

Mixed Effect Modelling in HIV-HCV Co-infected Children



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Introduction

HCV infection is a leading cause of morbidity in HIV infected patients. Worldwide, about 190million people are infected with chronic hepatitis C virus (HCV). Adult HCV-coinfected patients have been reported to have worse treatment outcomes[2]. However, very little is known in children who are also at increased risk of developing long term complications. As a result, there is presently no consensus amongst clinicians regarding management of HCV coinfecting children across Europe. A recent study containing 70 children revealed that the prognosis of liver disease is much more aggressive in children infected with HCV and HIV[3].

Aim

In this project, I investigate the effect of HCV infection on long term immune reconstitution of CD4 T cells in HIV infected children across Europe who are on anti-retroviral therapy (ART).

Materials/Methods

In a recent model developed by Lewis et al[1], it was shown that immune reconstitution in children commenced on antiretroviral therapy followed an asymptotic recovery in the first 5 yrs ($z_{ij} = asy_i - (asy_i - int_i)e^{-C \cdot t} + \epsilon_{ij}$)[1]. However, a linear mixed effects model provided a better fit for this new data and therefore was chosen over the asymptotic model. The data analysed was a retrospective observational data collected from 8 European paediatric HIV cohorts included in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC). The children were aged btw 18 months and 25yrs and had acquired HIV/HCV infection maternally or in childhood. Analysis was done using the principles of mixed effect modelling in R (nlme).

