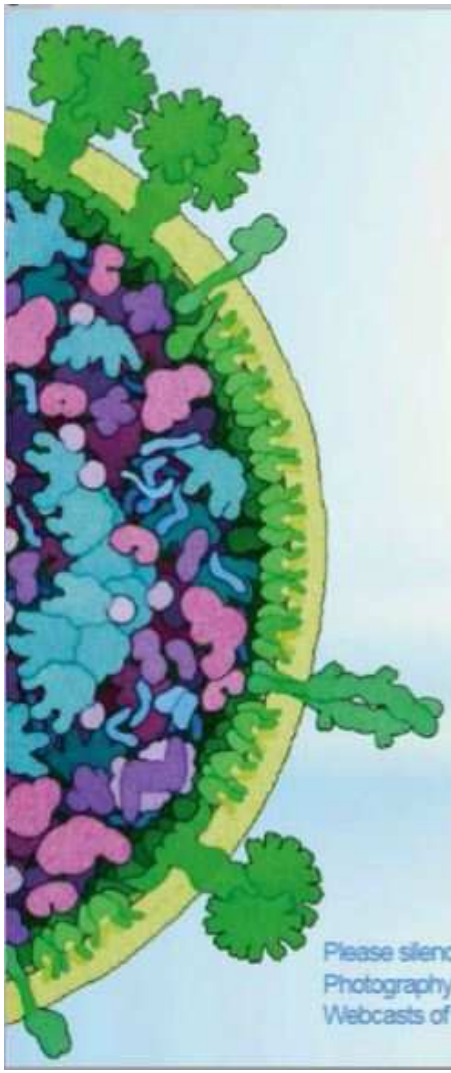
Overall and age-specific IRs (and 95% CIs) for ESRD



- **HIV-positive adults have a higher risk of ESRD age-associated events, but they occur at similar ages than those without HIV**

CI, confidence interval; IR, incidence rate; PY, person-years; PYFU, person-years of follow-up; VACS, Veterans Aging Cohort Study

Althoff KN et al. Clin Infect Dis 2015;60:627–638



SERIOUS CLINICAL EVENTS IN HIV-POSITIVE PERSONS WITH CHRONIC KIDNEY DISEASE (CKD)

Lene Ryom

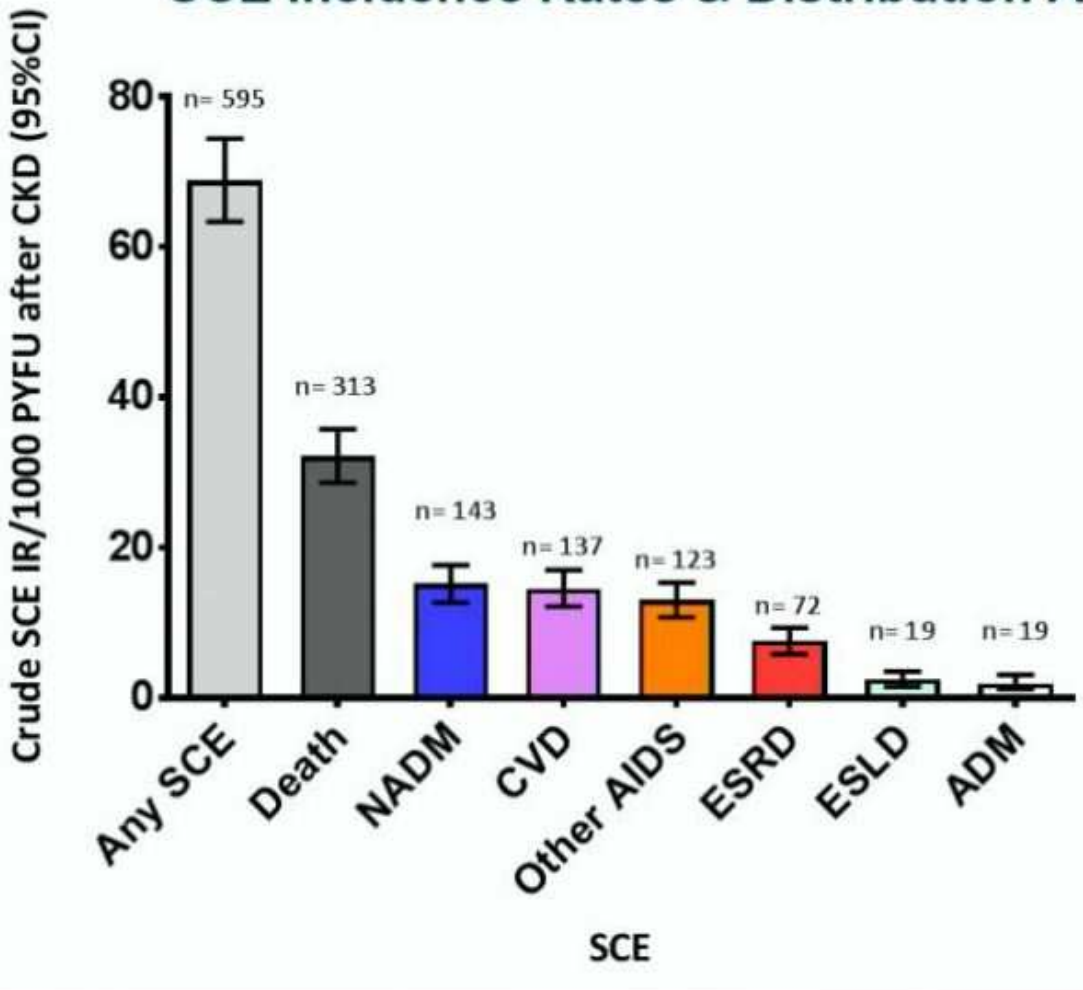
CHIP, Department of Infectious Diseases
Copenhagen, Denmark

Disclosure: Nothing to Disclose

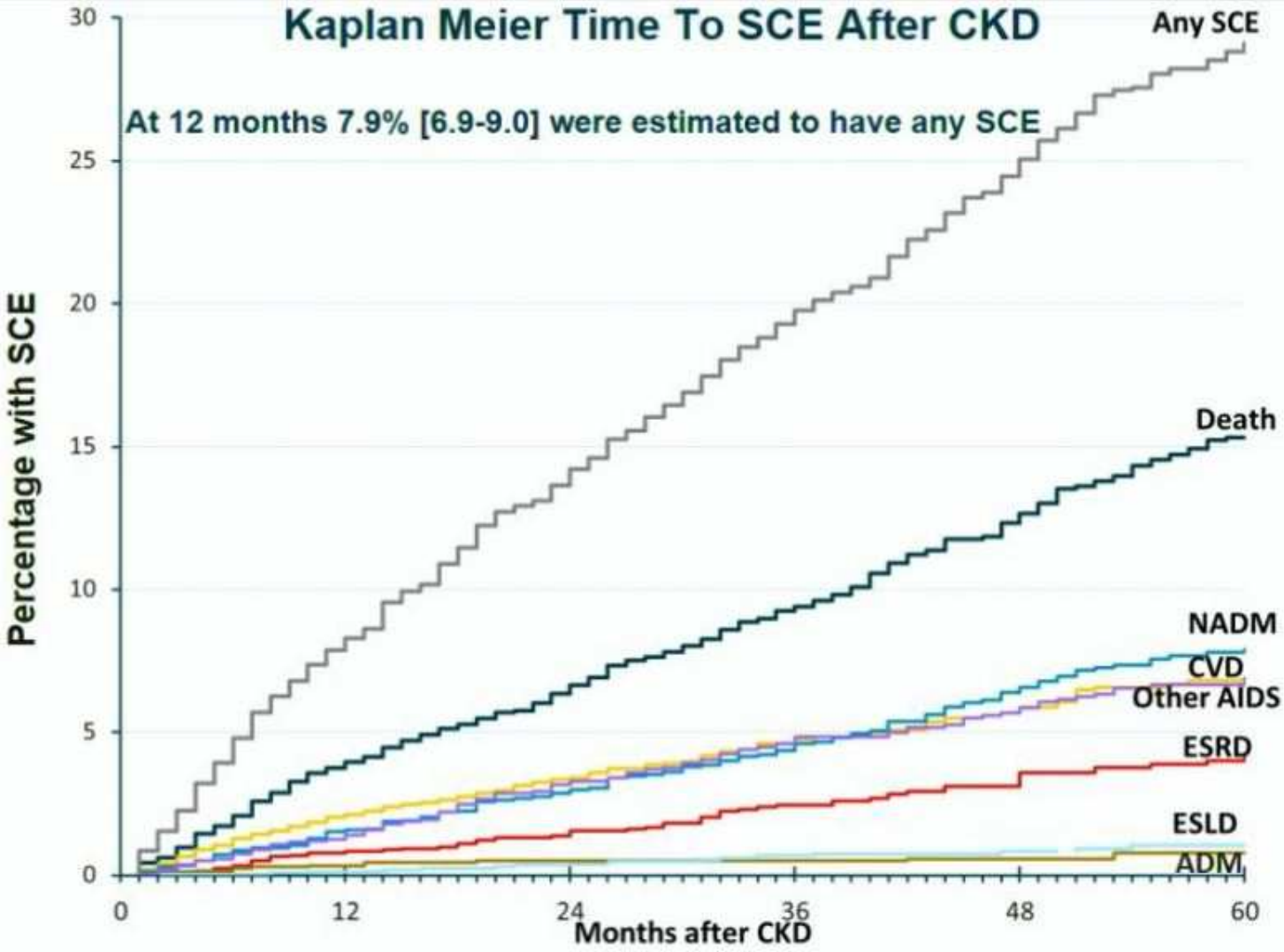
Please silence phones and devices.
Photography is not permitted in session room.
Webcasts of the lectures will be available at: www.CROIconference.org and www.CROIwebcasts.org

