Reviewer’s report

**Title:** Development of a definition for Rapid Progression (RP) of renal function in HIV-positive persons: the D:A:D study

**Version:** 2  
**Date:** 15 December 2013

**Reviewer:** Markus Bickel

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To assess abnormally rapid deterioration in renal function (Rapid Progression, RP). The authors established two definitions:

**RP definition A:** An average eGFR decline (slope) >5ml/min/year over four years of follow-up with ≥ 3 eGFR measurements/year, last eGFR<90ml/min/1.73m² and an absolute decline >5ml/min/1.73m/year in two consecutive years.

**RP definition B:** An absolute annual decline >5ml/min/1.73m/year in each year and last eGFR<90ml/min/1.73m.

These definitions use a steeper eGFR slope (>5 vs >3ml) as reported in other studies, to possibly reduce variation of serum creatinine and thus reduce “background noise”.

These definitions were assessed using data from the Data Collection on Adverse events of Anti-HIV Drugs (D:A:D) study between 2004 and 2011.

The average rate of eGFR decline found for all HIV+ participants was -3.91 ml/min/1.73m/year which is much higher compared to data from the general population with 1 ml/min/1.73m/year.

Using definition A with follow-up periods of 2 and 3 years, 3.1 and 3.3% of participants fulfilled the criteria. Using definition B: 4.4% fulfilled the criteria within a 2 year follow-up, but only 0.8% and 0.4% with a 3 and 4 year follow-up.

Whilst most individuals have a stable renal function over time, some experience a rapid deterioration of the eGFR. These patients are important to be identified in order to assess potential risk factors, especially those associated with the use of individual HIV drugs.

Especially because such patients, namely those with additional known risk factors for renal insufficiency (black race, IVDU, hepatitis B or C co-infected, diabetics…), are usually excluded from prospective studies, cohort studies will remain the mainstay for such investigations. This is further complicated by the fact, that as soon as the eGFR decreases, but still remains within a clinically acceptable range, most physicians will replace HIV drugs with a known nephrotoxicity. This limitation was earlier demonstrated by the same study group and for this reason various eGFR cut-offs were used in order to evaluate differences. Thus using a validated definition of an eGFR slope seems plausible and could guide future studies.

The main problem I could anticipate that, if the authors agree with my thoughts,
that this does not become clear in the background of the paper or the abstract. I am sorry that it took my so long to review the paper, but this is exactly why. I had to read it several times and kept asking me what this study might be good for. Moreover the work should be shortened by at least 30 % in order to reach more readers. The length strongly reminds me of discharge letters from nephrologists’.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests