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VALIDATION OF THE D:A:D CHRONIC KIDNEY DISEASE (CKD) RISK SCORE IN A LARGE AFRICAN COHORT

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BACKGROUND

- Chronic Kidney Disease (CKD) is a frequent complication in people living with HIV (PLWHIV), particularly among those living in sub-Saharan African.
- As renal replacement therapy is often unavailable or unaffordable in this part of the world, prevention and early detection of CKD is therefore critical in these populations.
- A risk score for predicting CKD in people with HIV has been developed using data from the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study, but this score has not been validated in sub-Saharan Africa (1).

To assess the performance of the D:A:D risk score to predict CKD using data from a large cohort of people living with HIV in West Africa

METHODS

- Data source : The International Epidemiological Databases to Evaluate AIDS (IeDEA) West Africa Collaboration.
- Population : PLWHIV initiating antiretroviral treatment between 1996 and 2018 in four clinics in Burkina Faso (CHU S. SANOU), Côte d'Ivoire (CEPREF, CIRBA) and Togo (CHUSO).
- Participants included had ≥3 creatinine measurements, a follow-up in the cohort ≥3 months and a baseline estimated glomerular filtration rate (eGFR) >60 ml/min/1.73m².
- eGFR was calculated using the CKD-EPI equation.
- The D:A:D score (short version) was calculated using the coefficients of the four variables available in the database : age, gender, nadir CD4 and baseline eGFR (Table 1).
- The score was categorized in low (<0), medium (0-4) and high (≥5) risk groups as proposed by Mocroft *et al*. (1).
- Discrimination was assessed by the C-statistics and calibration parameters were expressed as ratio of observed / expected events.

References

(1) Mocroft A, Lundgren JD, Ross M, et al. Development and validation of a risk score for chronic kidney disease in HIV infection using prospective cohort data from the D:A:D study. *PLoS Med*. 2015;12(3):e1001809

RESULTS

Of the 27,739 individual files recorded in the four outpatient clinics databases, 15,528 (56%) met the eligibility criteria and were further analyzed.

Table 1. Baseline characteristics and D:A:D score coefficients

Baseline visit characteristics	D:A:D score	IeDEA West Africa Cohort		D:A:D Cohort	
no. participants		15,528		17,954	
First visit, year		2010	[2008;2012]	2005	[2004;2007]
On ART		10,752	69.2	8,117	45.2
Gender					
Male	0	4,554	29.3	13,130	73.1
Female	1	10,974	70.7	4,824	26.9
Age, year		38.1	[32.1;45.1]	40	[34;47]
≤35	0	5,692	36.7		
> 35 to ≤50	4	7,759	50.0		
>50 to ≤60	7	1,744	11.2		
>60	10	333	2.1		
DFGe (1)		104.2	[87.1;116.5]	104	[90;120]
>60 to ≤70	6	1075	6.9		
>70 to ≤90	0	3383	21.8		
>90	-6	11,070	71.3		
Nadir CD4 (2)		186.0	[90.0;290.0]	290	[169;434]
≤200	0	6,154	46.3		
>200	-1	7,133	53.7		
IDU	2	Not available		2,081	11.6
HCV infection	1	Not available		2,262	12.6

Values are n, % for categorical variables and median [interquartile range] for continuous variables
(1) min/ml/1.73m². (2) cells/µl. ART, Antiretroviral treatment; IDU, intravenous Drug Use; HCV, hepatitis C virus

Participants were followed for a median duration of 6 years in both IeDEA and D:A:D cohorts. CKD incidence ranged from 7.5 to 9.2 ‰ PYFU in the clinics and was higher in the IeDEA cohort than in the D:A:D cohort.

Table 2. CKD incidence and risk score distribution

	IeDEA West Africa Cohort		D:A:D Cohort	
Median follow-up duration, years [IQR]	6.0	[3.3;8.6]	6.1	
Median renal assessment frequency, per year [IQR]	1.9	[1.5;2.2]	3	[2;4]
Developed CKD, n %	692	4.5	641	3.6
Incidence of CKD, per 1000 PYFU [95% CI]	7.6	[7.0;8.1]	6.2	[5.7;6.7]
Median D:A:D Score [IQR]	-2	[-5 to 2]	-2	[-4 to 2]
Median D:A:D Score for those who developed CKD [IQR]	6	[1 to 11]	10	[5 to 13]

IQR, Interquartile Range; CKD, Chronic Kidney Disease; PYFU, Person-years of Follow-up; CI, Confidence Interval

Figure 1. Crude CKD incidence (A) and progression to CKD at 5 years (B) and 95% confidence interval by CKD risk groups

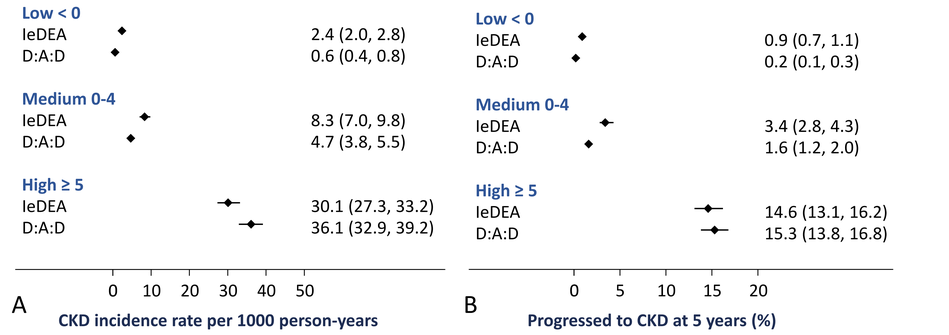


Table 3. Performances of the D:A:D score to predict CKD in the IeDEA cohort

Discrimination	Sensitivity	Specificity
Cut-off ≥ 0	78.5	59.0
Cut-off ≥ 5	67.4	85.5

Calibration (O/E)		
Low (score < 0)	2.46	[2.09-2.88]
Medium (score 0-4)	0.76	[0.60-0.95]
High (score ≥ 5)	0.42	[0.35-0.50]
Total	1.30	[1.21-1.40]

Calibration O/E : Observed/Expected CKD events

- CKD incidence increased markedly across the risk score groups. Among the 2,566 participants with a high score, the CKD incidence reached 30.1 ‰ PYFU.
- The discrimination of the model was good (C-statistics of 0.80; 95% CI : 0,79;0,82). With a cut-off at 0, 78.5% of people who progressed to CKD during their follow-up were identified at baseline (sensitivity) and 67.4% of people identified did progressed to CKD (specificity).
- Calibration was modest with overall underestimation of the risk. Addition of parameters like HCV coinfection and hypertension could improve the performances.

This study confirms the validity of the D:A:D score in identifying people at high risk of CKD who could benefit from prevention intervention in HIV outpatient clinics in West Africa

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