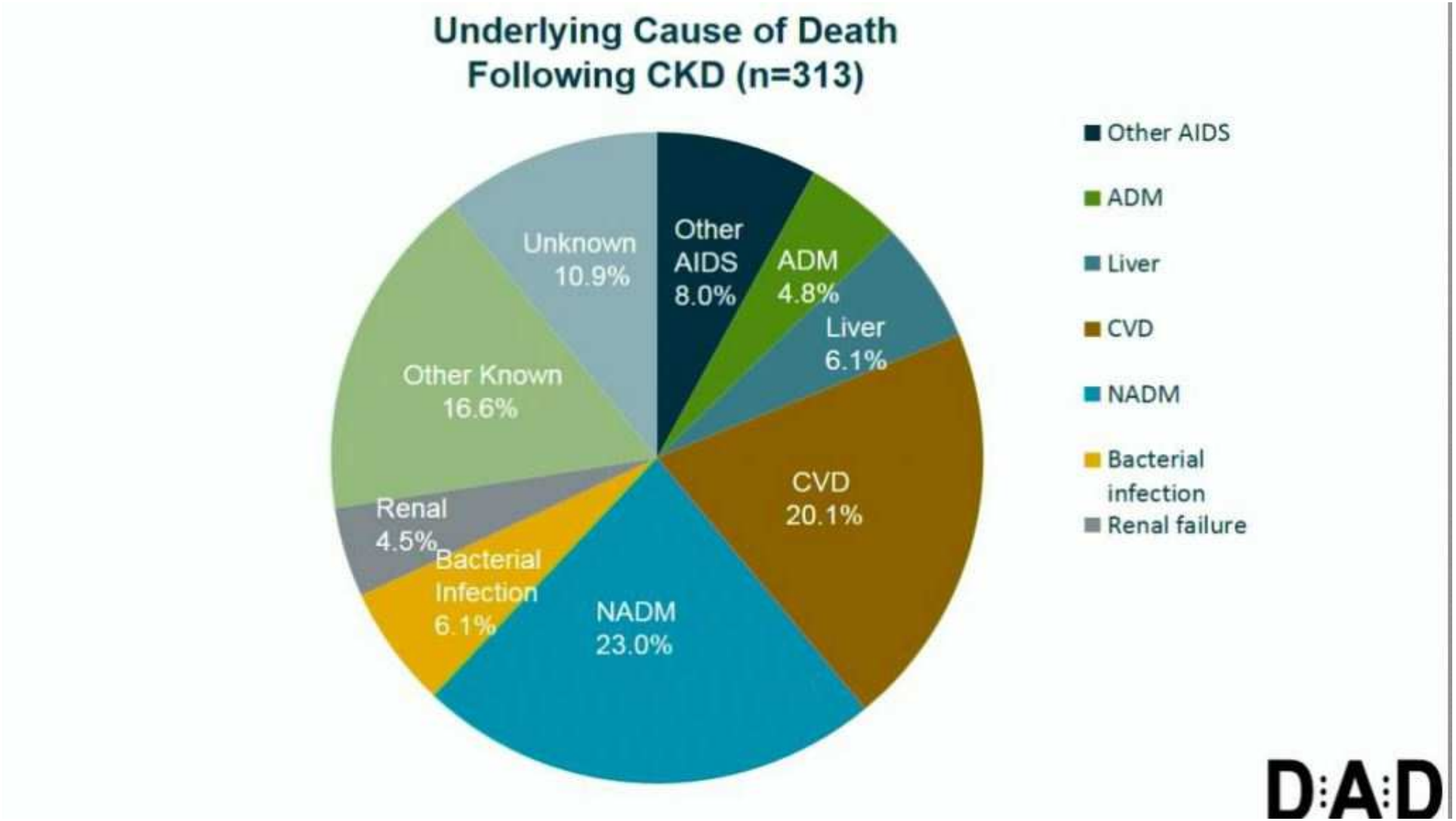
25th CROI

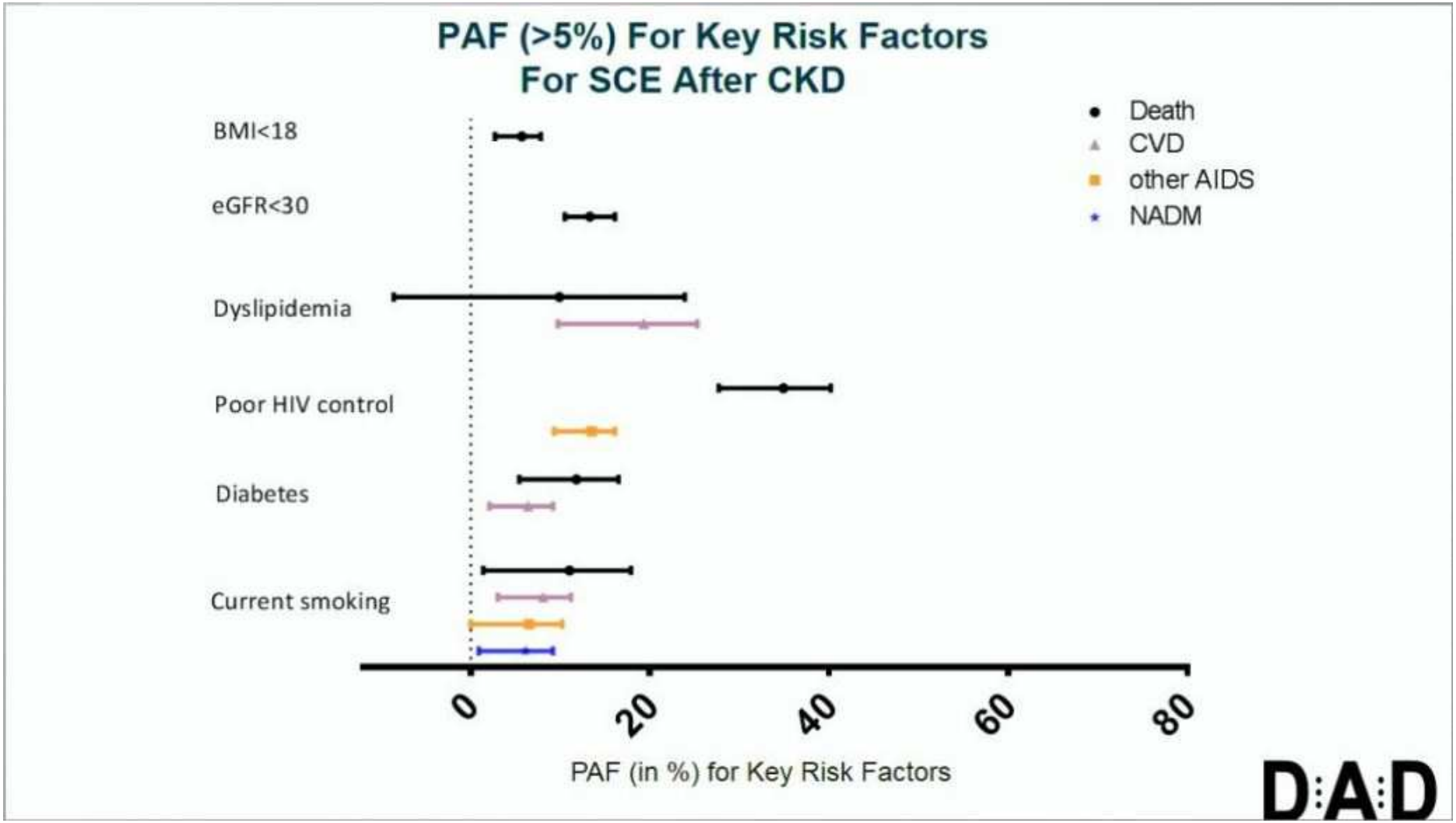
SCE Incidence Rates & Distribution After CKD



