Optimising Renal Care

Optimising Care Series 2020

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Outline – Optimising Renal Care

- Case discussion
  - What would you do?
- Measurement of renal function
- AKI vs. CKD vs. ESRF
  - What are they?
- Managing CKD
  - When to refer
  - What to do about proteinuria

Q1: How comfortable are you managing patients with chronic kidney disease?

1. Not at all comfortable
2. I rarely do, and try to avoid it
3. Somewhat comfortable
4. Comfortable
5. Very comfortable

Case Study

- 52 year old. From the Philippines
- Recently diagnosed HIV and commenced on ART + Resprim for PJP prophylaxis 3 months earlier. CD4 90. VL now UD

- PMH
  - Diabetes
  - Anxiety
  - Previous heavy ETOH and IVDU
  - Hypertension: stopped taking tablets ~3 years ago

- Medications:
  - Descovy 200/25
  - Raltegravir bd
  - Metformin
  - Resprim half daily

- Investigations:
  - serum creatinine 205µmol/L (normal <90µmol/L)
  - U/A Protein+++ no blood

Q2: What is the renal diagnosis?

1. Acute Kidney Injury from Resprim
2. Acute Kidney Injury secondary to ART-induced nephrotoxicity
3. Acute Kidney Injury related to immune reconstitution inflammatory syndrome
4. Acute kidney Injury on a background of chronic kidney disease
5. Chronic kidney disease secondary to diabetes

AKI vs CKD vs ESRF

AKI → **CKD** → **ESRF** → **DIALYSIS** / **TRANSPLANT**

Change in renal function over days
Doubling of serum creatinine 48hrs **or** increase by >26.5µmol/L

If left untreated can result in permanent damage

Change in renal function over months
CKD = eGFR <60 one two separate measurements 3 months apart

Usually slowly progresses.

Risk factors for progression like those For CVD.

eGFR< 15

Stages of kidney disease

- 5 eGFR <15
- 4 eGFR 30-15
- 3 eGFR 60-30
- 2 eGFR 90-60
- 1 eGFR >90 – markers of damage

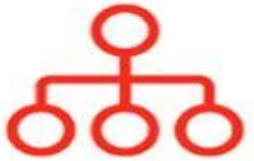
Kidney Health Australia

Are you at increased risk?

Diabetes

High blood presure

Heart problems or stroke



Family history

Obesity

Smoker

60 years or older

Aboriginal or Torres Strait Islander

History of acute kidney injury

#KHW17 #kidneysfirst

HIV
IDVU
ART

The Kidney Check

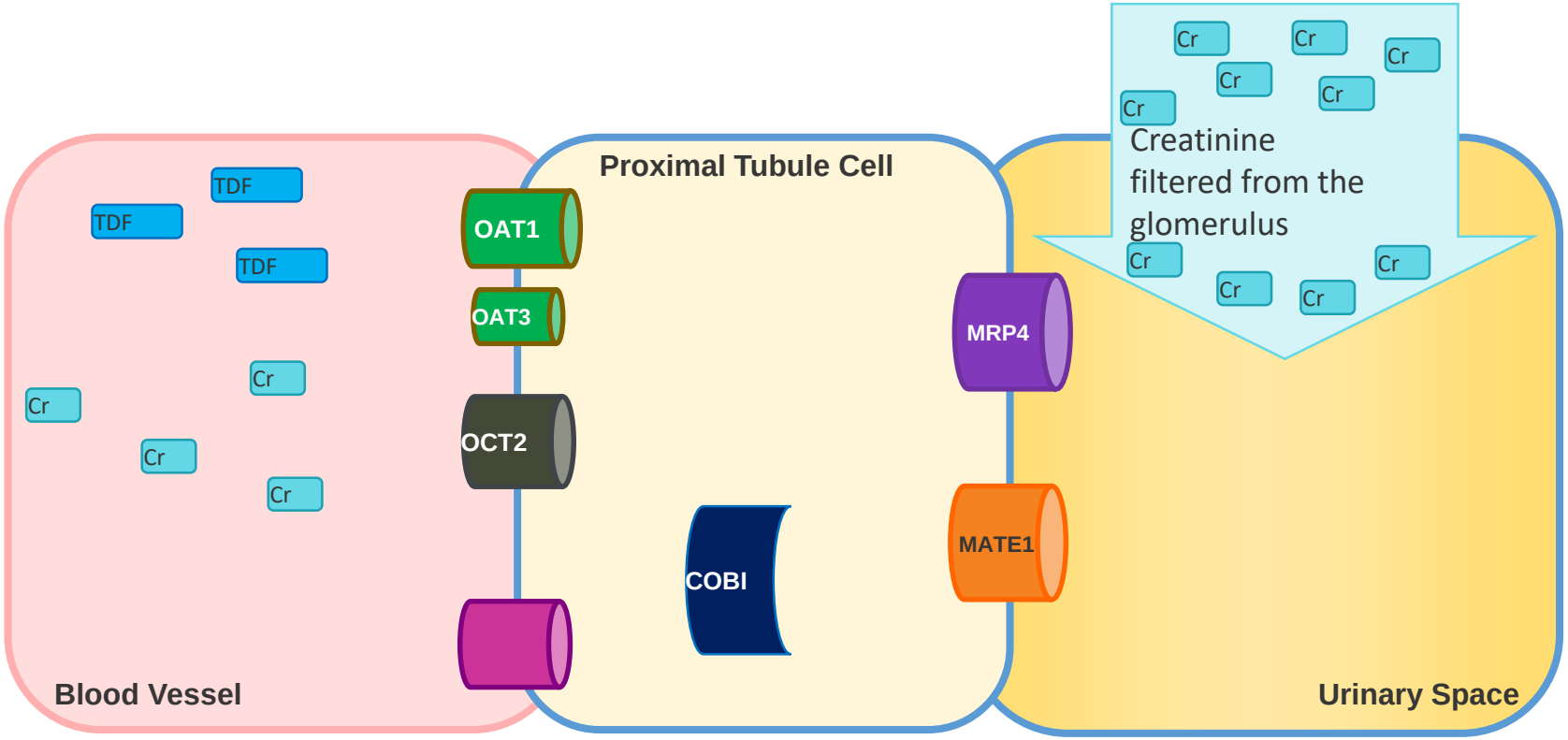
- Should be performed in ‘at risk’ patients at least annually
- Risk factors for kidney disease very similar to heart disease (+ FHx, AKI, nephrotoxic Rx)
- Earlier detection of CKD results in better outcomes
- Clinically:
  - Blood pressure
  - uACR and U/A (blood and protein)
  - eGFR

Measuring renal function

- eGFR calculated automatically from serum creatinine (adjusted for age and sex)
  - Remember renal function declines with age (~1ml/min/year after 35yo)
- Creatinine is a breakdown product of muscle metabolism. More muscle = higher creatinine, Less muscle = lower creatinine
- Dietary intake, protein powders, supplements and bone broth soups
- Extremes of BMI, racial differences
- Medications can interfere with serum creatinine (Resprim, COBI)
  - actual vs. estimated GFR

COBI and TDF - Effect On Creatinine Tubular Secretion

- TDF undergoes active tubular secretion with uptake via OAT1/OAT3 and secretion by MRP4. COBI does not inhibit these transporters[1-3]



German P, et al. *J Acquir Immune Defic Syndr*. 2012;61:32-40.
[2] Lepist EI, Ray AS. *Expert Opin Drug Metab Toxicol.* 2012;8:433-448.
[3] Lepist EI, et al. ICAAC 2011; abstract A1-1724.

