Reviewer’s report

Title: A Prognostic Model for Estimating the Time to Virologic Failure in HIV-1 Infected Patients Undergoing a New Combination Antiretroviral Therapy Regimen

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Reviewer: Fatima Laher

Reviewer’s report:

This work, which compares RSF to Cox multivariate regression analysis in the application of the prediction of time to virologic failure in antiretroviral therapy, is lucid and has intriguing implications.

In particular, the study title and aims are clear, the design was thoughtfully constructed, the chosen variables were clinically appropriate and consistent with current understanding of important factors in virologic science, and the manuscript was sufficiently explanatory. The application of a machine learning technique to the field of HIV Medicine is innovative. It is interesting to note that the findings of both models are corroborated by data from randomised clinical trials about factors associated with virologic failure.

MINOR ESSENTIAL REVISIONS NOT FOR PUBLICATION

In minor comments, there are suggestions to improve readability: grammatical corrections and sometimes a request for greater summarisation.

Publication of this manuscript is recommended after comments are addressed.

Minor:

1. "Combination antiretroviral therapy (cART) nowadays is able to push down the plasma viral load to undetectable levels in a large proportion of HIV-1 infected patients."

Suggest:

Modern combination antiretroviral therapy (cART) can suppress plasma viral load to undetectable levels in a large proportion of HIV-1 infected patients.

2. "Indeed, the risk for a patient to experience a virologic failure has been decreasing consistently during the last decade in high-income countries [1, 2, 3, 4, 5]."

Suggest:
Indeed, the risk for a patient to experience virologic failure has been decreasing consistently during the last decade in high-income countries [1, 2, 3, 4, 5].

3. "Part of this outstanding success is due to the increased ability of physicians in designing the best cART regimens depending on the patients' background, and in prompt managing treatment failure. In this context, the availability of more potent and tolerable drugs, with the increased range of molecular targets has greatly increased the rate of virologic success."

Suggest:

Part of this outstanding rate of virologic success may be due to the increasing availability of more potent and tolerable antiretroviral drugs targeting a wider range of molecular targets; this provides physicians the opportunity to tailor cART regimens according to patient background, and to manage treatment failure promptly.

4. "The concomitant understanding of mechanisms of drug resistance emergence allows to optimize treatment regimens based on the patient's virus genotype."

Suggest:

Additionally, better understanding of the mechanisms of drug resistance allows optimization of treatment regimens based on an individual's HIV genotype.

5. "Although the virus cannot be eradicated [6], the prevalence of drug resistance seems to be decreasing during more recent calendar years [7]."

These two ideas are not well linked. Suggest remove the phrase leading up to reference 6 and summarise the rest of the paragraph as follows:

Although the prevalence of drug resistance seems to be decreasing in recent years [7], and despite modern cART options [9], drug resistance remains a concern in chronically infected patients with a long treatment history, and in treatment-naïve patients who have been infected with drug resistant isolates [8].

6. "A model that is able to predict how long a cART will last would be a substantial improvement over the actual state-of-the-art tools for patient tailoring cART, which are currently limited to fixed time point outcomes."

Suggest:
A model that could predict an individual's duration of success with a cART regimen would provide valuable information in tailoring cART regimen choice.

7. "Further selection criteria were a cART duration non-inferior to 90 days"

Suggest:
Further selection criteria were a cART duration more than 90 days

8. "changes of one or more drugs associable to tolerability/adherence issues."

Suggest
changes of one or more drugs associated with tolerability/adherence issues.

Discussion:

9. "Low GSSs of cART, a less recent calendar year, administration of 2NRTI+1NNRTI, as compared to 2NRTI+1PI/r, older age, higher HIV-1 RNA, lower CD4+ counts, and previous drug class exposure were independently associated with an increased hazard of virologic failure."

Suggest:
In contrast to 2NRTI+1PI/r, older age, higher HIV-1 RNA, and lower CD4+ counts, an increased hazard of virologic failure was associated with low GSSs of cART, a less recent calendar year, administration of 2NRTI+1NNRTI and previous drug class exposure.

10. "HIV-1 RNA and GSS remained associated with the endpoint also when considering treatment-naïve patients in a sensitivity analysis."

Suggest:
HIV-1 RNA and GSS remained associated with the endpoint when considering only treatment-naïve patients in a sensitivity analysis.

11. "Such an expert system could provide a more clinically oriented treatment decision tool and help building patient tailored regimens."

Suggest:
Such a system could build a more clinically-oriented treatment decision tool and help tailor patient regimens.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I declare that I have no competing interests.