Supplemental Content

Tocilizumab in COVID-19 Related Critical illness: A Propensity Matched Analysis

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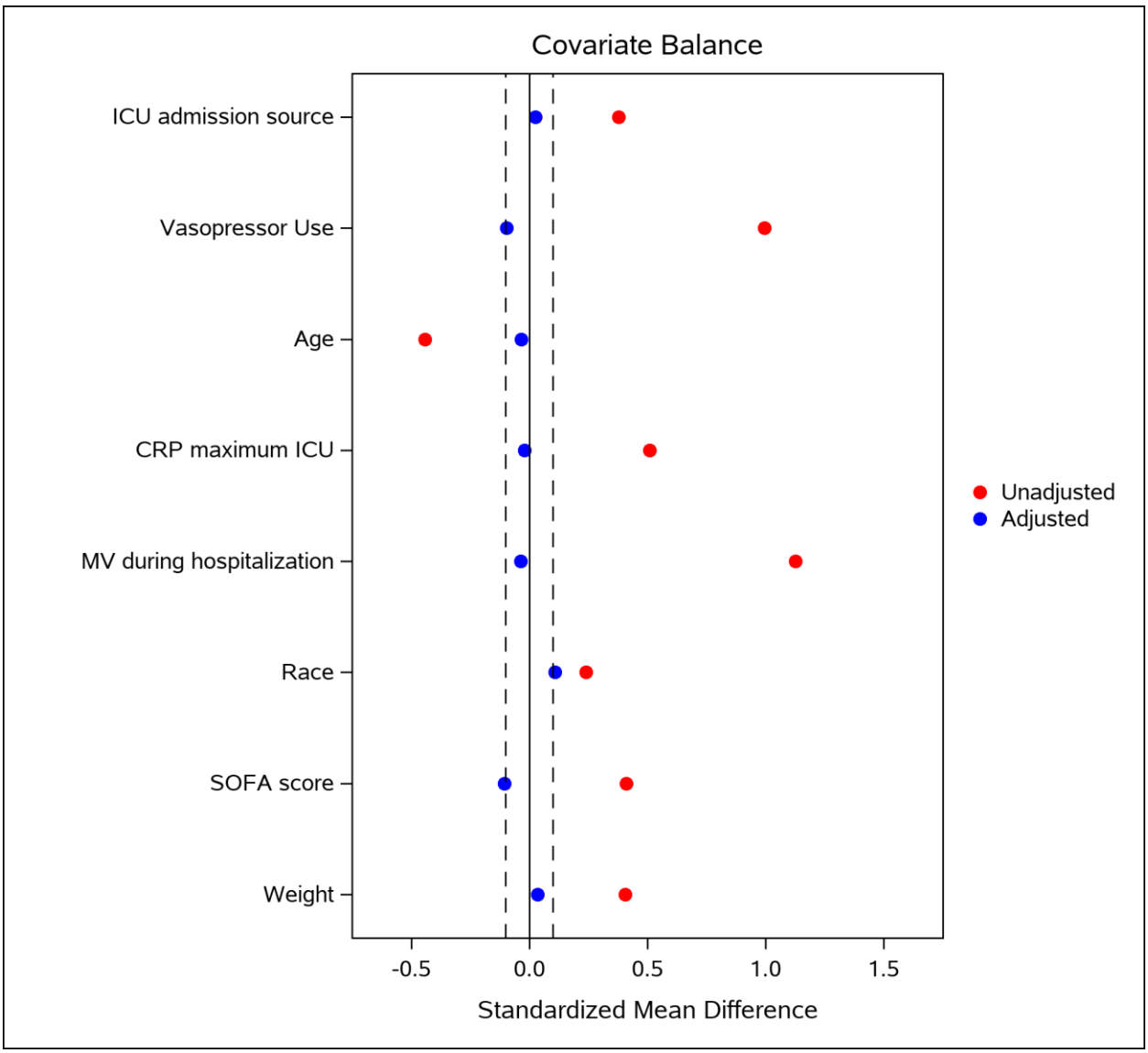
eTable 1: Definitions of Select Clinical Outcomes