Case continued…

- In order to answer my first question we needed more information:
- What was her baseline renal function? (creatinine 12 months before 188µmol/L, eGFR 26 – at first review eGFR 24)
- Acute vs. Chronic vs. Acute-on-chronic

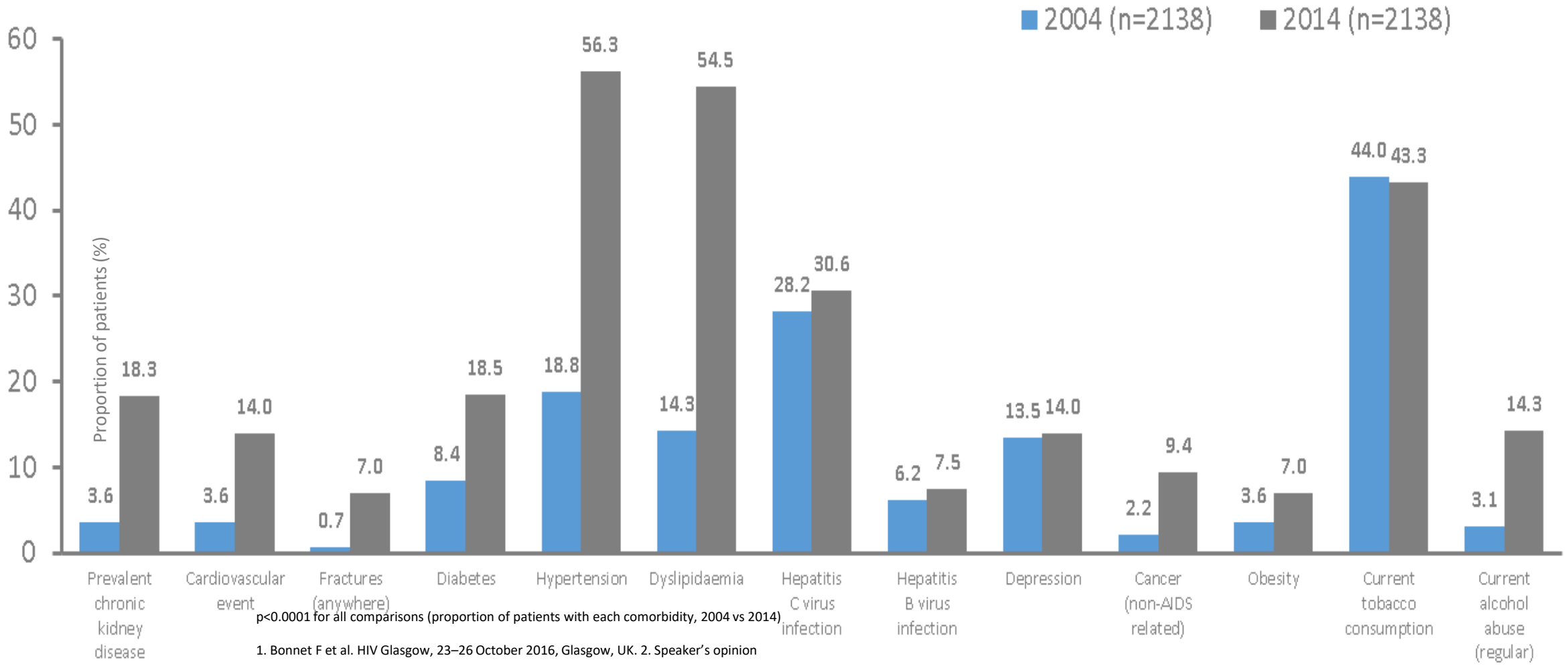
- **Our patient was at high renal and cardiovascular risk**
- Diabetes, hypertension, smoker, HIV, non-compliance, previous IVDU (HCV-associated renal disease?), proteinuria, established CKD; advanced and progressive
- Need to intervene stringently and aggressively on modifiable risk factors to prevent progression

Q3: The most important aspect of managing our patient is:

1. Improving diabetic control
2. Blood pressure management
3. Modifying ART
4. Smoking cessation
5. Referral to a renal physician

Comorbidities: Aquitaine Cohort

- High rate of comorbidities in 2004, significantly increased by 2014
- Dyslipidaemia (+40.2%) and hypertension (+37.5%). Chronic kidney disease (+14.7%) and cardiovascular events (+10.4%)