Figures

Fig. 1 Linear mixed effects model with Ukraine cohort only

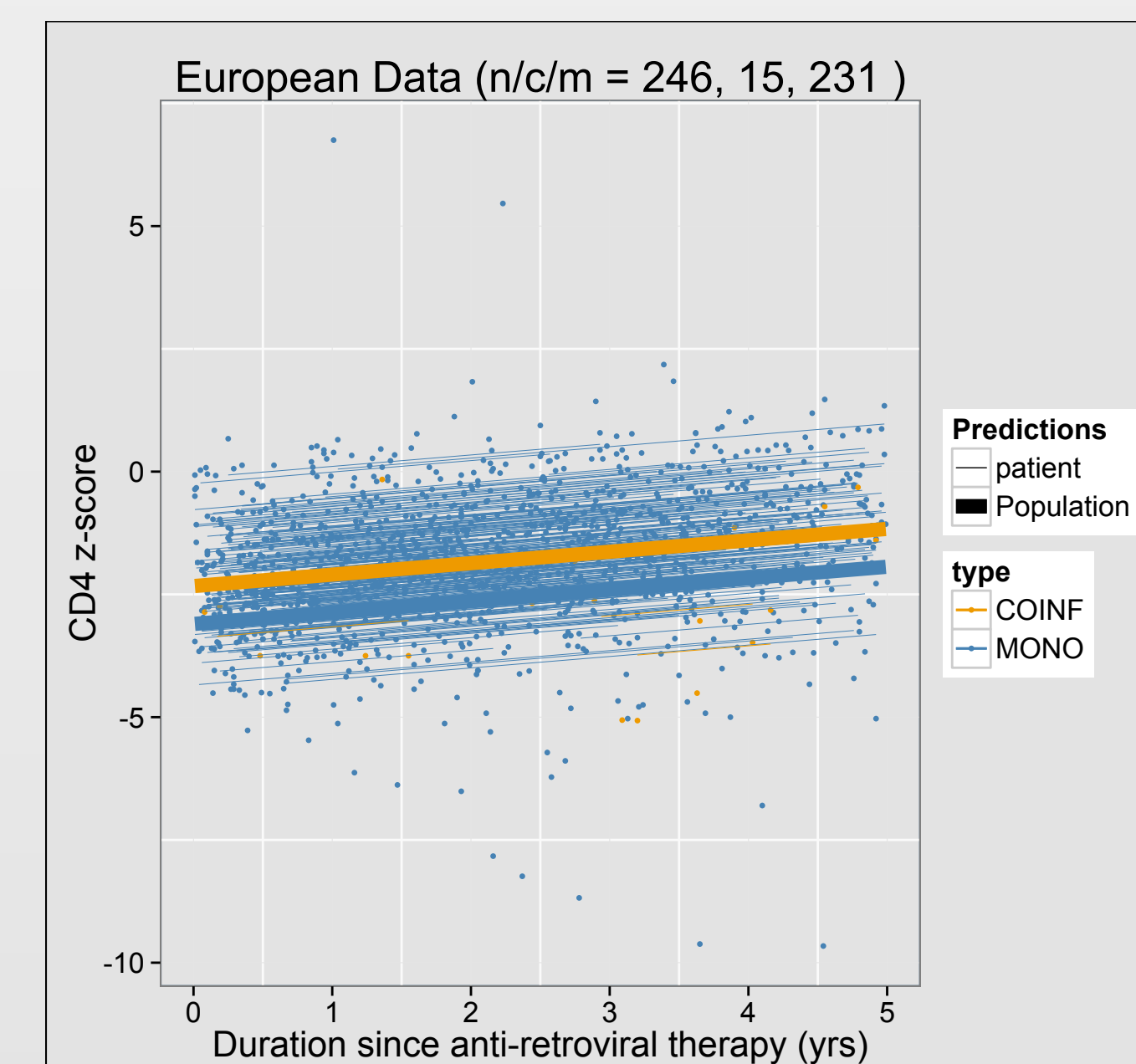


Fig. 2 –Linear mixed effects model with entire European data