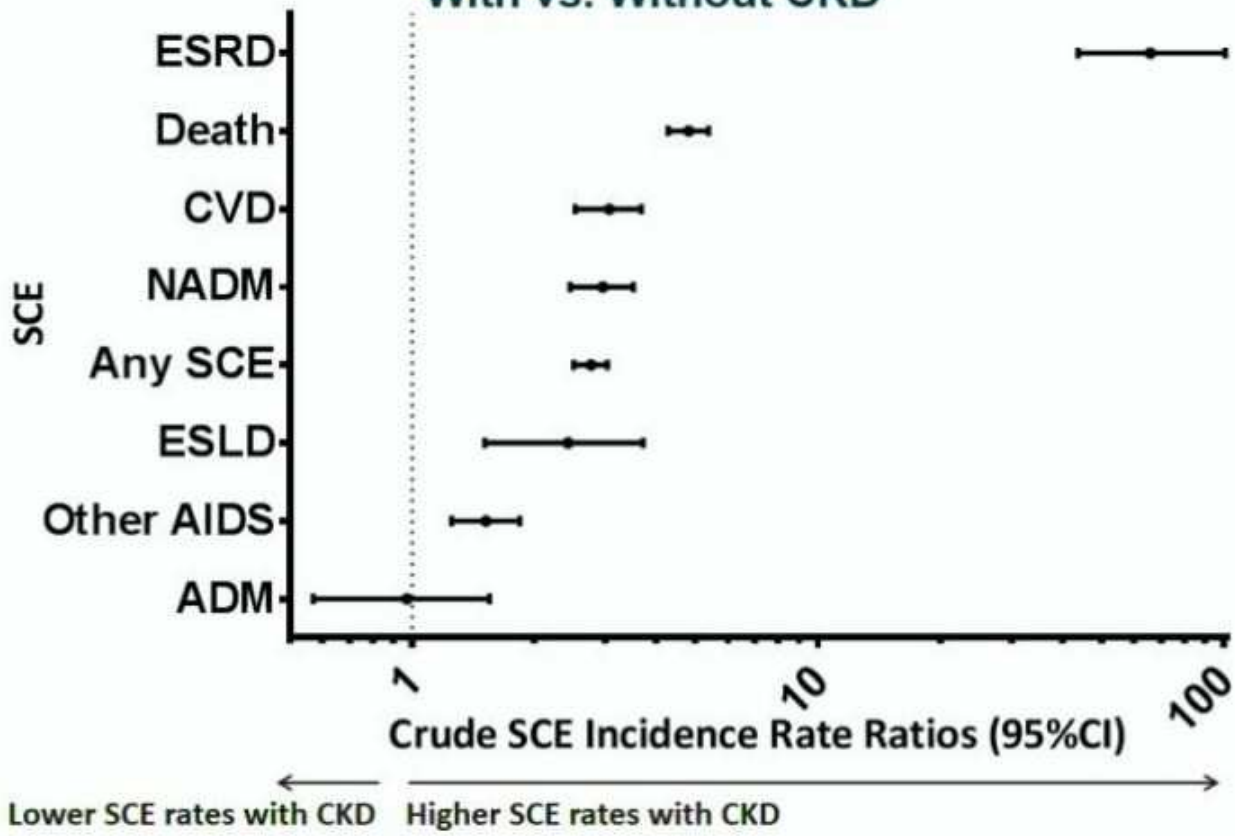
D:A:D


Kaplan Meier Time To SCE After CKD
At 12 months 7.9% [6.9-9.0] were estimated to have any SCE
Percentage with SCE
Months after CKD
0
5
10
15
20
25
30
0
12
24
36
48
60
Any SCE
Death
NADM
CVD
Other AIDS
ESRD
ESLD
ADM


Underlying Cause of Death
Following CKD (n=313)
Other AIDS 8.0%
ADM 4.8%
Liver 6.1%
CVD 20.1%
NADM 23.0%
Bacterial Infection 6.1%
Renal 4.5%
Other Known 16.6%
Unknown 10.9%
Other AIDS
ADM
Liver
CVD
NADM
Bacterial infection
Renal failure
D:A:D


PAF (>5%) For Key Risk Factors
For SCE After CKD
BMI<18
eGFR<30
Dyslipidemia
Poor HIV control
Diabetes
Current smoking
Death
CVD
other AIDS
NADM
0
20
40
60
80
PAF (in %) for Key Risk Factors
D:A:D

Results in Perspective (II)
Crude SCE Incidence Rate Ratios in those With vs. Without CKD



D:A:D

Conclusions I

- In an era where many HIV-positive persons require less monitoring due to effective antiretroviral treatment, those living with CKD have a high SCE burden with almost 1/5 developing SCE within 3 years, which require closer monitoring

- Compared to persons without CKD, those living with CKD have substantially higher rates of organ dysfunction, NADM and non-malignant AIDS events

D:A:D

Conclusions

- Our data further suggest modifiable risk factors including
  - *Smoking for Death, CVD, Other AIDS & NADM*
  - *Dyslipidemia for Death & CVD*
  - *Poor HIV-control for Death & Other AIDS*
  - *Diabetes for Death & CVD*
  - *Low BMI and low eGFR for Death*

  play a central role for post-CKD morbidity and mortality and highlight the need of increased awareness, effective treatment and preventive measures for those living with CKD

D:A:D

Definition of CKD (chronic kidney disease)

- Chronic Kidney Disease (CKD) is defined as abnormalities of kidney structure or function, present for > 3 months, with implication for health

Criteria for CKD (either of the following present for > 3 months)

Markers of kidney damage (one or more)	• Albuminuria (AER > 30 mg/24 h); ACR (> 30 mg/g; > 3 mg/mmol) • Urine sediment abnormalities • Electrolyte and other abnormalities due to tubular disorders • Abnormalities detected by histology • Structural abnormalities detected by imaging • History of kidney transplantation
Decreased GFR	• GFR < 60 ml/min/1.73 m^2 (GFR categories G3a – G5)

2012 KDIGO

CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health and CKD is classified based on cause, GFR category, and albuminuria category (CGA).