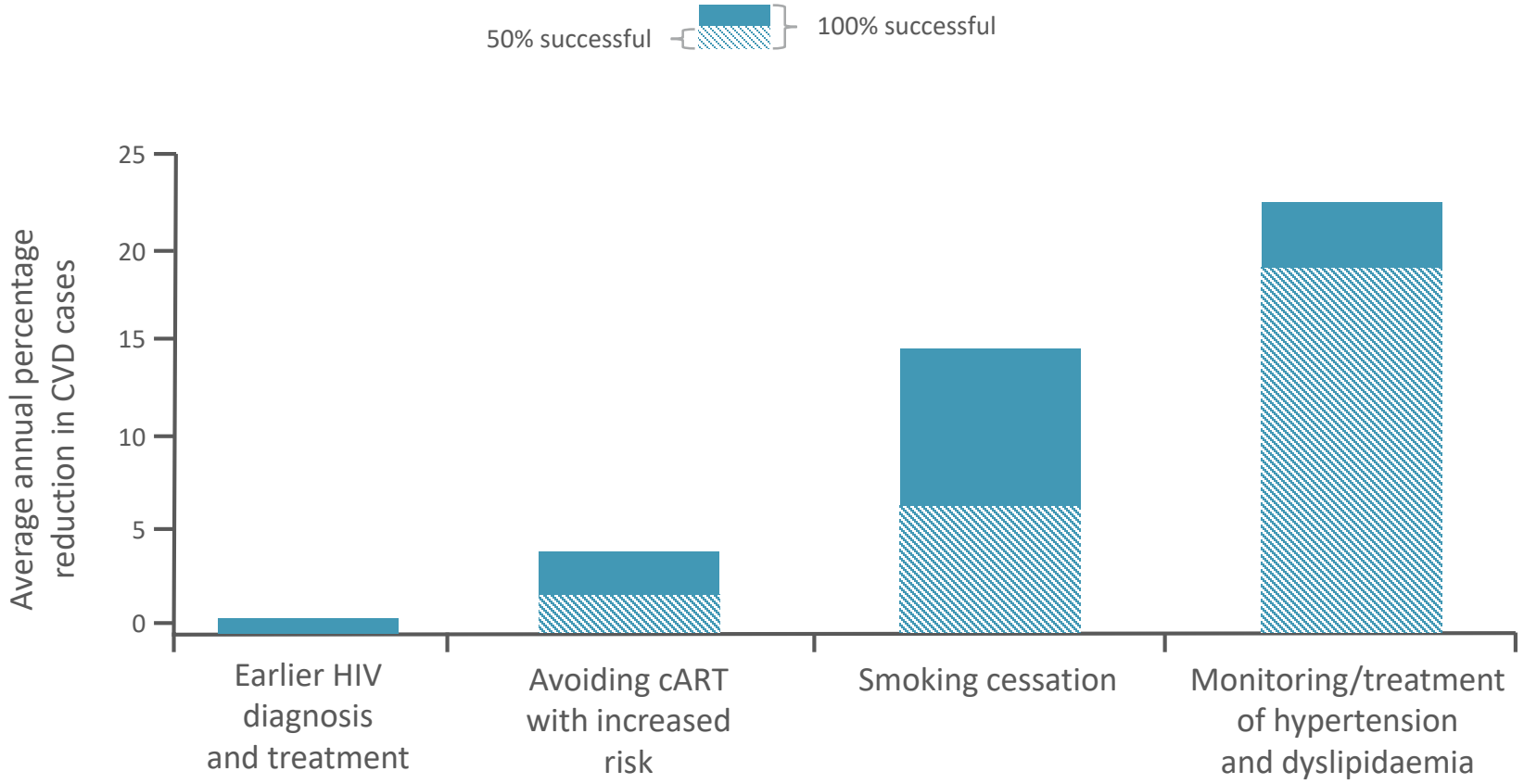


p<0.0001 for all comparisons (proportion of patients with each comorbidity, 2004 vs 2014)

1. Bonnet F et al. HIV Glasgow, 23–26 October 2016, Glasgow, UK. 2. Speaker's opinion

Modelling: Intervention and change in CVD/renal risk

- INTENSIFIED MONITORING AND DRUG TREATMENT OF HYPERTENSION AND DYSLIPIDAEMIA WILL PREVENT 17–20% OF CVD CASES ANNUALLY



cART, combination antiretroviral therapy
Adapted from: van Zoest R et al. CROI 2017; Abstract 129

