

Appendix I: Supplementary information on time series analysis and data simulation

ARIMA model selection

To allow for empirically based simulation of data, the autocorrelation structure of the outcomes in the Nijmegen early RA cohort was inspected. To this end, residual fluctuation in the PROM-score over time was assessed in 29 patients with 30 months of stable DMARD and/or biologic therapy and at least 10 assessments.

As a first step, sequence charts, autocorrelation function (ACF) charts and partial autocorrelation function (PACF) charts for individual patients were inspected to assess stationarity of the data. Figure A1 illustrates how the PROM-scores fluctuate around a stationary mean.

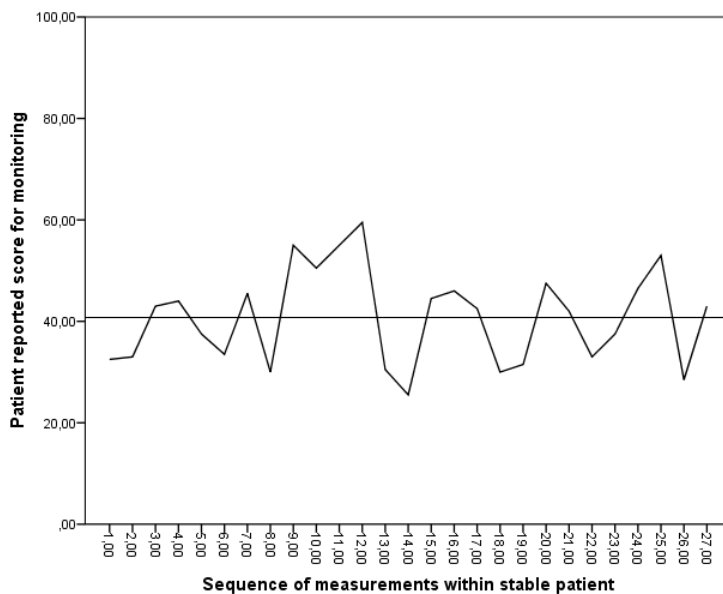


Figure A1 Example of one patient's sequence chart

The second step involved inspection of each patient's ACF and PACF charts, to choose the best fitting ARIMA model.[1] Over all patients ACF values showed a general tendency to decline gradually (Figure A2).

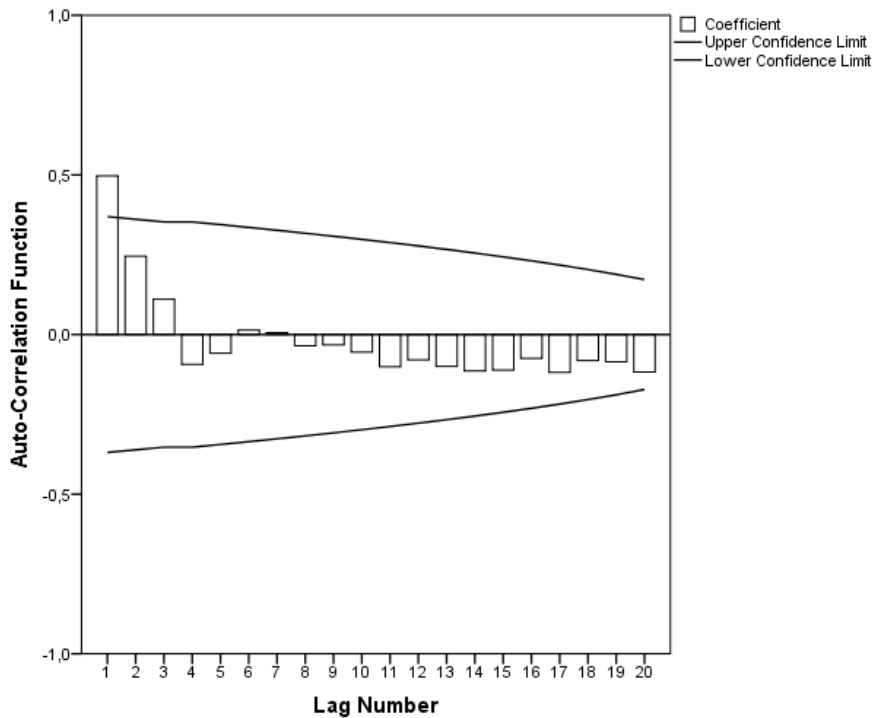


Figure A2 Example of one patient's autocorrelation function plot

This was contrasted by a steep decline after the first lag for PACF values (Figure A3). In correspondence with these findings an autoregressive first order (1,0,0) ARIMA model, best suited the data at hand and was selected to generate residual variance for imputed weekly data.[1]