Outcome free days at day 28*	Includes ICU, hospital, mechanical ventilation, and vasopressor free days at day 28. Calculation example: Using vasopressor free days as an example, this was calculated by adding the number of days the patient was alive and off of all vasoactive agents starting at the time of the last vasoactive agent discontinuation for that patient's hospital encounter. For example, if a patient was off vasopressors from days 5 to 10 but required vasopressors from day 12-20 yet survived the hospital encounter, there would be no credit for the days 10-12 off vasopressors. If patients died while receiving vasopressors, they were counted as 0 days alive and free from vasopressors.
Secondary Infection	Evaluated within the first 30 days after ICU admission (for control group) or the first 30 days after tocilizumab administration (for tocilizumab group) and was defined as the presence of any active infection from any source. Candida spp. Detected in the urine or from respiratory samples and respiratory samples growing only normal flora, pathogen quantity of rare that was not speciated or further worked up by microbiology, or samples with rare polymorphonuclear leukocytes indicating colonization versus active infection were not considered to be a secondary infection. Additionally, *Clostridioides difficile* infections that were PCR positive but the confirmatory toxin enzyme immunoassay was negative, indicating colonization versus active infection, were not considered to be a secondary infection. Three independent reviewers (GS, PR, and AD) manually reviewed each patient and adjudicated colonization vs. active infection, any discrepancies were discussed among the three reviewers.
SOFA Score change	Change in SOFA score at 72 hours from SOFA score at baseline

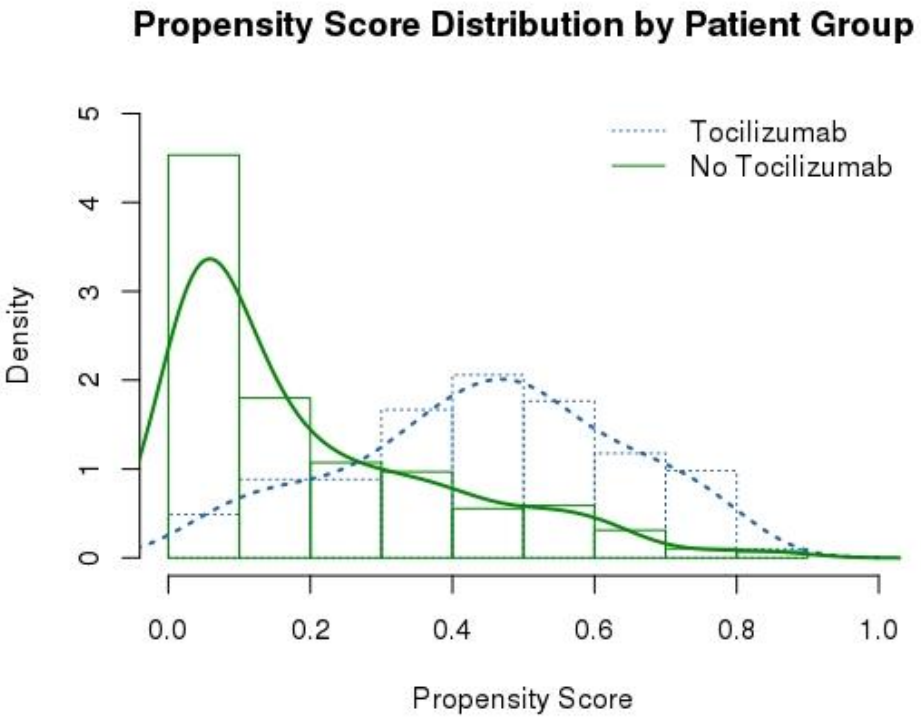
*Reference: Russell JA, Lee T, Singer J, De Backer D, Annane D. Days alive and free as an alternative to a mortality outcome in pivotal vasopressor and septic shock trials. J Crit Care. 2018;47:333-337. 10.1016/j.jcrc.2018.05.003