DOI: 10.1111/hiv.12637
HIV Medicine (2018), 19, 5–23

ORIGINAL RESEARCH

HIV in practice: current approaches and challenges in the diagnosis, treatment and management of HIV infection in Australia

DE Smith,[1,2] LJ Woolley,[3,4] DB Russell,[5,6] F Bisshop[7] and V Furner[1]

- Development of comorbidities was the commonest reason for switching ARVs
- Managing comorbidities the second most commonly identified critical challenge facing PLWH in Australia

AIDS Res Ther. 2018 Mar 8;15(1):6. doi: 10.1186/s12981-018-0193-z.

Non-AIDS complexity amongst patients living with HIV in Sydney: risk factors and health outcomes

Derek J Chan [1 2], Virginia Furner [1], Don E Smith [3 4], Mithilesh Dronavalli [1], Rohan I Bopage [1 2], Jeffrey J Post [1 5 6], Anjali K Bhardwaj [7]

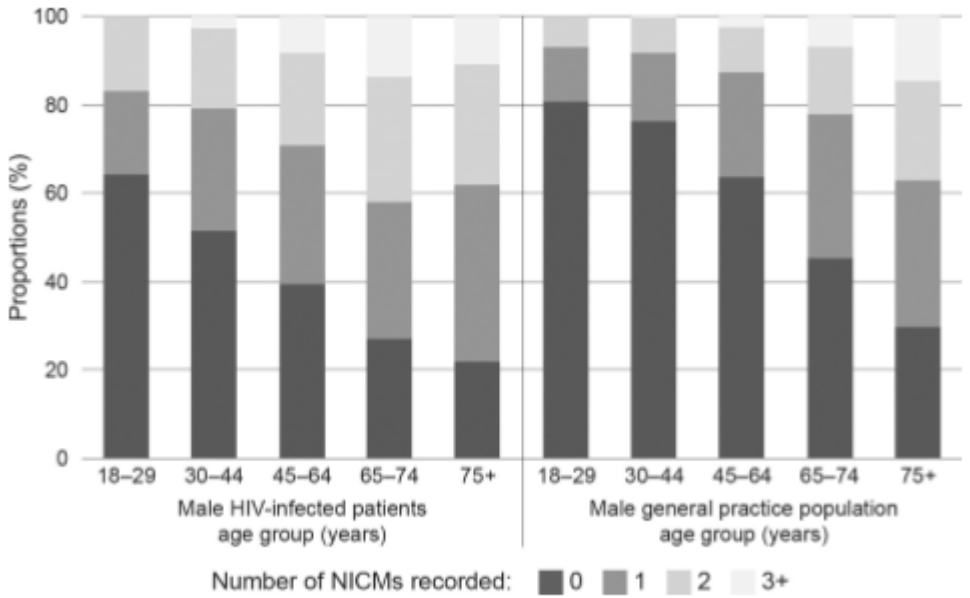
- At Albion Centre, publically funded HIV clinic in central Sydney
- 50% no GP
- 25% no Medicare
- CVD 25%, 20% diabetes
- 50% Hx cigarette smoking

RESEARCH ARTICLE

The prevalence and risk of non-infectious comorbidities in HIV-infected and non-HIV infected men attending general practice in Australia

Jack Edward Heron[1‡], Sarah M. Norman[2‡], Jeannie Yoo[2], Kirsty Lembke[2], Catherine C. O'Connor[3,4], Clare E. Weston[2*], David M. Gracey[1]