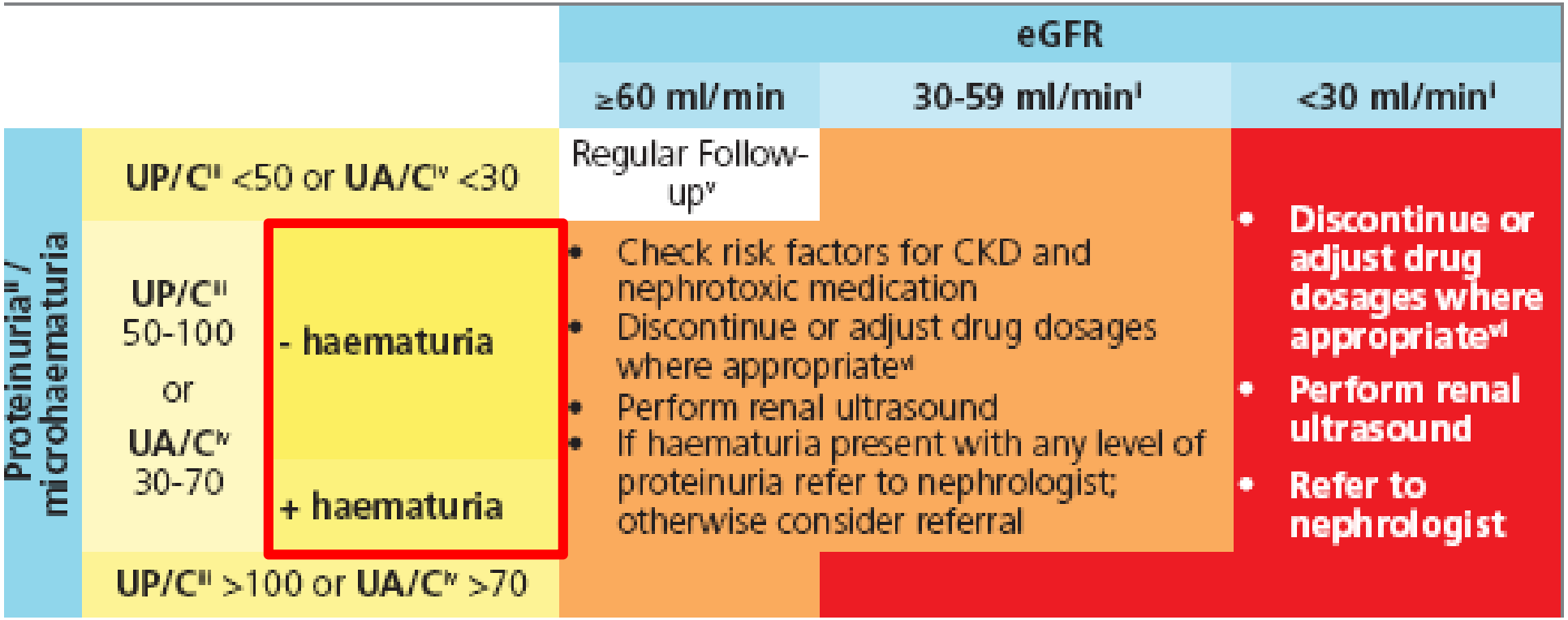
Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

2012 KDIGO


eGFR
≥60 ml/min
30-59 ml/min[i]
<30 ml/min[i]
Proteinuria[ii] / microhaematuria
UP/C[ii] <50 or UA/C[iv] <30
Regular Follow-up[v]
UP/C[ii] 50-100 or UA/C[iv] 30-70
- haematuria
+ haematuria
UP/C[ii] >100 or UA/C[iv] >70
• Check risk factors for CKD and nephrotoxic medication
• Discontinue or adjust drug dosages where appropriate[vi]
• Perform renal ultrasound
• If haematuria present with any level of proteinuria refer to nephrologist; otherwise consider referral
• Discontinue or adjust drug dosages where appropriate[vi]
• Perform renal ultrasound
• Refer to nephrologist

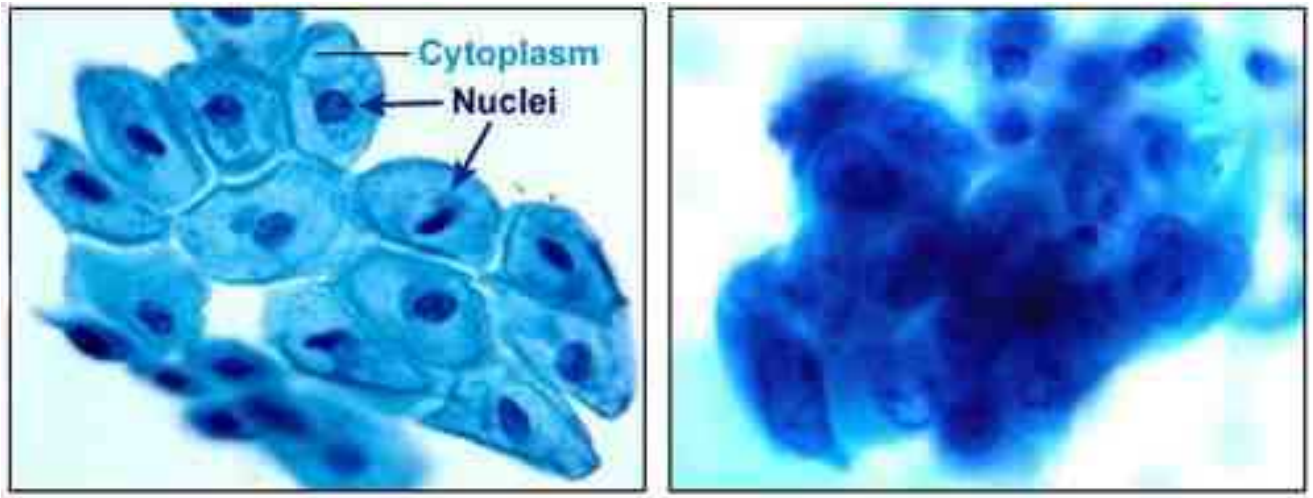
L'ematuria: il secondo driver

Haematuria?
First step:

Repeat the test!!

