

Addressing adherence improves the accuracy of neural networks' predictions of virological treatment response

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Introduction

- Artificial Neural Networks (ANN) trained using genotype, viral load (VL) and drug treatment data, can successfully predict virological response to combination therapy
- Data from non-adherent patients used in training may reduce the accuracy of the ANN, for example causing them to incorrectly predict virological failure despite a 'benign' genotypic context
- This study was designed to address whether censoring training data for adherence improves the predictive accuracy of ANN.

Methods

- Treatment adherence (%) was estimated using prescription refill data from the BC Centre for Excellence in HIV/AIDS
- Two sets of 623 treatment change episodes (TCEs) were identified with < or ≥90% adherence respectively, for ANN training
- High and low adherence 'committees' of 10 ANN models each were trained using genotype, baseline VL, drugs in new regimen and time to follow-up as input variables, and follow-up VL as the output variable
- 50 TCEs from a separate clinic (NIAID) were used as an independent test set: the ANN models were given the input variables of the test TCEs and predicted the VL response (Δ VL)
- The models' performance was assessed in terms of the 'committee average' (the average prediction of Δ VL of all 10 models for each test TCE)
- These prediction were compared to the actual follow-up viral loads from the test TCEs in terms of:
 - Correlations (Pearson's Product-Moment) between the ANN models' predictions and the actual Δ VL values
 - The mean absolute difference between the models' predictions and the Δ VL
 - The percentage of the models' predictions that had the correct trajectory, positive or negative.

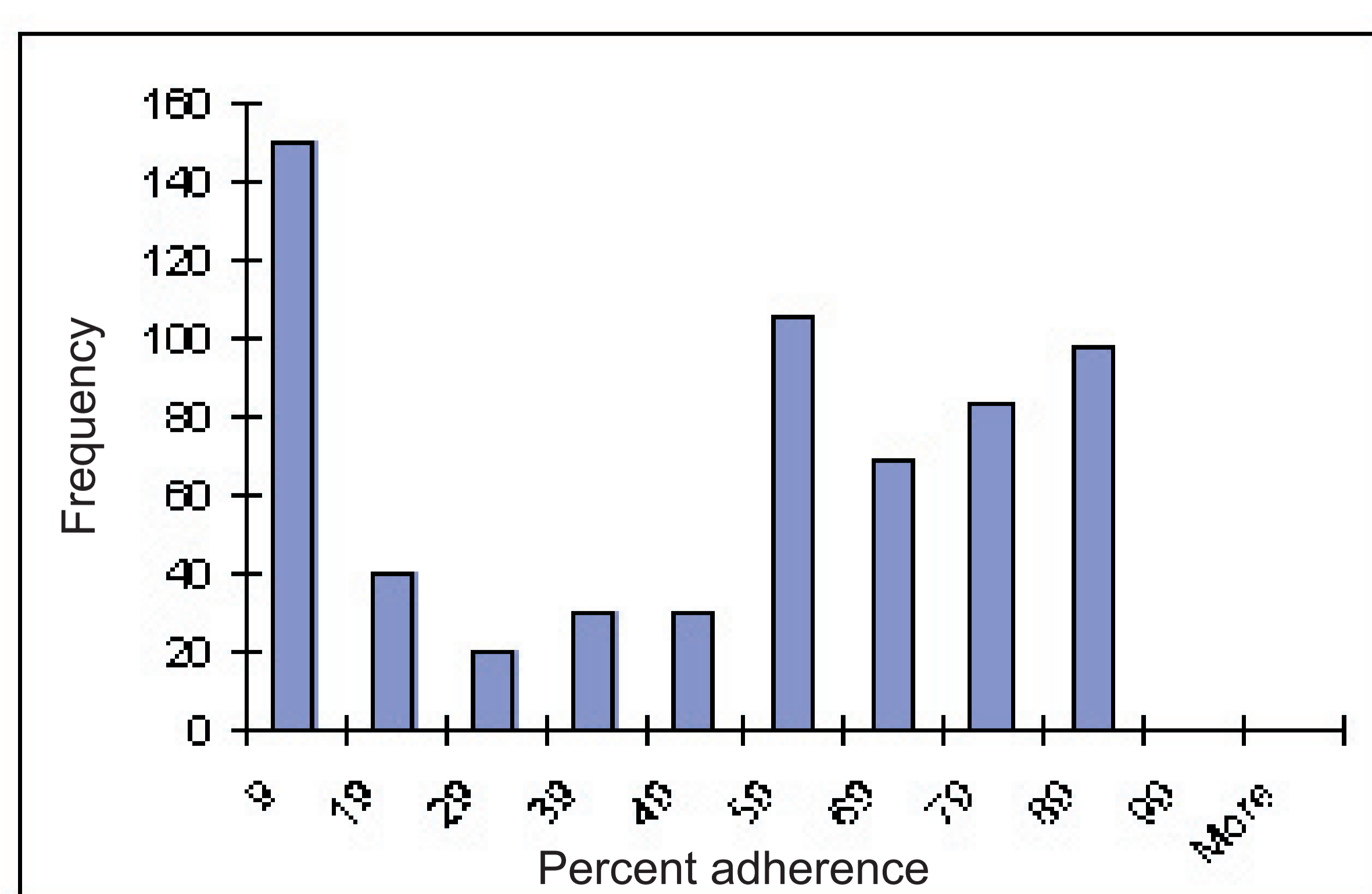
NB a detailed description of the methodology by which ANN committees are developed is presented in Poster WePe12.6CO4.