HIV+



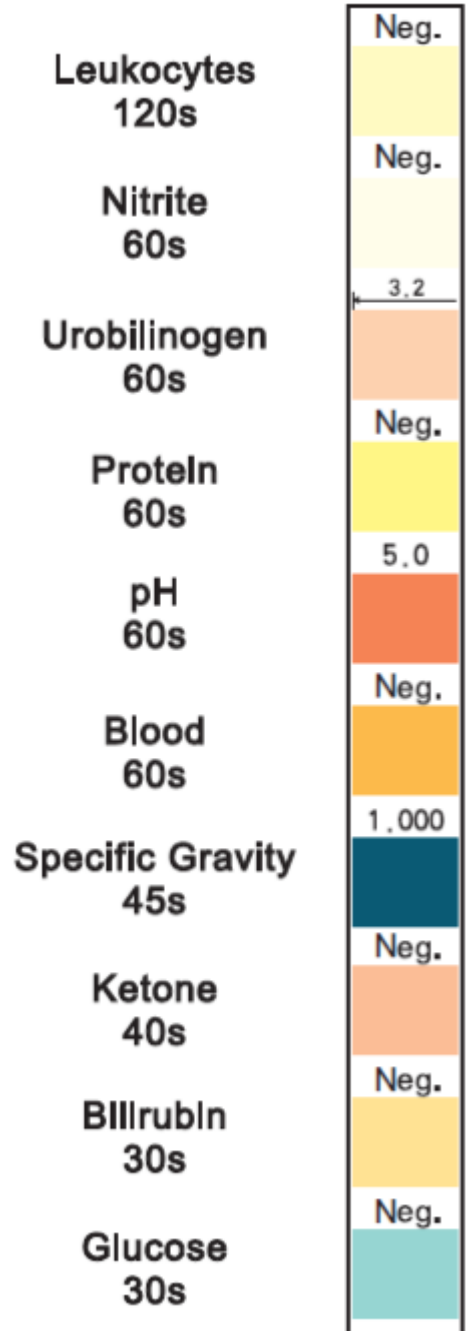
HIV-

Fig 2. Multiple NICMs recorded by HIV status and age group.

PLOS ONE

Measurement of proteinuria

- Dipstix urinalysis: detects albumin, not other proteins. Does not detect <300mg protein / day. Other inclusions can be useful
- uACR: detects urinary albumin down to a very low level. Recommended for screening for CKD
  - ‘albuminuria’ vs ‘proteinuria’
- uPCR: detects proteins other than albumin (can be useful with ‘tubular’ proteinuria and TDF)
- 24 hour urinary protein excretion: cumbersome, sometimes usef



Modifying renal risk – proteinuria

- Consider what is the cause? Need for further Ix (refer) ?
- Reducing blood pressure reduces amount of proteinuria
- Preferentially use anti-hypertensive agents with additional anti-proteinuric effects: ACE-inhibitors and ARBs
- Use cautiously in people with CKD (K+ and worsening of CKD)
- Be careful if on other medications which may increase K+ (aldactone, avoid NSAIDs)
- SGLT-2 inhibitors: effect in reducing proteinuria and improving renal survival is even greater than ACEi/ARB in selected patients
- Diet: not too high in protein

SGLT-2 inhibitors and diabetic CKD

Explosion of recent evidence – more and more publications every week

- For selected patients
- Reno-protective and cardio-protective
- Reduces proteinuria
- Benefit > ACEi
- Will result in glycosuria
- Can worsen renal function
  - Not in advanced CKD

Good for non diabetic CKD?

Slows progression

CLINICAL RESEARCH www.jasn.org

Canagliflozin Slows Progression of Renal Function Decline Independently of Glycemic Effects

The effect of SGLT-2 inhibitors on albuminuria and proteinuria in diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials

Alexia Piperidou[a], Pantelis Sarafidis[b], Afroditi Boutou[c], Costas Thomopoulos[d], Charalampos Loutradis[b], Maria Eleni Alexandrou[e], Apostolos Tsapas[f], and Asterios Karagiannis[a]

Modifying renal risk - Hypertension

- In the presence of CKD aim for BP<130/80
- Lifestyle factors important. Reduce salt diet. Weight loss.
- Start with ACEi/ARB, especially if proteinuria/diabetes
- Monitor creatinine and K+ - both may go up a little
- If diabetic not on ACE, but on something else ? switch
- Maximise dose of ARB/ACE first, but may need to add more than one agent; second line ?CCB ?β-blocker ?diuretic
- If resistant or difficult to control, refer.

