

**Supplementary material**Table S1: **Number of participants/missing data**

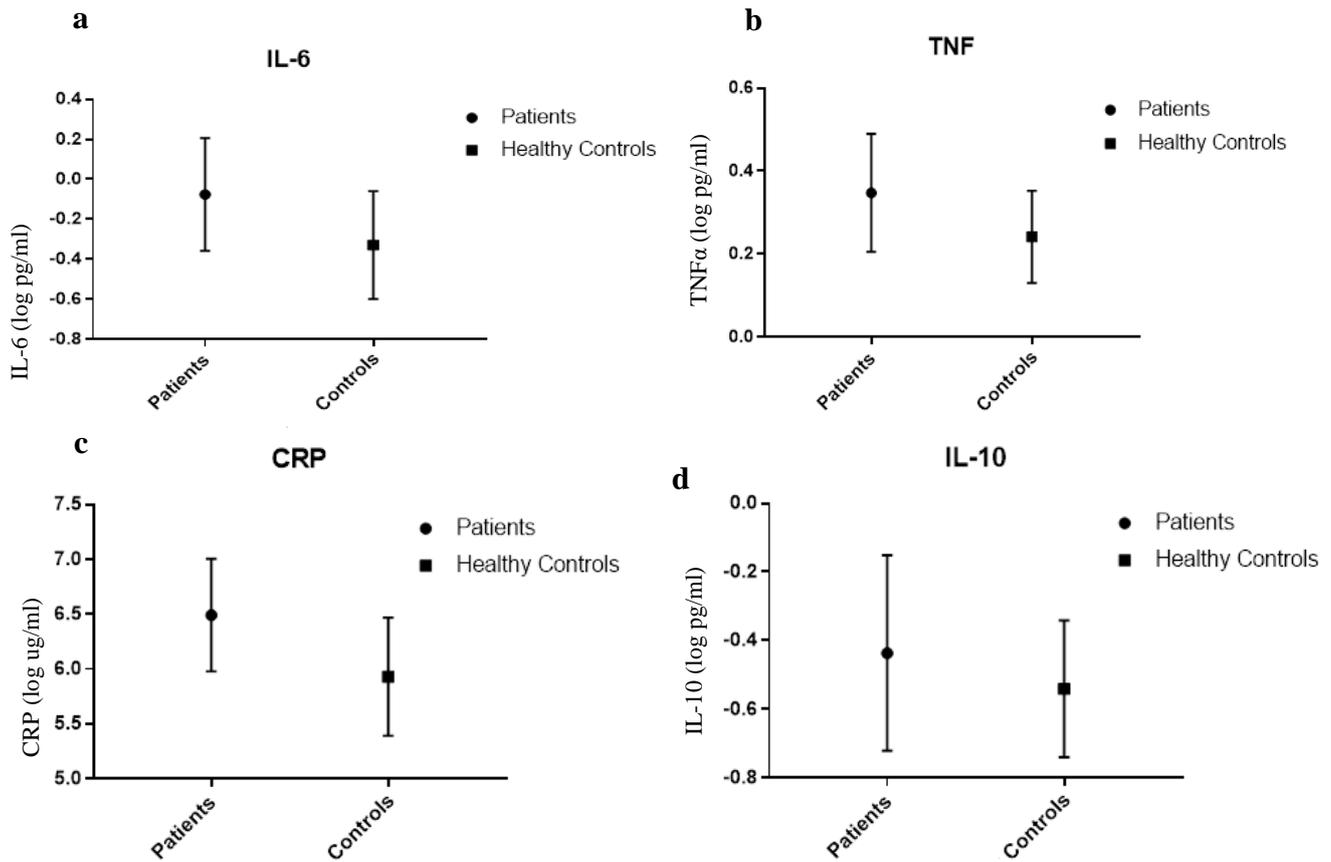
|   |                   |                | <b>Total TRD</b> | <b>Controls</b> |
|---|-------------------|----------------|------------------|-----------------|
| Total number of ADD participants with baseline inflammatory and clinical data                                       |                   |                | <b>143</b>       | 31              |
|   | <b>Metyrapone</b> | <b>Placebo</b> | <b>Total TRD</b> | <b>Controls</b> |
| Total numbers after exclusions for inflammatory conditions <sup>a</sup>   | 63                | 66             | <b>129</b>       | 28              |
| Number after exclusion of non-adherent metyrapone patients <sup>b</sup>   | 40                | 66             | <b>106</b>       | -               |
| Number of participants (excluding metyrapone non-adherent) with clinical and inflammatory outcome data <sup>c</sup> | 40                | 57             | <b>97</b>        | -               |

<sup>a</sup> included in baseline patient/control comparisons, and the mITT moderation and mediation analyses