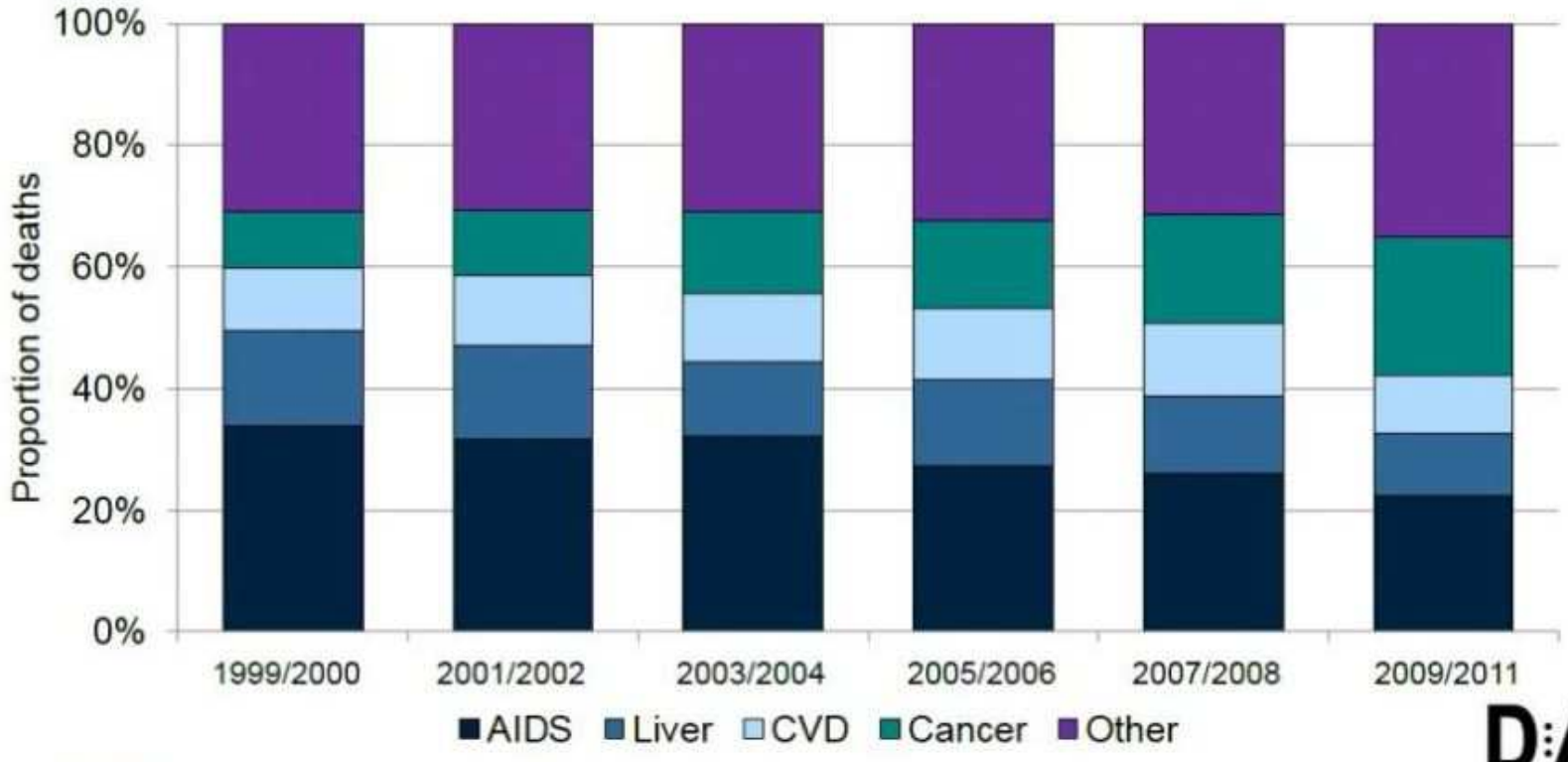
- Normal water intake (specific gravity <1020)
- No physical activity
- No sexual activity
- Far from menstrual period
- 1 sample/month along 3-6 months (if no progression in kidney failure)

Haematuria?
Second step:
Rule out Cancer!!



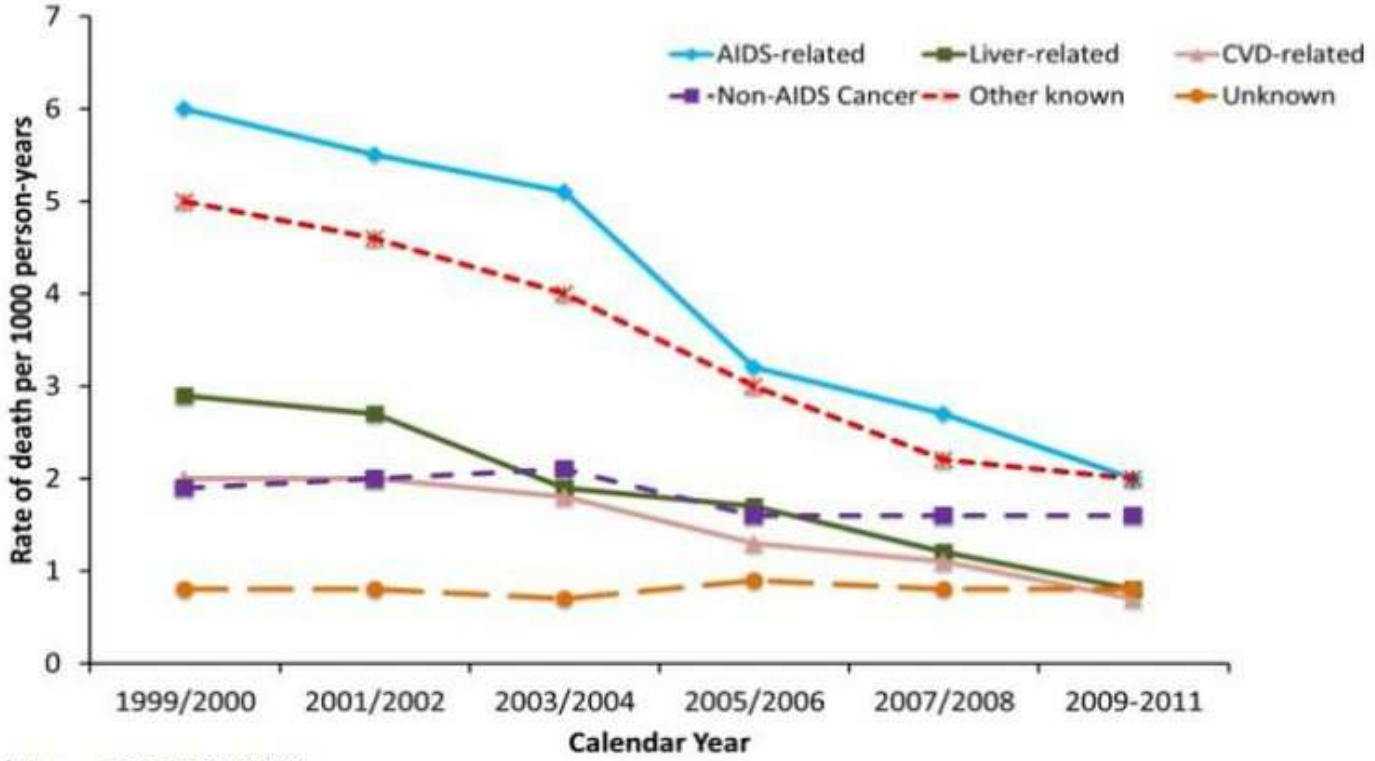
US, Citology, PSA, Cistoscopy

Causes of death



D:A:D Merger 14 dataset

Age-standardised mortality rates



Smith CJ et al. *Lancet* 2014;**384**:241-8.

D:A:D

Haematuria?
Third step:

Rule out Infection!!

- Perform Urinocolture and treat accordingly

If persistent and/or high leukocituria

- Consider <u>first catch</u> urine (Chlamydia, Mycoplasm, Ureaplasm)
- Treat the partner
- Counsel for hygiene
- Consider profylaxis or Uro-Gynecologic referral

Haematuria?
Fourth step:

Fairley Test

- Fresh sterile urine sample
- 12 ml, Centrifuge 1200 RPM for 10 minutes
- Contrast phase urinary sediment
- Eumorphic (Simil-peripheral / Non glomerular) vs Dismorphic (Glomerular) erithrocytes
- Casts
- Crystals

Test di Farley

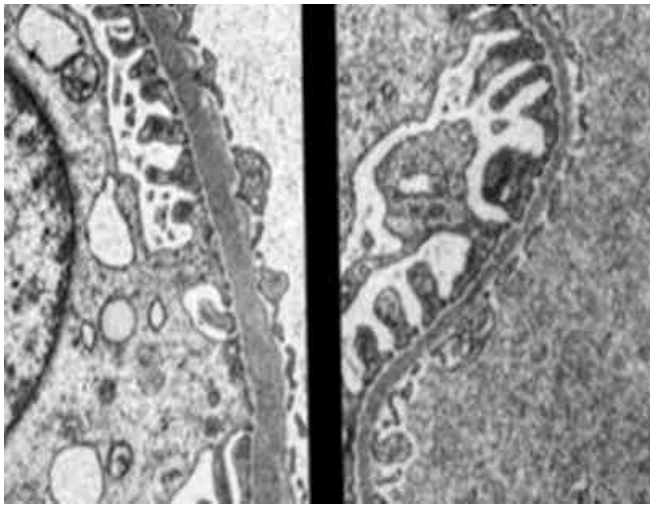
- Si esegue in presenza di eritrociti nel sedimento urinario.
- Il test di Farley è un esame morfologico eseguito con un microscopio in contrasto di fase.
- Se rivela un dismorfismo superiore al 75% degli elementi osservati, l'ematuria è compatibile con una origine glomerulare

In pratica il test di Farley è usato per definire l'origine glomerulare o non glomerulare dell'ematuria.