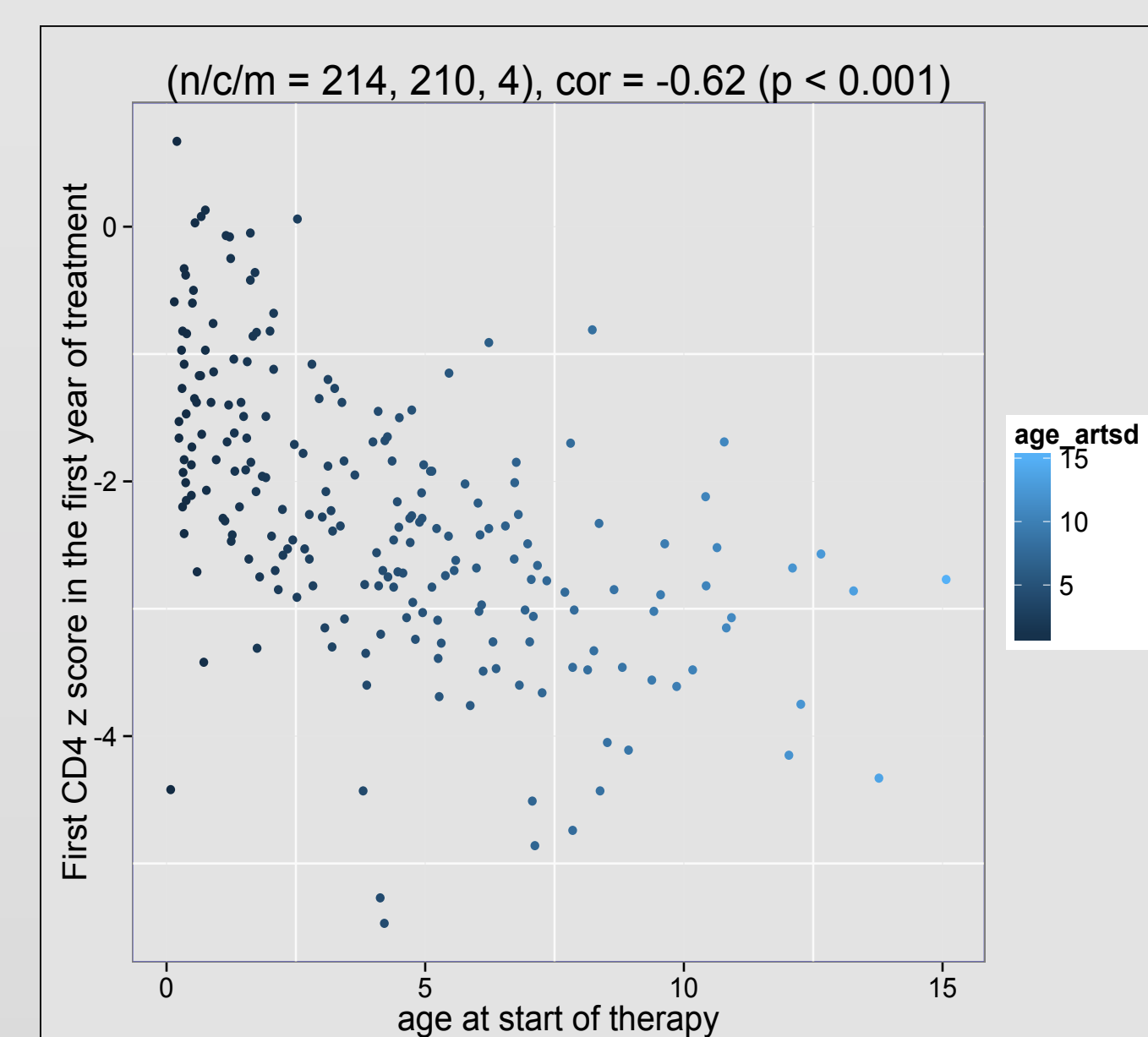
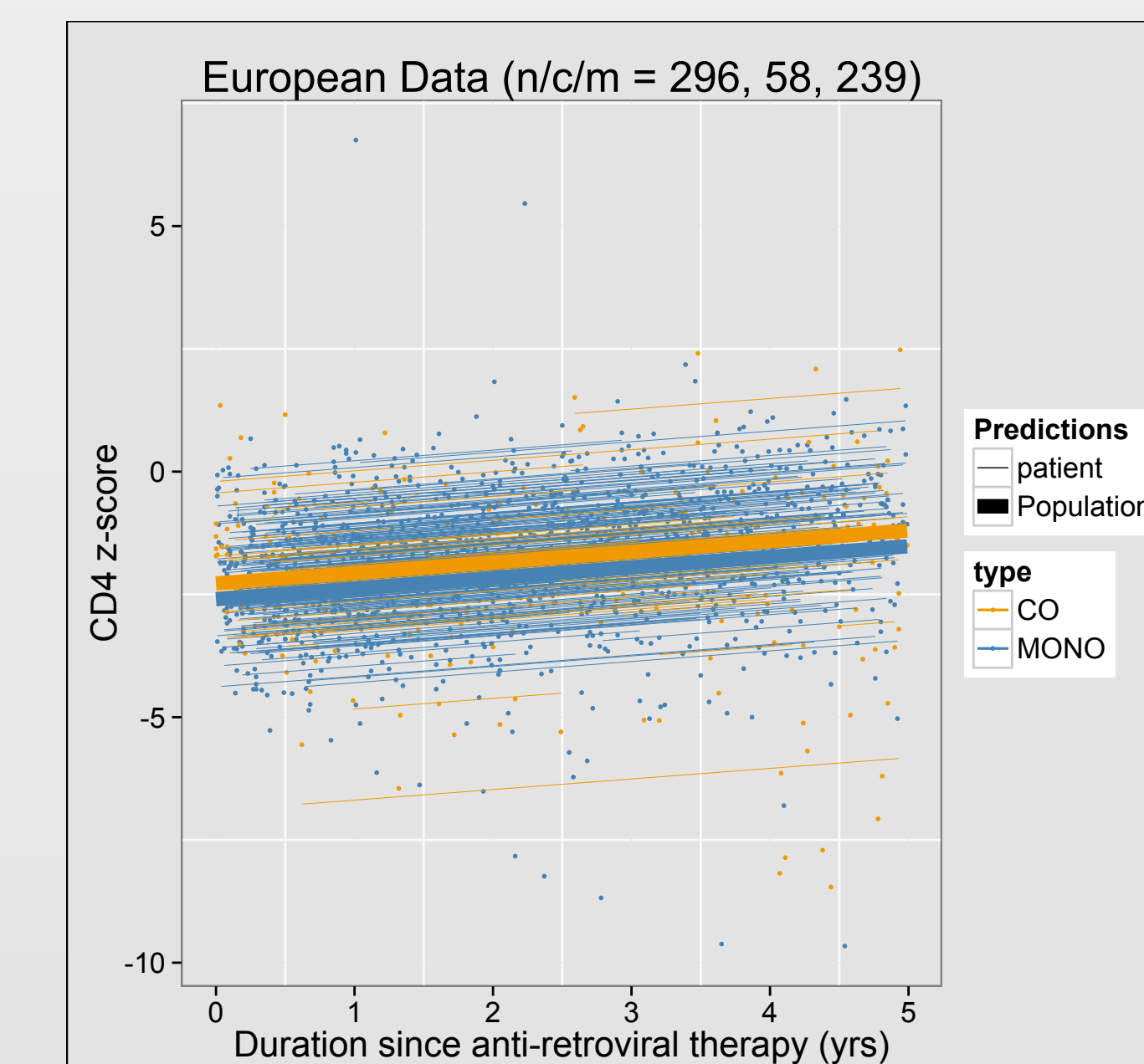


Fig. 3 above shows that younger children have higher cd4 z-score compared to older children.