eFigure 1: Love Plot of Included Covariates

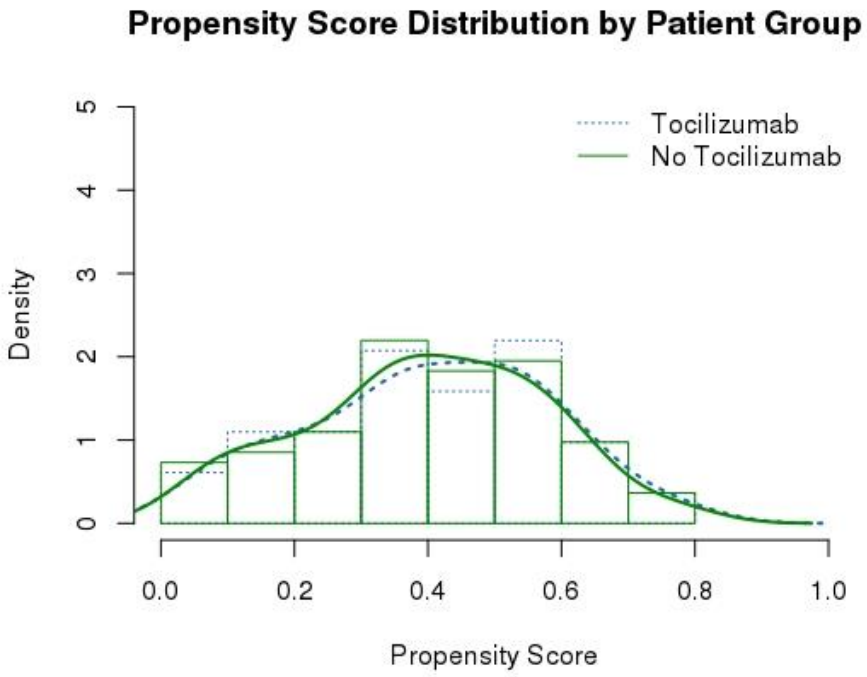


Love plot depicting covariate balance before and after matching with the dashed line representing a standardized mean difference of 0.10.