Results

Baseline characteristics

- Adherence in the low adherence group ranged from 0 to 89% (Figure 1)
- The distribution suggested two distinct populations: non-adherers and partial adherers, with most of the latter achieving adherence levels of more than 50%

Figure 1: distribution of adherence (low adherence group)

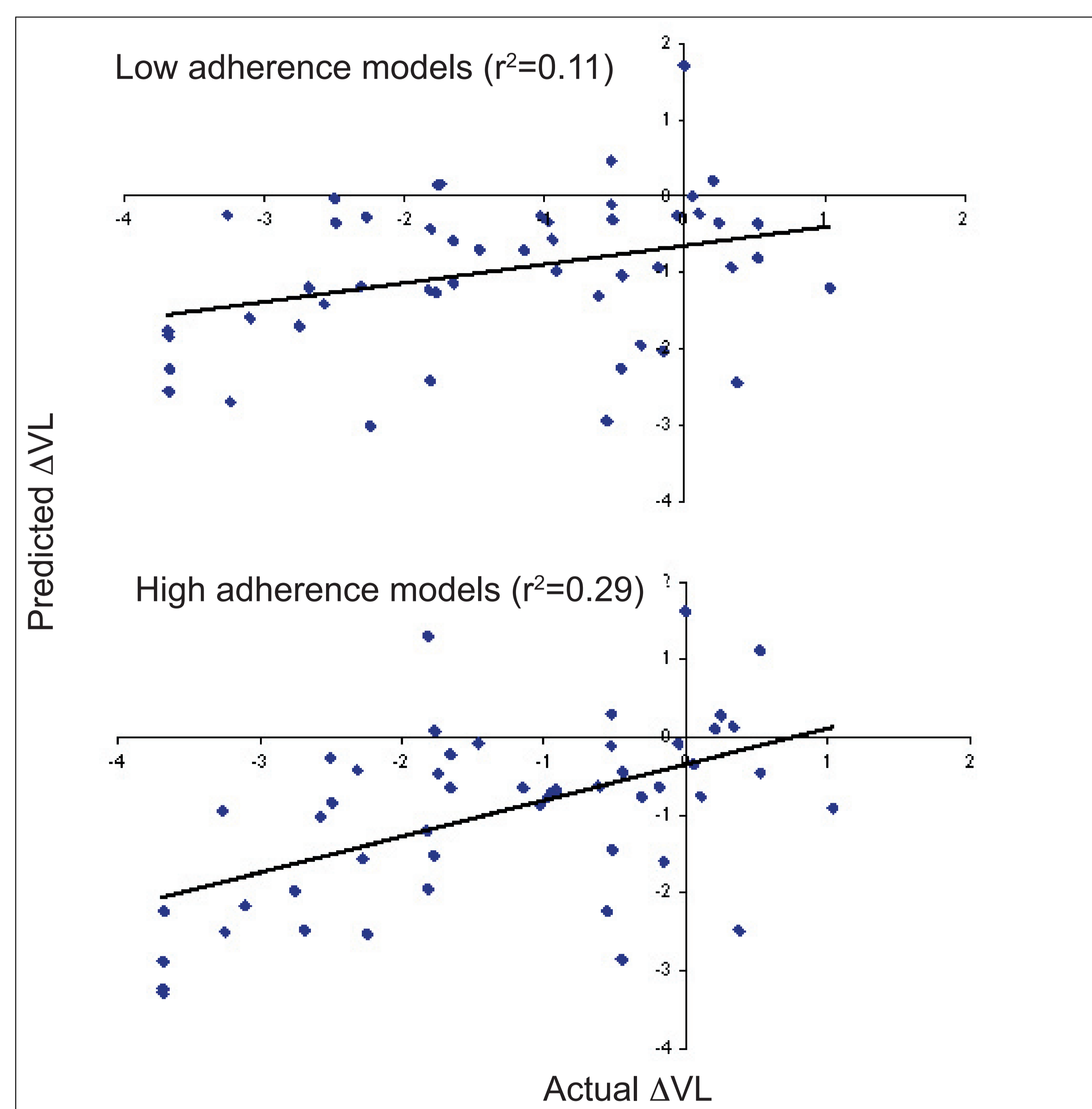


- In general the low adherence group had lower viral loads (4.02 vs 4.49, $p < 0.001$) and fewer RT mutations (2.24 vs 4.54, $p < 0.001$) and PI mutations (2.47 vs 3.50, $p < 0.001$) at baseline than the high adherence group.

Results of ANN modelling

- Correlations between predicted and actual Δ VL for the low and high adherence committees gave r^2 values of 0.11 ($p < 0.05$) and 0.29 ($p < 0.0001$) respectively (Figure 2)
- The difference in this measure of accuracy between low and high adherence models was statistically significant ($p < 0.01$)
- The mean absolute difference between predicted and actual Δ VL (\log_{10} copies/ml) was 1.16 for the low adherence and 0.94 for the high adherence models ($p < 0.01$)
- The percentage of correct VL trajectory predictions was 78% for the low adherence and 84% for the high adherence models (ns).

Figure 2: Scatterplots of predicted vs actual Δ VL for ANN models



Discussion

- ANN models trained using data from highly adherent patients were significantly more accurate in their predictions of virological response to combination therapy than those trained with data from less adherent patients**
- The low adherence group covered a wide range of adherence (ie: non-adherent and partially adherent)
- The presence of patients with adherence over 50% in the low adherence group may have contributed to the accuracy of the low adherence models, reducing the superiority of the high adherence models
- Further study is required to identify an appropriate adherence cut-off for inclusion of patients in ANN training sets**
- The performance of the high adherence models was encouraging given the small training sets and rigorous test.**

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