- L'esame va eseguito sul secondo mitto del mattino, e non sulle urine presenti in vescica al risveglio, che sono rimaste nella vescica per un periodo di alcune ore, per evitare che anche i globuli rossi isomorfici possano deformarsi.

Causes of glomerular haematuria

- Glomerular disease (>5 RC/HPF)
  - IgAN : gross haematuria during upper air tract or gastrointestinal infections
  - Postinfectious: gross haematuria 1-2 weeks after
- Hypercalciuria: U-Ca > 4mg/kg/die
  - Diet
  - Tubular damage
- Thin Base Membrane disease:
  - Benign, electron microscopy



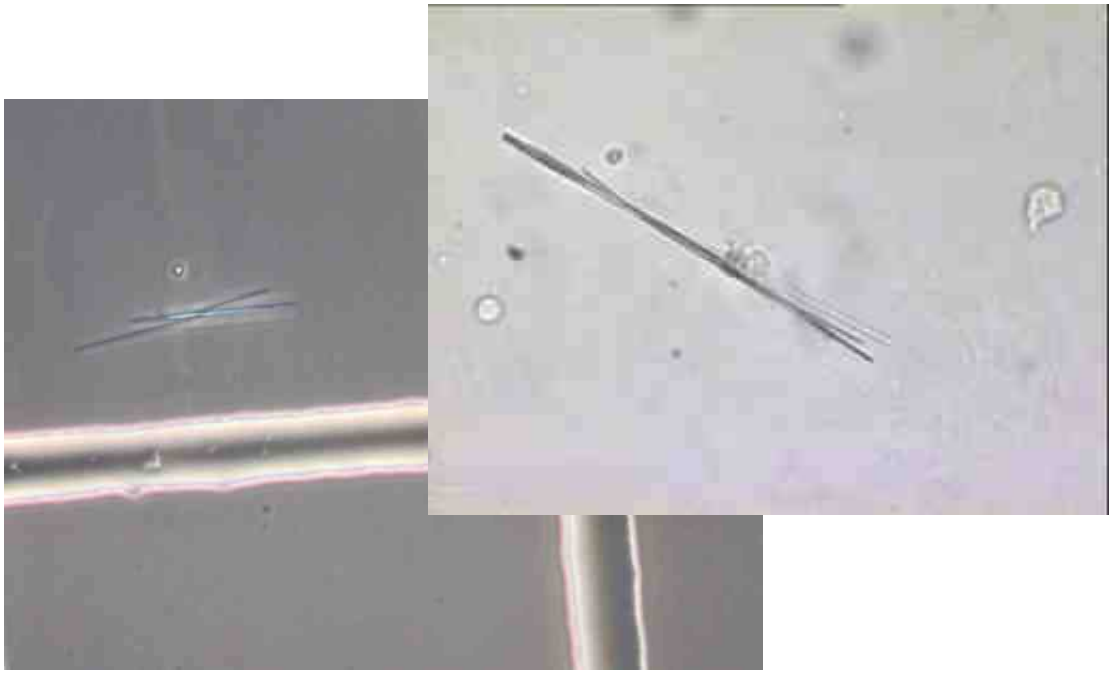
Causes of non-glomerular haematuria

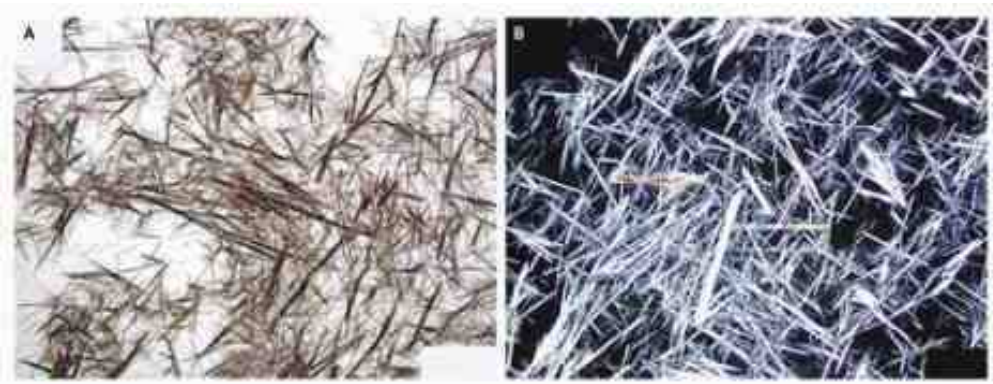
- Urothelial Cancer
- Urolithiasis
- Inflammation
- (Oral Anticoagulation)

If MIXED Haematuria (<50% dismorfic erithrocytes) always **rule out cancer**!

Fairley test

Fairley test: drug crystals





Is lab diagnosis of haematuria enough?

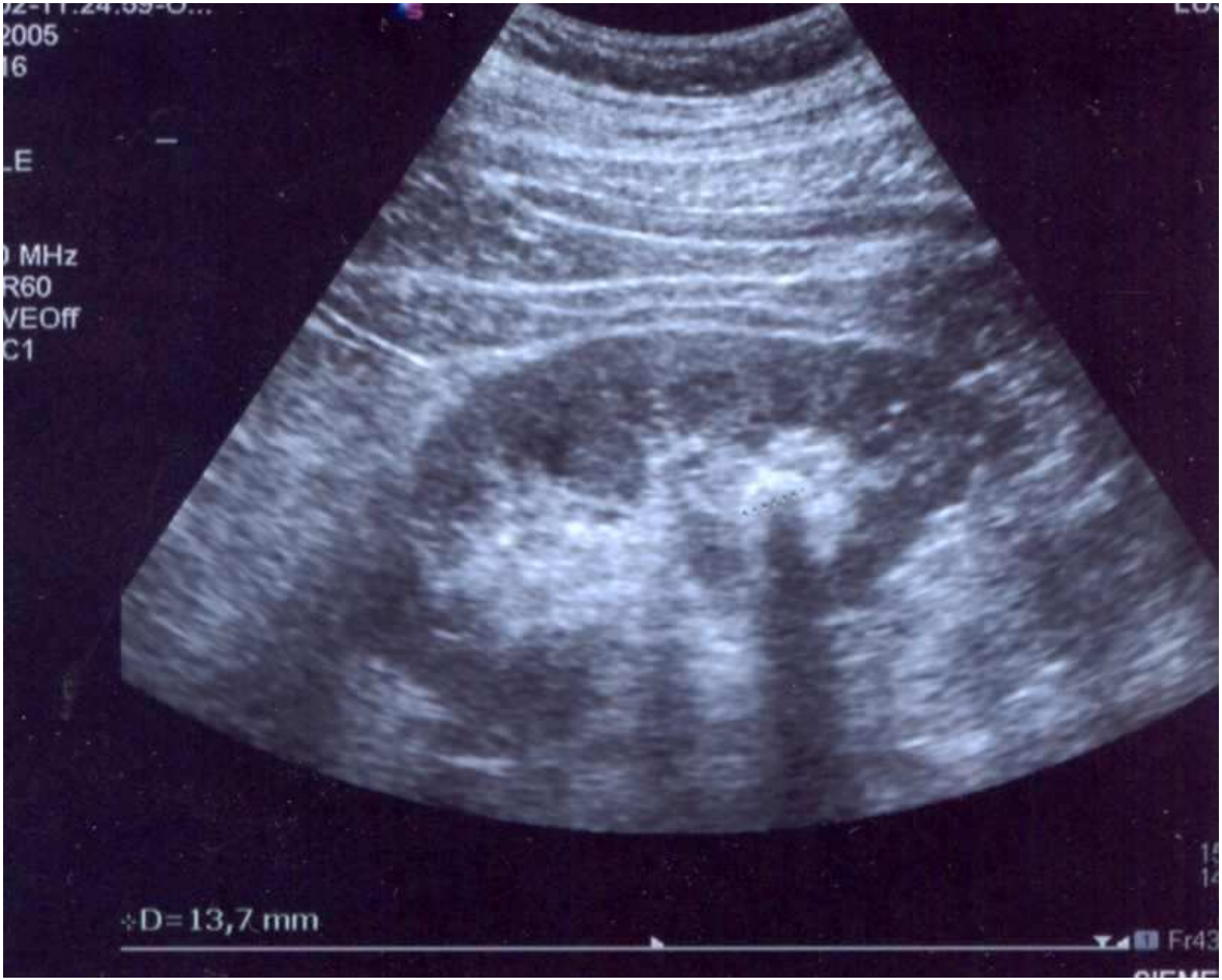
NO!