eFigure 2: Propensity Score Distribution Before and After Matching

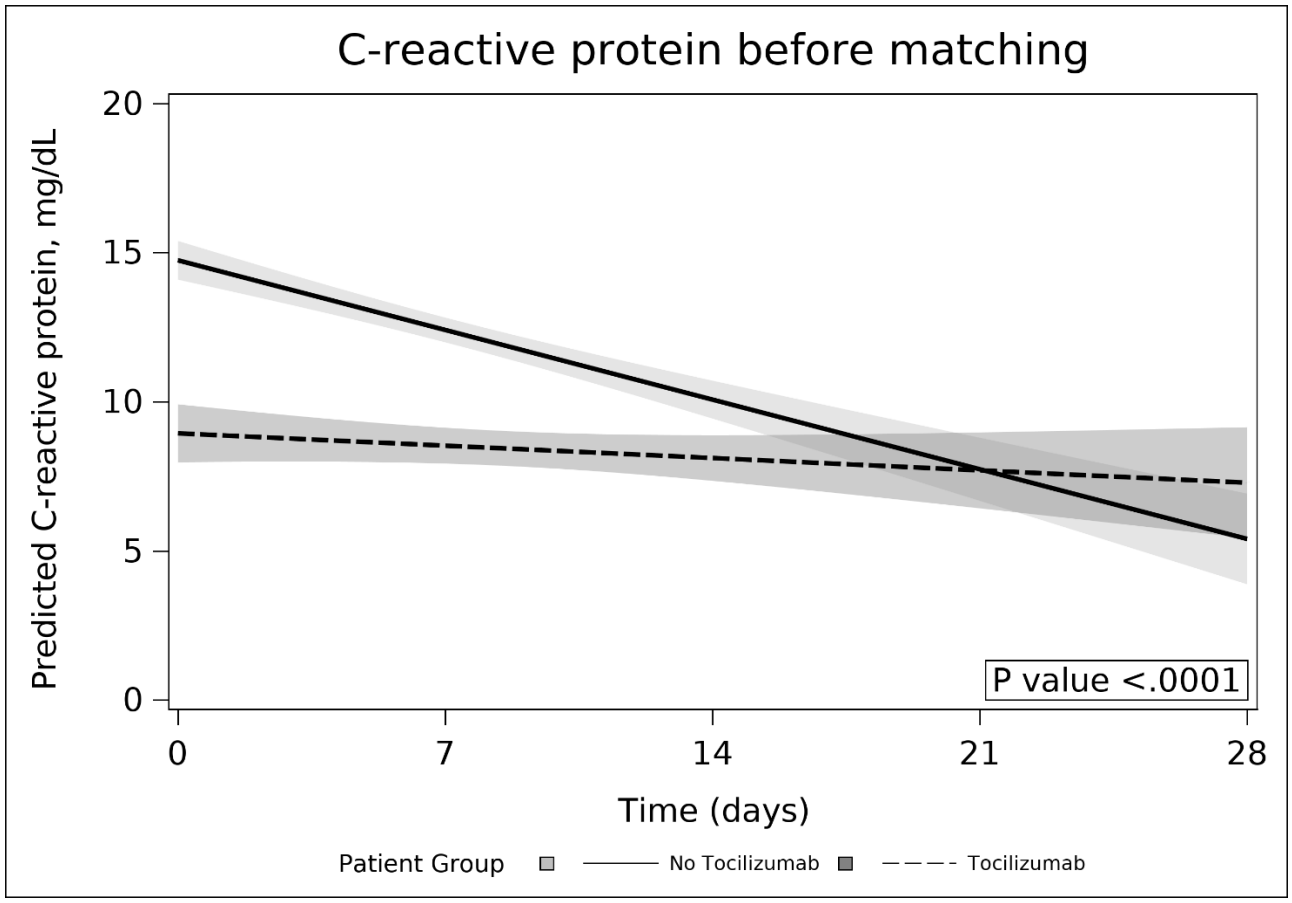