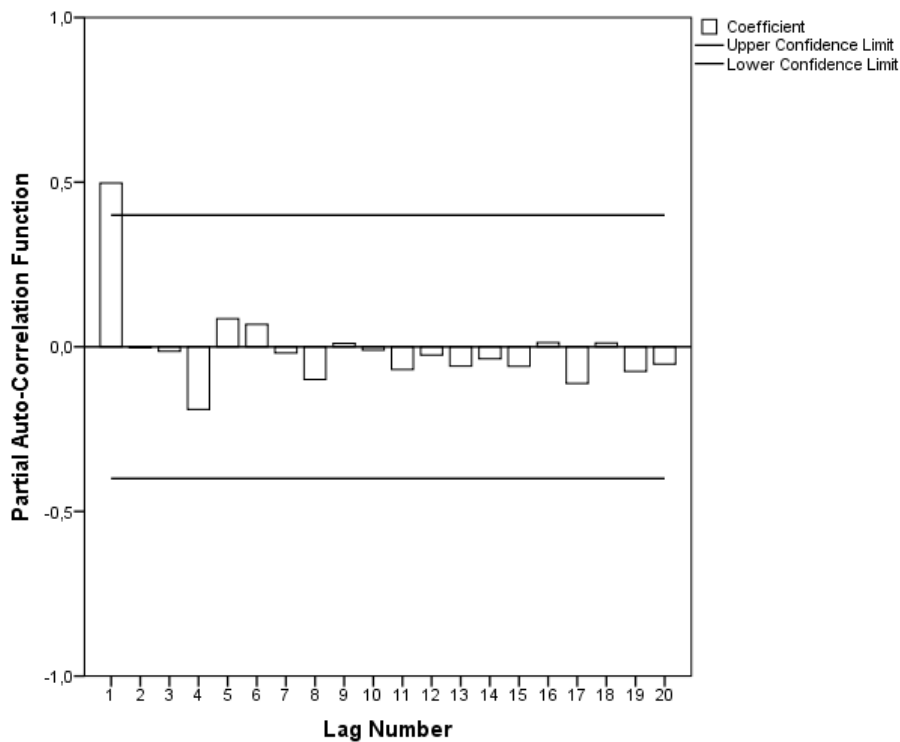


Figure A3 Example of one patient's partial autocorrelation function plot.

Advanced data interpolation

The idea behind more advanced interpolation is that observed scores are compiled of “true” scores and error variance (Figure A4). To interpolate weekly measures, residual variance determined in the patients stable on medication was subtracted from registered PROM-score to obtain “true” PROM-scores. These values were then linearly interpolated. To then obtain weekly simulated scores that could be have been observed in real life, random error variance had to be added to the linearly interpolated scores. This was done by taking the linearly interpolated score and adding residual variance by randomly drawing from a standard normal distribution with a mean of 0 and a standard deviation of $\sqrt{(1 - \text{weekly autocorrelation}^2)}$ and multiplying this times the Standard Deviation of PROM-scores of stable patients at each time point (approximately 12).

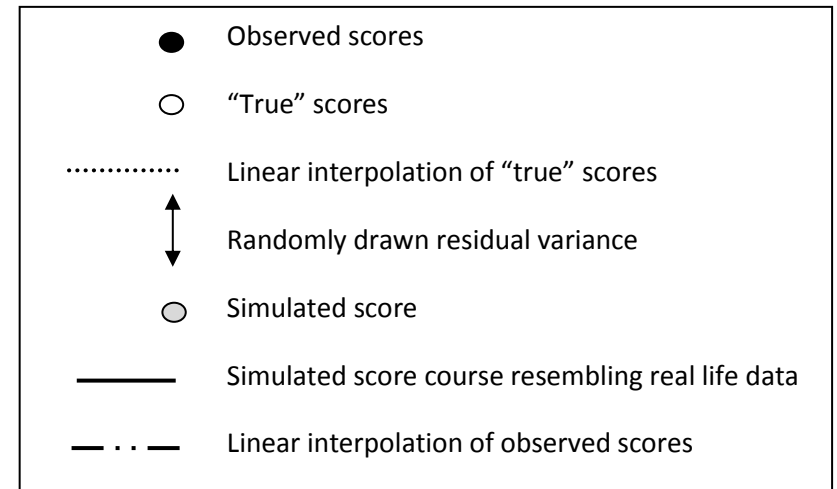
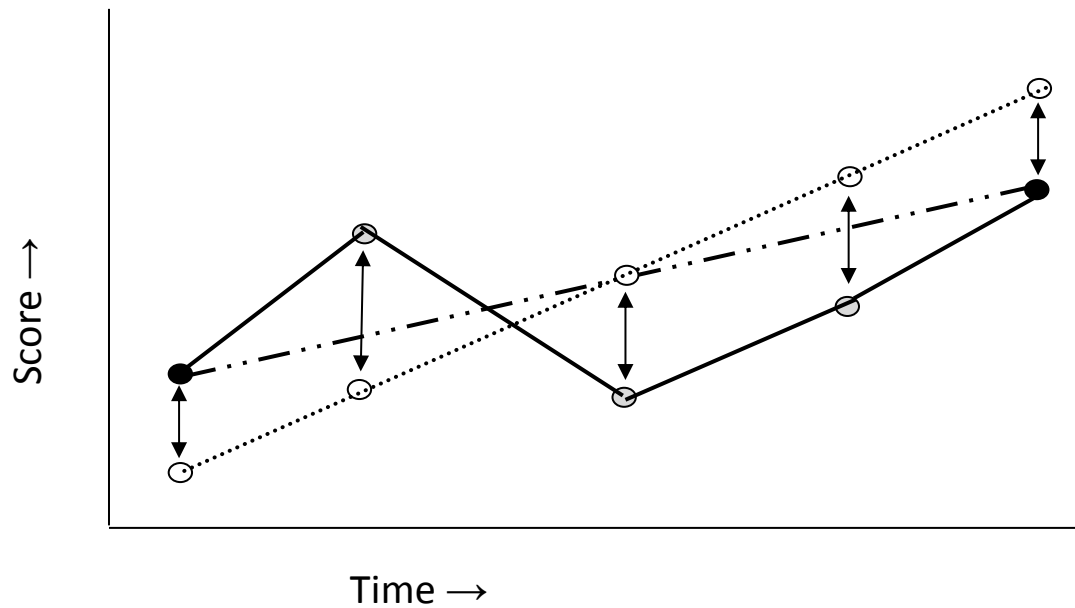


Figure A4 Example of advanced interpolation

1. Imhoff M, Bauer M, Gather U, Lohlein D. Time series analysis in intensive care medicine. *Acp-Applied Cardiopulmonary Pathophysiology*. 1996; 6(4):263-281.