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D:A:D

A clinically useful risk-score for chronic kidney disease (CKD) in HIV infection

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BACKGROUND

Development of a simple, widely applicable risk-score for CKD would allow comparisons of the risks/benefits of starting potentially nephrotoxic antiretrovirals (ARVs).

MATERIALS AND METHODS

18055 HIV+ persons from the Data on Adverse Drugs (D:A:D) study with ≥3 eGFRs ≥1/1/2004 were included. Persons with use of TDF, ATV/r, ATV, LPV/r, and other bPI before baseline (first eGFR>60 ml/min/1.73m^2 after 1/1/2004) were excluded. CKD was defined as confirmed (>3 months apart) eGFR<60. Poisson regression was used to develop a score predicting low (≤0 points), medium (1-4 points) and high (≥5 points) risk of developing CKD. Increased incidence of CKD associated with starting ARVs was modelled by including ARVs as time-updated variables. The risk-score was externally validated on 2 independent cohorts.

RESULTS

- Characteristics of the included persons are shown in **Table 1**
- 641 persons developed CKD during 103278.5 PYFU (incidence 6.2/1000 PYFU, 95% CI 5.7–6.7)
- Older age, intravenous drug use, HCV+ antibody status, lower baseline eGFR, female gender, lower CD4 nadir, hypertension, diabetes and cardiovascular disease predicted CKD and were included in the risk-score (**Figure 1**)
- There was good discrimination between those at low, medium and high risk and incidence of CKD (**Figure 2**) with good discrimination
- The risk-score was externally validated on 2603 persons from the Royal Free Hospital clinic cohort (94 events, incidence 5.1/1000 PYFU; 95% CI 4.1–6.1) and 2013 persons from the control arms of SMART/ESPRIT (32 events, incidence 3.8/1000 PYFU; 95% CI 2.5–5.1). External validation showed consistent CKD rates across the low, medium and high risk groups (**Figure 2**).
- NNTH at 5 years in persons starting ATV or LPV/r was 1395, 142 and 20 respectively among those with low, medium or high risk of CKD. NNTH were 603, 61 and 9 for those with a low, medium or high risk of CKD starting TDF, ATV/r or bPI.

CONCLUSIONS

Traditional and HIV-related risk factors were predictive of CKD; all are routinely available, making the risk-score easy to incorporate into clinical practise and of direct relevance for clinical decision making. NNTH in persons starting potentially nephrotoxic ARVs at high risk of CKD were low, and alternative ARVs may be more appropriate

Table 1

Baseline characteristics of 18055 HIV+ persons from D:A:D

		Did not develop CKD		Developed CKD	
		N	%	N	%
All		17414	96.5	641	3.6
Gender	Male	12741	73.2	459	71.6
Race	White	8087	46.4	321	50.1
HIV Risk	Homosexual/IDU	8086/2015	46.4/11.6	264/86	41.2/13.4
Hypertension	Yes	1338	7.7	120	18.7
CVD	Yes	251	1.4	44	6.9
HCV +	Yes	2192	12.6	89	13.9
AIDS	Yes	2490	14.3	159	24.8
Diabetes	Yes	498	2.9	68	10.6
VL < 400	Yes	7552	43.4	398	62.1
		Median	IQR	Median	IQR
Age	Years	40	33 – 46	56	47 – 64
CD4	/mm^3	460	320 – 644	440	300 – 615
Nadir CD4	/mm^3	292	170 – 438	202	93 – 337
Baseline	mm/yy	6/05	5/04 – 2/07	1/05	5/04 – 1/06
eGFR	mL/min/1.73m^2	105	91 – 121	73	65 - 84

Baseline : first eGFR > 60 after latest of 1/1/2004 and enrolment to D:A:D. IQR; interquartile range.

Figure 1

D:A:D risk score for CKD and example of how to calculate the score

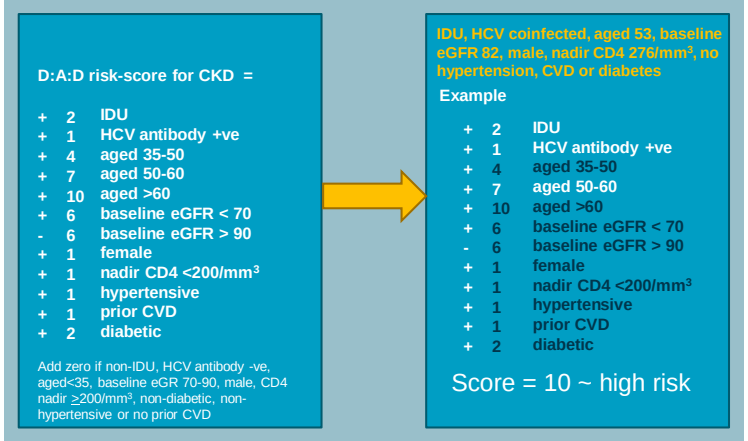


Figure 2

Validation of D:A:D renal risk score in 2 independent cohorts

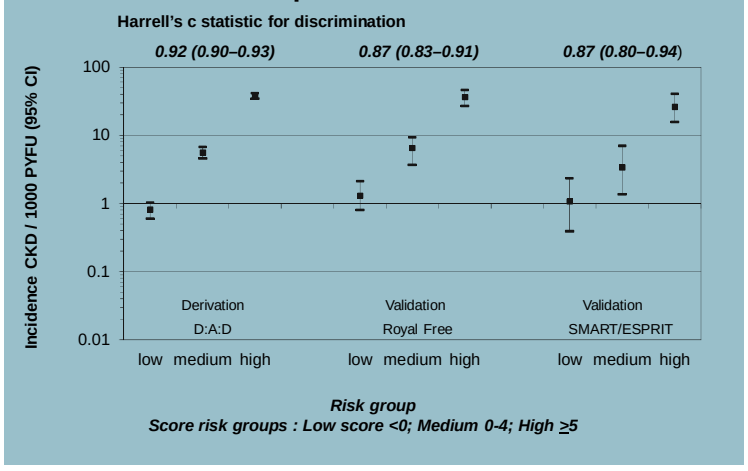
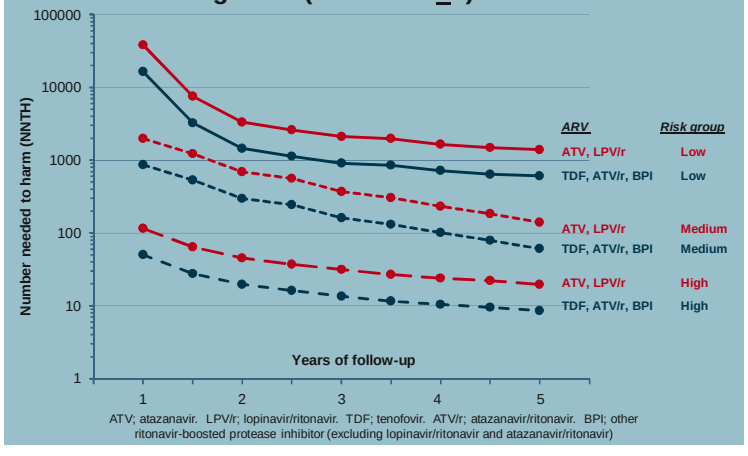


Figure 3

Number Needed To Harm (NNTH): Adding antiretrovirals to those at low (risk-score <0), medium (risk-score 0-4) or high risk (risk-score≥5) of CKD



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SMART/ESPRIT

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(1) Abrams D et al. N Engl J Med 2009;361:1548-59. (2) El-Sadr WM et al. N Engl J Med 2006;355:2283-96.