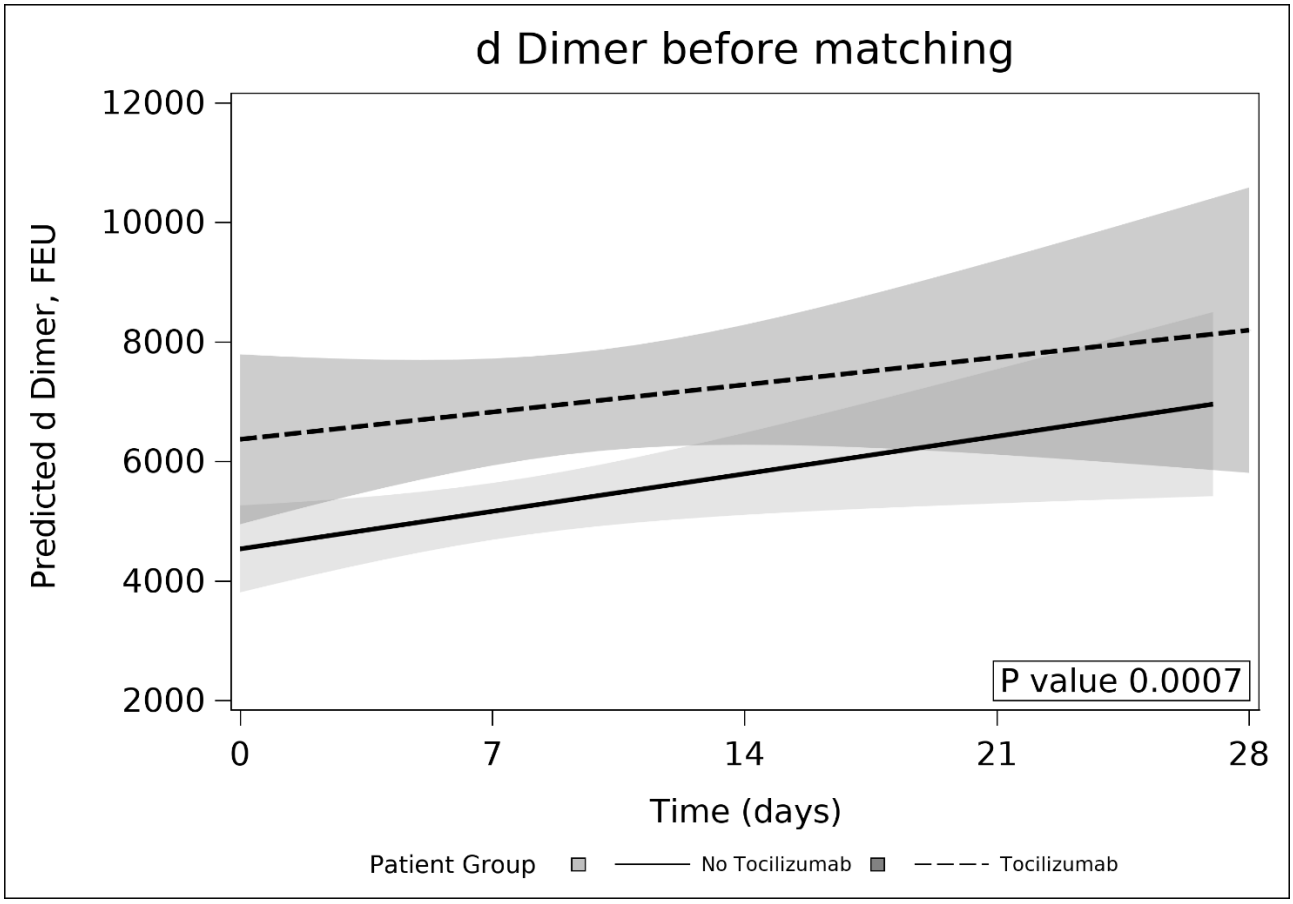
Propensity score distribution plot before matching