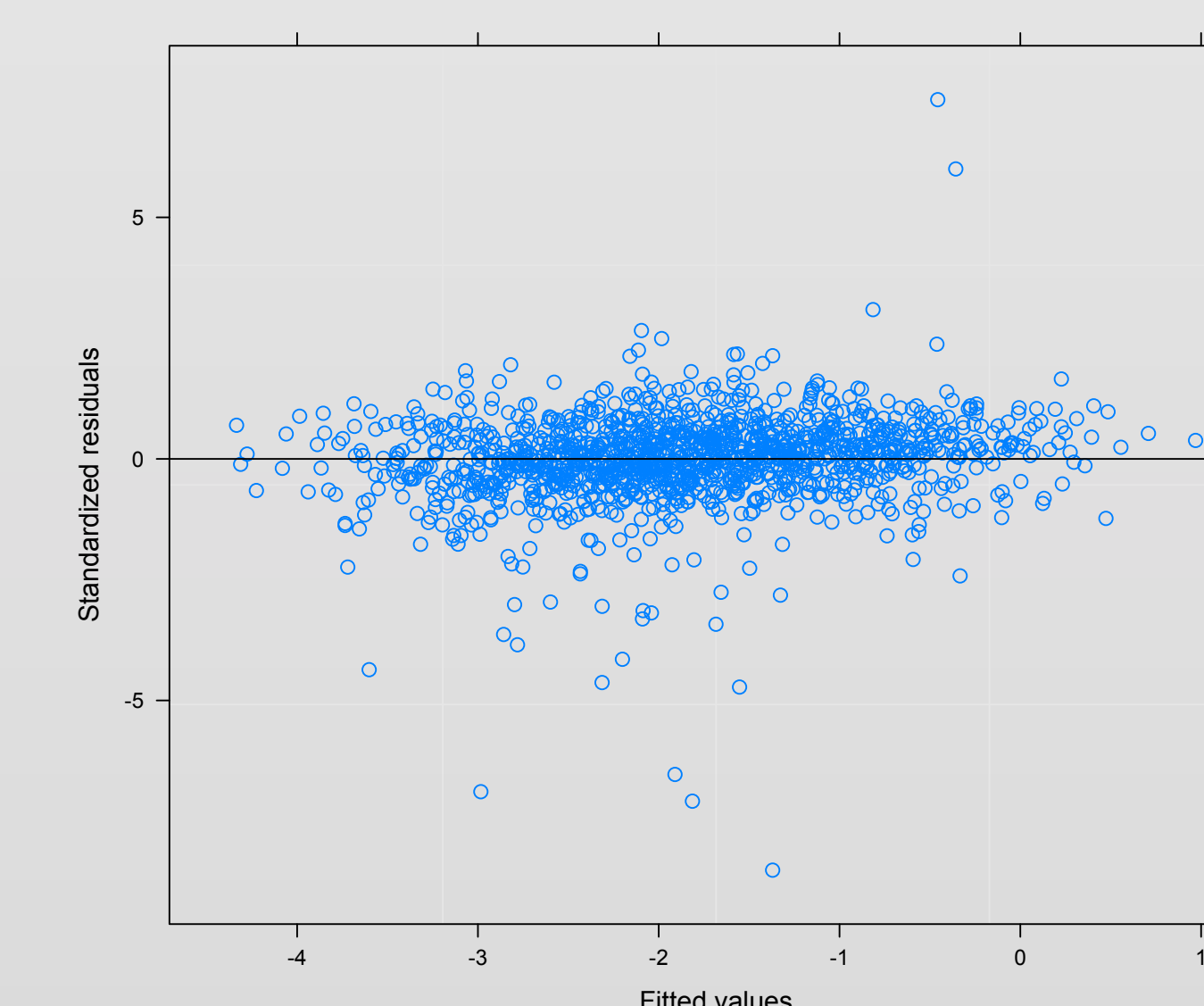


Fig. 4 Residual plot of the linear model for the Ukraine cohort.