<sup>b</sup> included in per-protocol moderation and mediation analyses

<sup>c</sup> included in analyses with missing data addressed using full information maximum likelihood

Figure S1

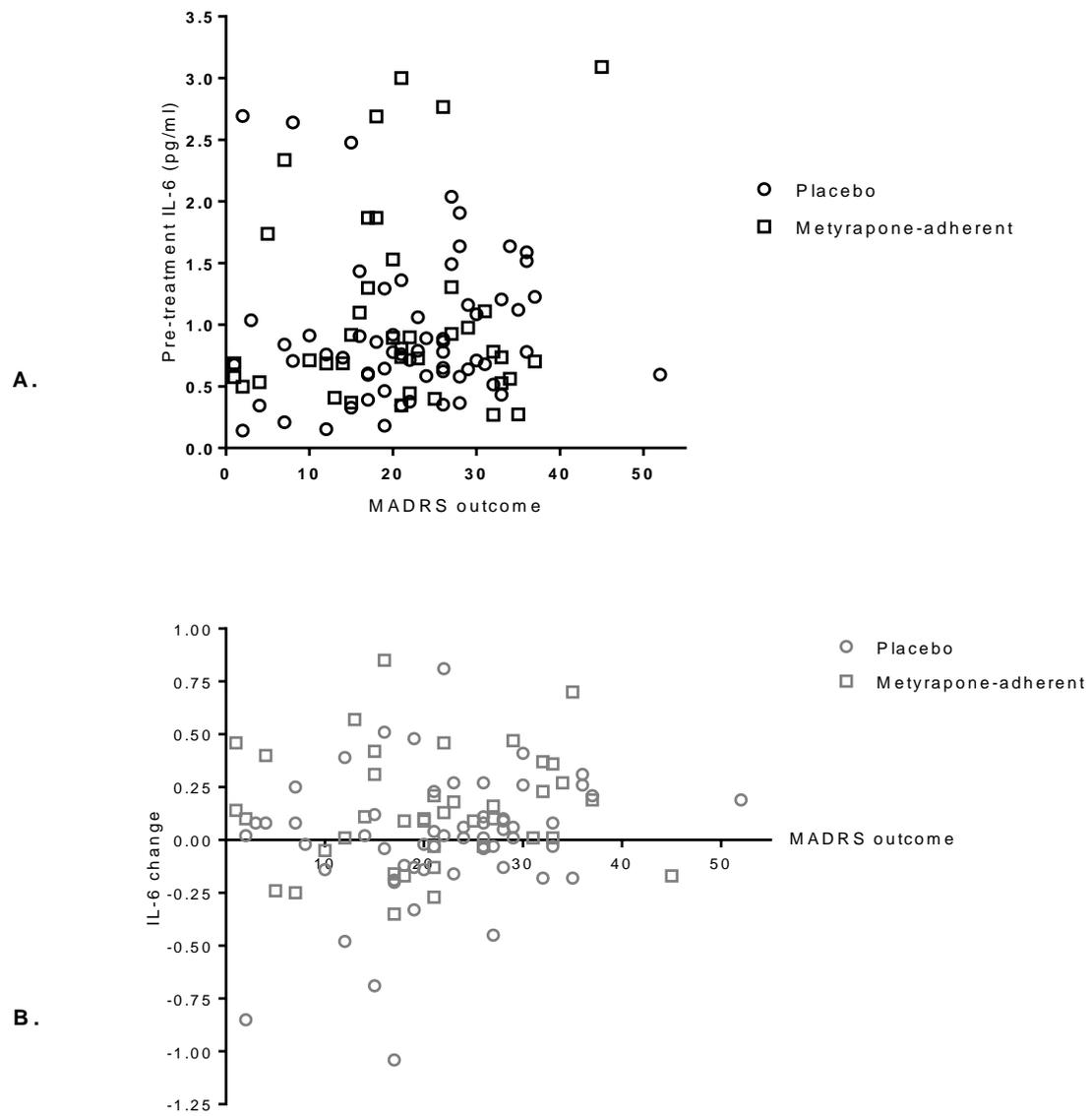


**Figure a-d:** Patients' and controls' baseline levels of

- a) IL-6
- b) TNF $\alpha$
- c) CRP
- d) IL-10

Log transformed mean values of the cytokines assessed are presented. Error bars represent standard deviation (SD).  
CRP = C-reactive Protein; IL-6 = Interleukin 6; IL-10 = Interleukin 10; TNF- $\alpha$  = Tumour Necrosis Factor  $\alpha$ .

Figure S2



**Figure A / B:** IL-6 associations with treatment group and clinical outcome, as examined in linear regression and mediation analysis  
a) Pre-treatment IL-6 as a predictor of subsequent clinical outcome  
b) Change in IL-6 during treatment and association with clinical outcome