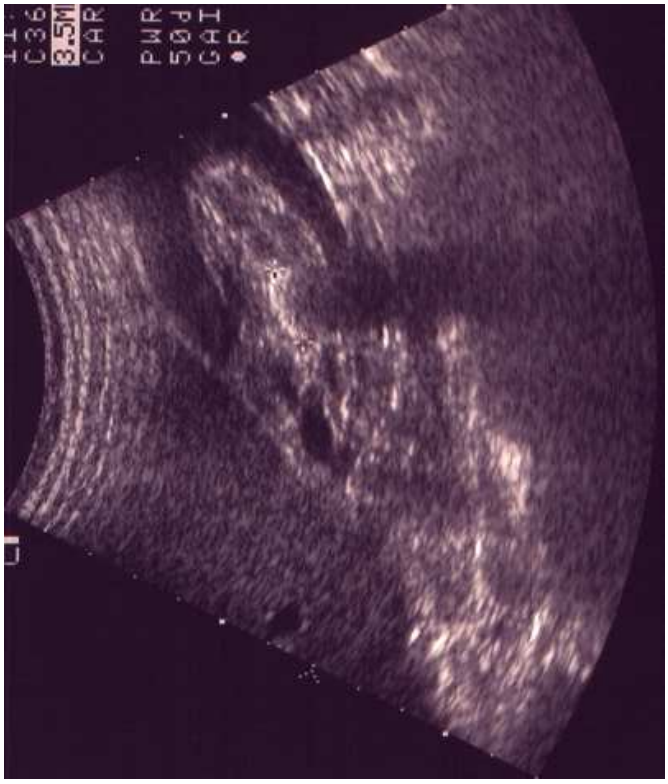
Kidney Biopsy as a Gold Standard

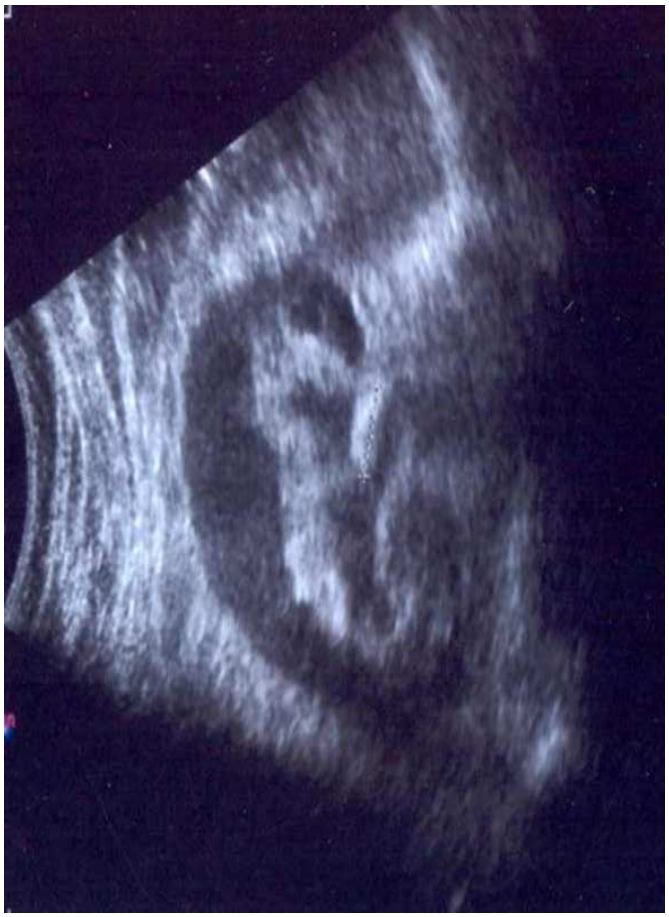
- Absent microalbuminuria minimizes positive predictive value of KB
- No proteinuria = Conservative management (ACEi, BP control, CV Risk control…)

Value of renal biopsy

- **Provides diagnosis**
  - alters clinical diagnosis in 25%-50% of cases
- **Guides treatment**
  - changes therapy in 30-40%
  - Determines reversibility and activity
- **Predicts prognosis**
  - Specific pathologic features and extent of changes
- **Reveals pathogenesis**
  - Molecular and cellular mechanisms
- **Validates outcome**
  - Used as endpoint in clinical trials


2005
16
LE
MHz
R60
VEOff
C1
D=13,7 mm


C36
3.5M
CAR
PWR
50Hz
GAIN



Renal toxicity associated with indinavir (and atazanavir)