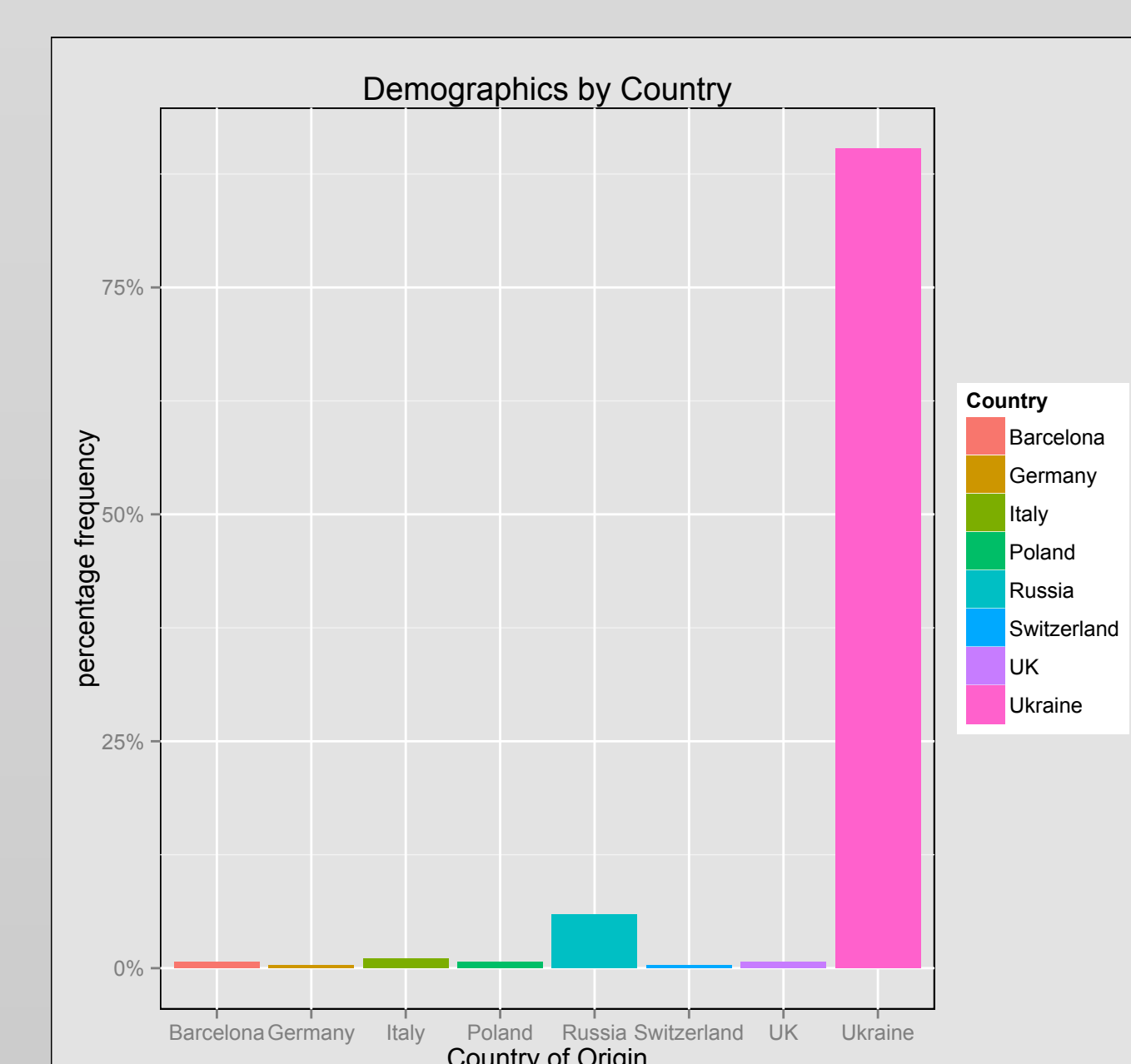


Fig. 5 shows the dominance of Ukrainian children in this data.