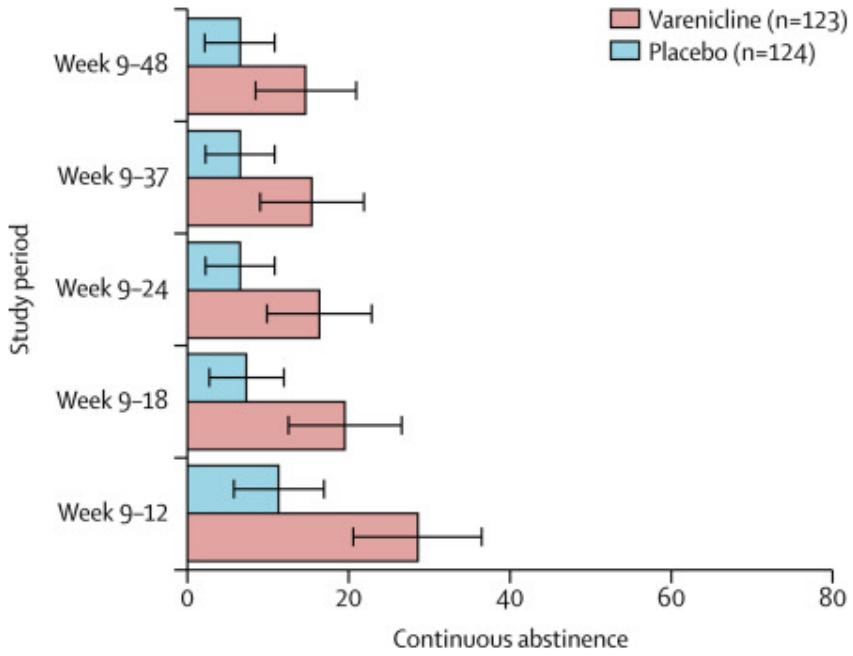
Modifying renal risk – Diabetes

- Lifestyle factors – diabetic diet. Note diabetics with CKD have a VERY restrictive diet. Often difficult to adhere to
- Aim HbA_1c <6%
- Caution with agents in CKD, including Metformin (GI sx and lactic acidosis) and SGLT2 inhibitors
- Start with oral agents; may need insulin
- If cannot achieve targets, refer
- Remember cardio- and reno-protection with SGLT2, but not a first line agent

Modifying renal risk – smoking

- The most common modifiable risk factor for CVD/CKD in PLWHIV worldwide
- Smoking history, vaping history important
- Previous attempts at quitting
- One of the most important motivators to stop smoking is persistent, repeated and systematic medical advice
- Quitline, smoking cessation aids, vaping.

Varenicline (champix)



- PLWHIV France 2018
- Effective at increasing abstinence rates, although still a high rate continued to smoke (18% vs. 7%)
- Few side effects