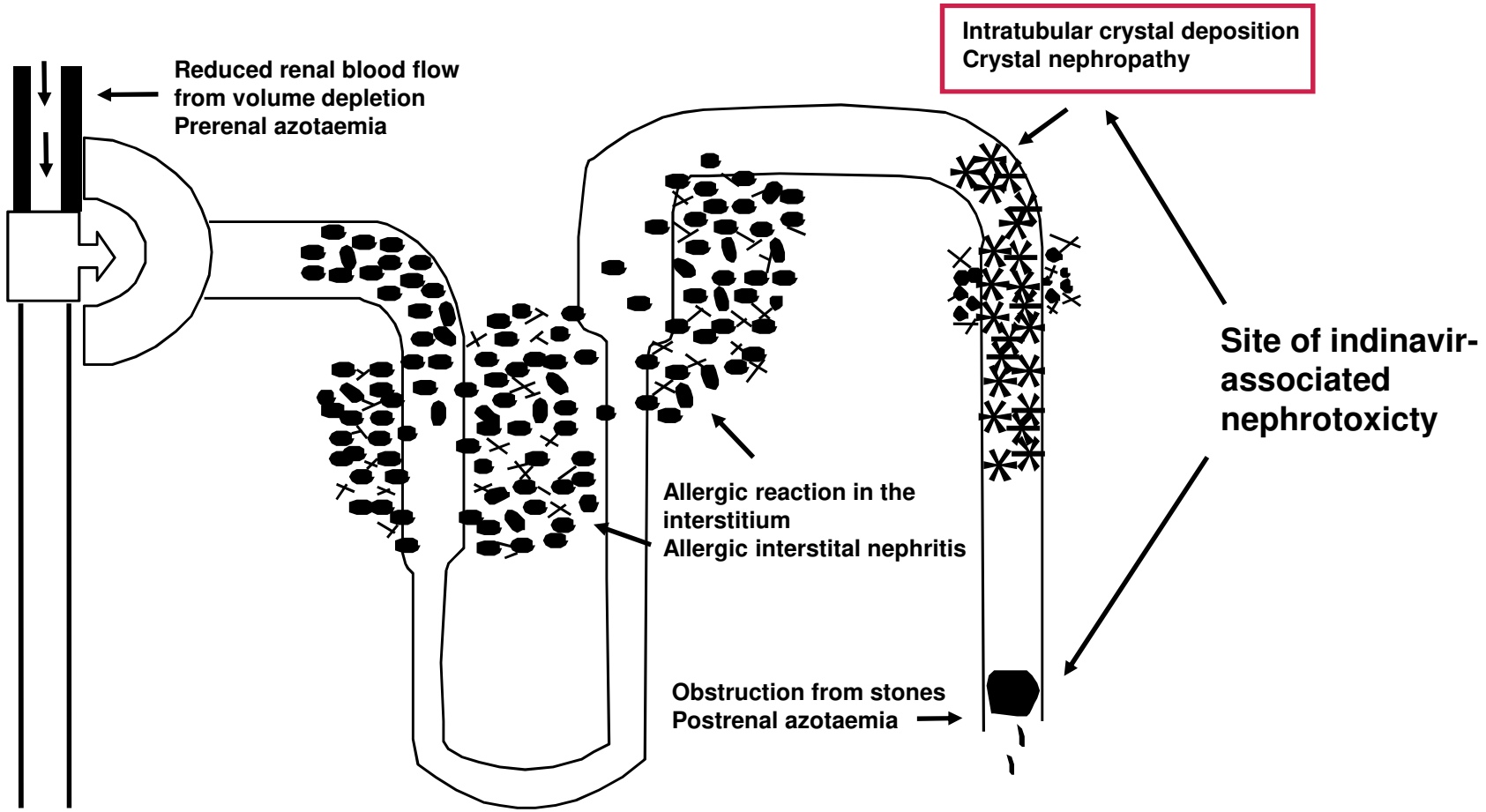


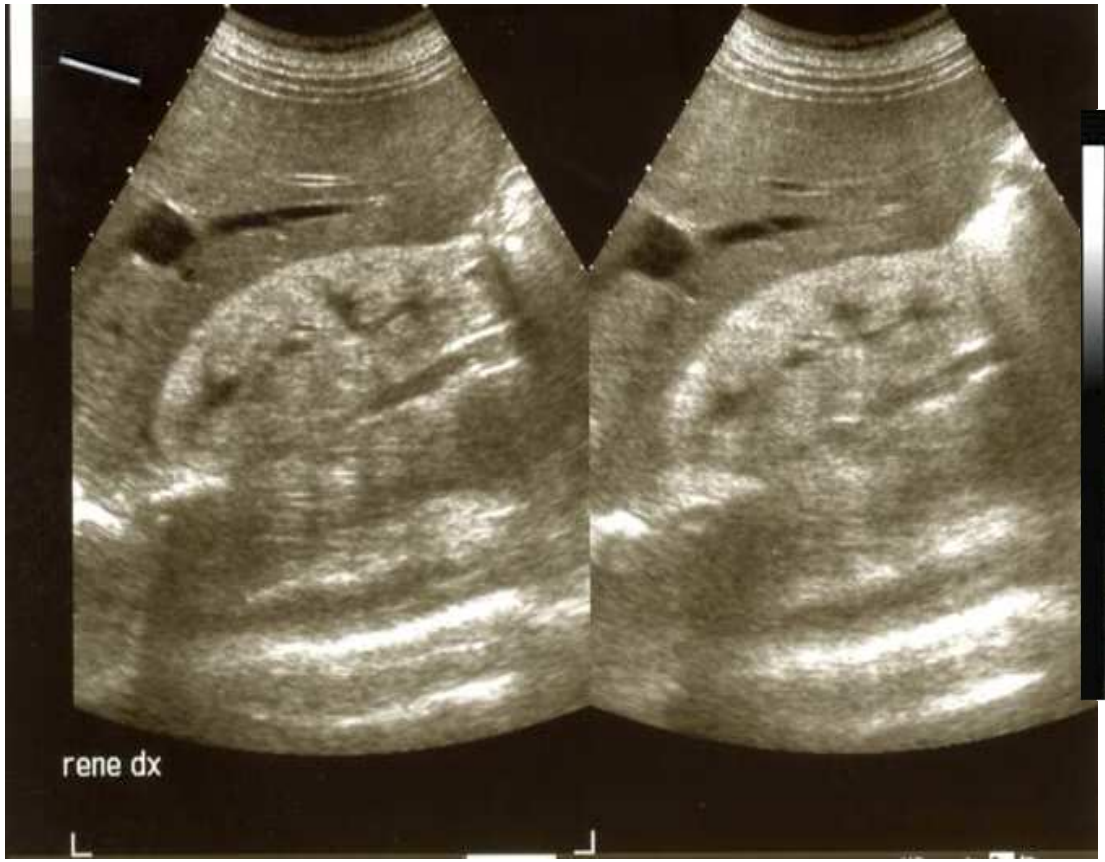
Illustration adapted from: Reilly RF & Perazella M. Nephrology in 30 days. McGraw-Hill, 2005

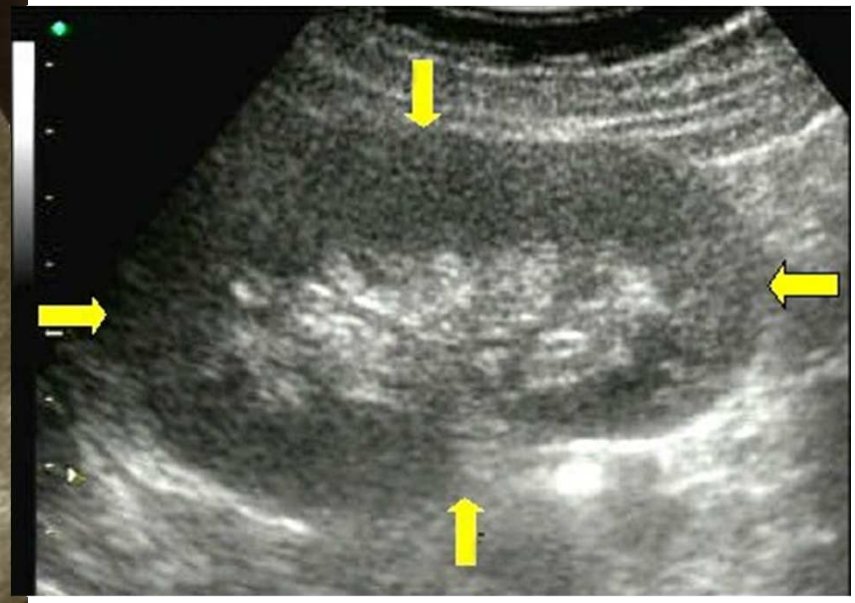
Nephrolithiasis

- Nephrolithiasis (kidney stones) is common, with a lifetime prevalence in the general population of 5–10% and increasing[1]
- Nephrolithiasis is
  - associated with several factors including low urine volume, **high sodium and protein intake, obesity**, urine infection, inflammatory bowel disease etc
  - usually reversible and frequently recurs
  - can occasionally (3.2% of cases) lead to end-stage renal disease[2]
- In patients with HIV, nephrolithiasis has been frequently associated with indinavir use[3] but has also been reported in association with other protease inhibitors[4]

1. Hall. Cleve Clin J Med 2009;76:583–91.
2. Jungers et al. Am J Kidney Dis 2004;44:799–805.
3. Huynh et al. Int Urol Nephrol 2011;43:571.
4. Chan-Tack et al. AIDS 2007;21:1215–8.

HIVAN – aspetto ecografico dei reni



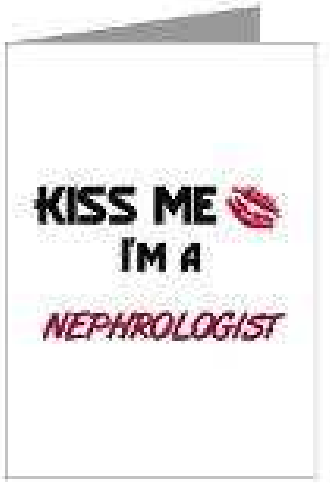


Rene normale

Take home messages

Non dimentichiamoci cosa abbiamo imparato nell'era TDF:

- Valutare la proteinuria
- Valutare la funzione renale



Nell'era TAF dobbiamo imparare a:

- Diagnosticare per tempo una CKD
- Individuare tempestivamente e valutare un'ematuria (renale o periferica)

E sapere quando chiamare il nefrologo……

Grazie per l'attenzione


Grazie