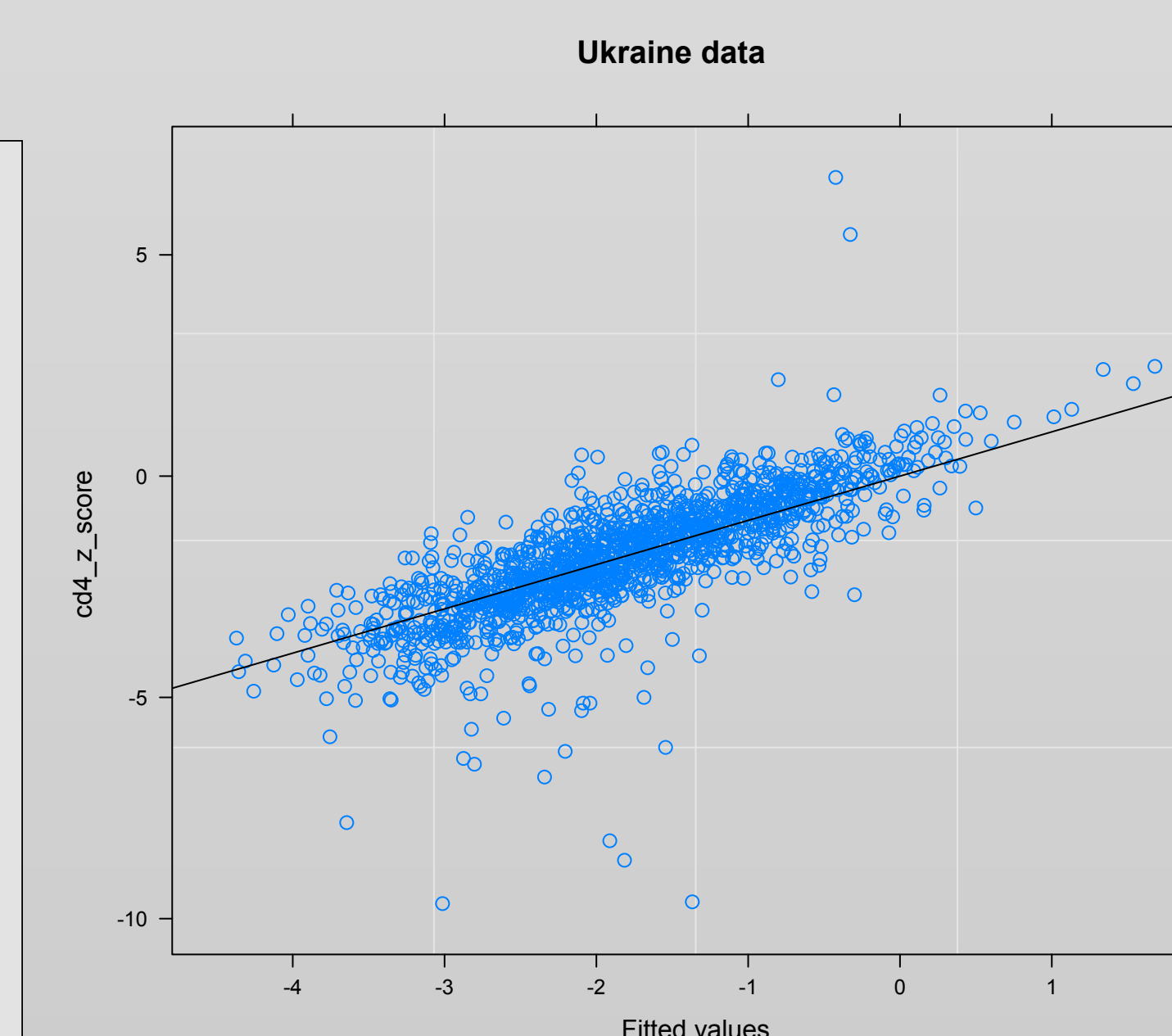


Fig. 6 This shows a strongly positive correlation between the predicted and actual cd4 z-scores for the linear model (cor 0.83, p-value < 0.001).

Results

Coinfected children appear to have higher cd4 z-scores throughout the first 5 yrs of treatment. However, this was only statistically significant in the Ukraine cohort (Fig. 1 $p < 0.001$). Covariate analysis revealed that **age at start of antiretroviral therapy and HCV status both had significant interaction** with the initial cd4 z-score (intercept) of the model ($p < 0.001$, 0.022). **Age at start of antiretroviral therapy also had a significant impact on the rate of increase of cd4 z score over a 5 yr period** ($p = 0.0016$). Older children have lower cd4 z-scores compared to their younger counterparts (Fig. 3).

Conclusions

Coinfected children from Ukraine appear to have a significantly higher cd4 z-score at start of ART. **This is an unexpected finding when compared with coinfecting adults who are known to have lower cd4 recovery profiles[2].** A possible explanation for this could be additional homeostatic mechanisms in repopulating T cells in children. However, larger studies are needed to fully characterize immune profiles of these patients.

Future Work/Acknowledgement

To investigate homeostatic mechanisms responsible for immune reconstitution in HIV coinfecting children using mechanistic models.

Acknowledgement

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References

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2. Van Griensven et al- Hepatitis B/C Co-infection among HIV-infected Adults while on Antiretroviral Treatment: Long-Term Survival, *PLOS One*, Vol. 9, Feb 2014.
3. Claret-Teruel et al- Impact of HIV coinfection on the progression of mother- to-child transmitted HCV infection. *Paed. Infect. Dis. Journal*. Vol. 30, 2011.