Mercie et al, Lancet HIV 2018-03-01

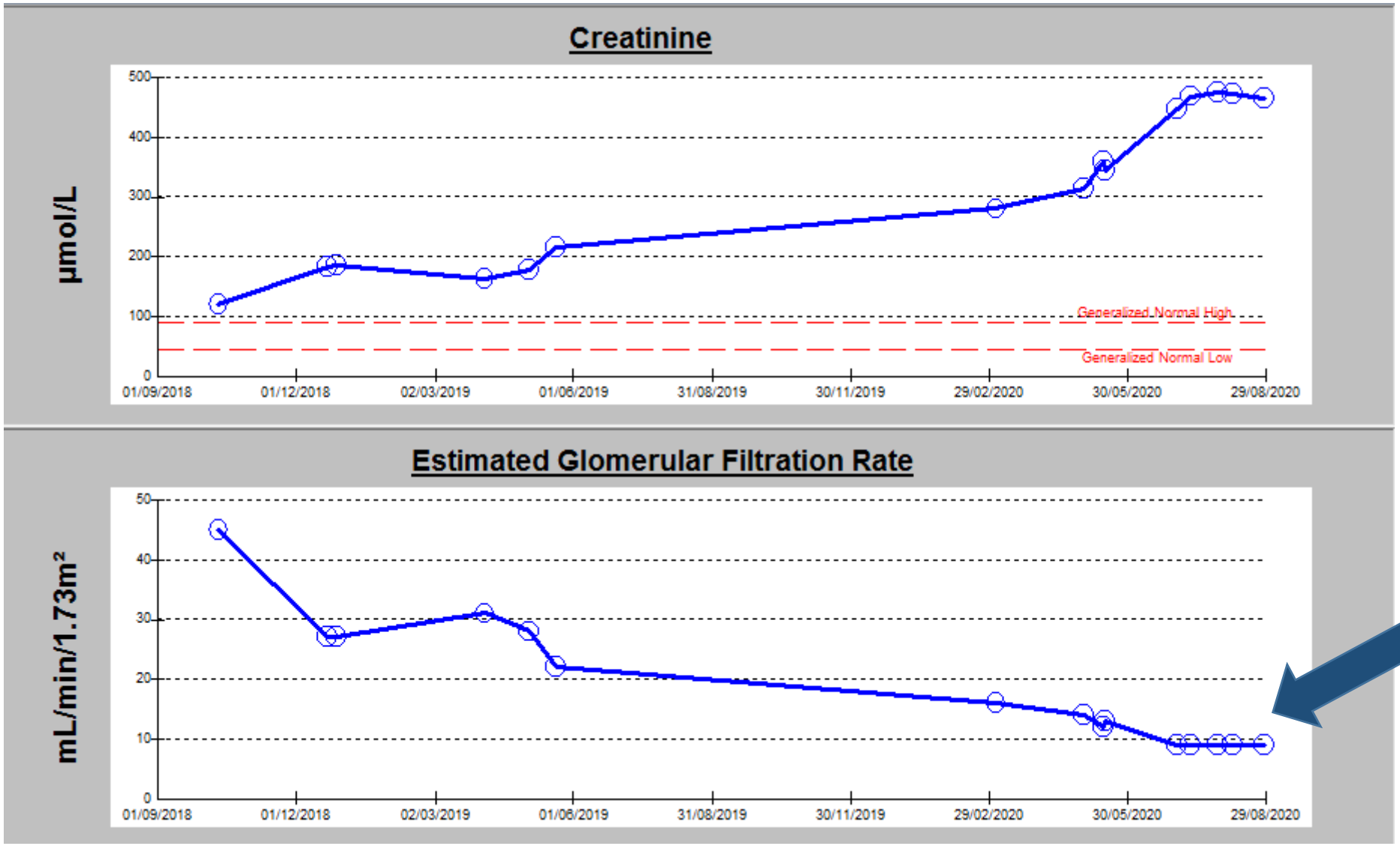
Modifying renal risk – Medications

- Consider medications in CKD, both nephrotoxicity and correct doses
- Nephrotoxic medications: stop NSAIDs, and specific advice to avoid them, including topical preparations.
- ART – esp. TDF
- Remember renal effects of COBI and Dolutegravir: changes eGFR not aGFR.

Case – progress

- Continued non-adherence
- Went back to the Philippines for 3 months to find her teenage son, missing in the jungle, no Rx
- Severe hypertension, viraemia
- Attempts at engagement not very successful
- Worried about other co-morbidities
- Unfortunately, continued deterioration in eGFR, about to start dialysis. ? Suitable for transplantation

A sad downwards spiral



Fistula and start dialysis, Sept 2020
? Tx suitability

Multiple comorbidities

- Addressing each can be time-consuming
- Need a comprehensive approach, often in conjunction with multiple specialists
- Interactions and poly-pharmacy
- Lifestyle factors just as important as medications, perhaps more so
- Danger of therapeutic nihilism
- “*my blood pressure is always better than that on my home machine*”

When to refer: CKD

- Complex patients at high risk of kidney disease, multiple comorbidities. Shared care, sometimes with cardiologists, diabetes centre, dietician etc.
- Difficult to control hypertension
- Unexplained haematuria
- Proteinuria >1g/day
- eGFR< 60 OR rapid loss of renal function (~10-20%p.a.)
- Advanced CKD eGFR< 30 or rapid loss of function – urgent
- AKI
- Concerns regarding ART/nephrotoxicity

Questions?