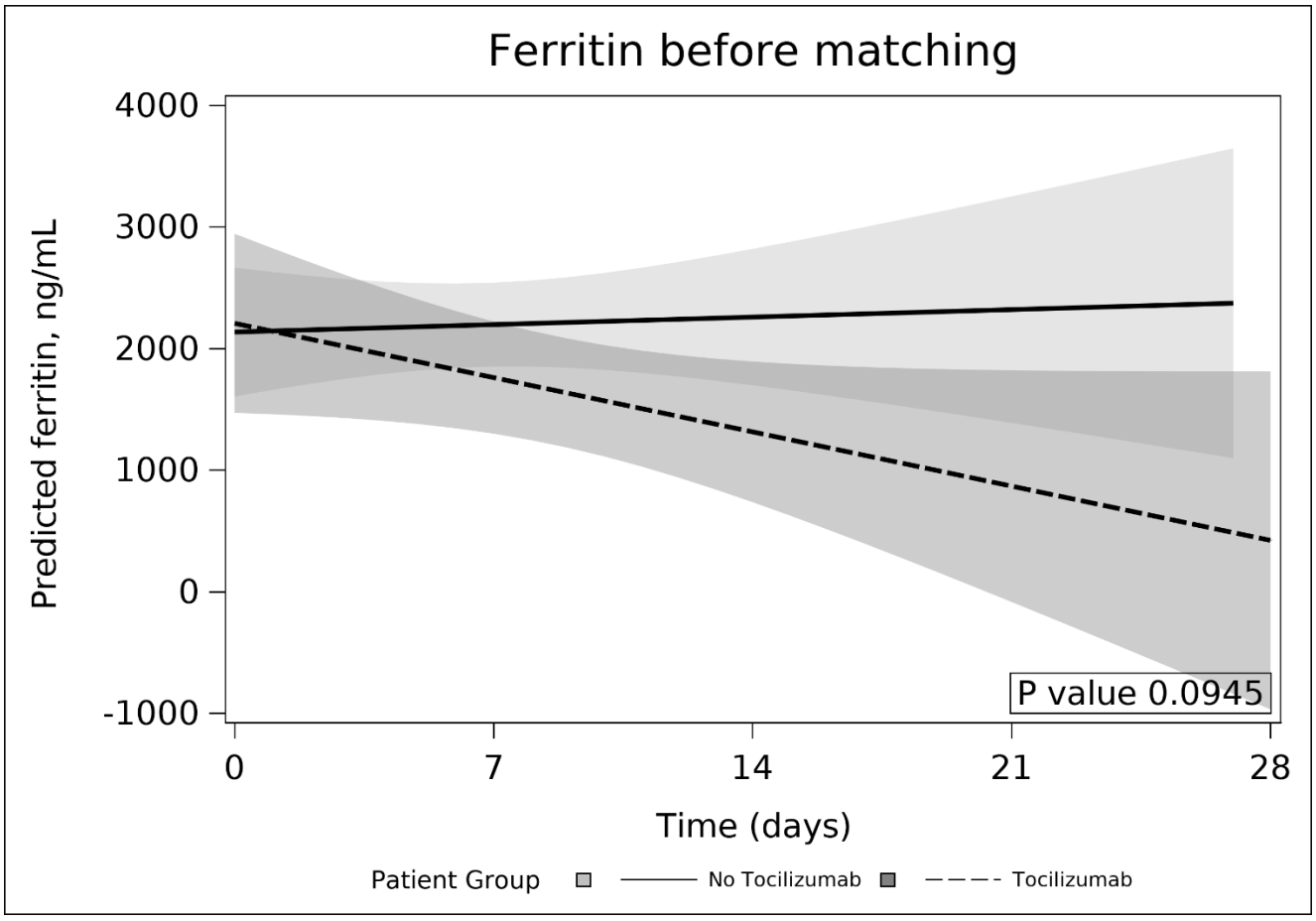


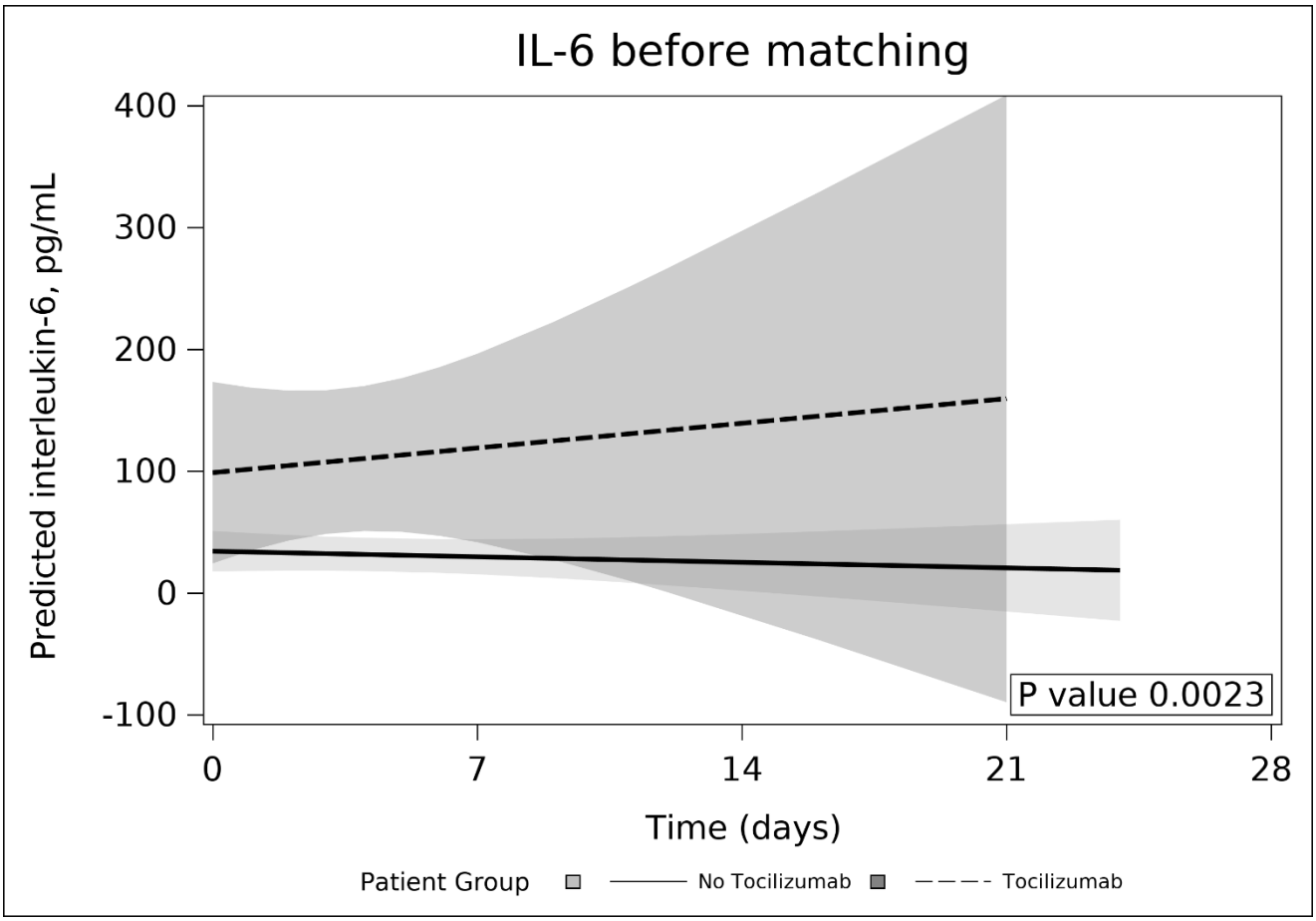
Propensity score distribution plot after matching

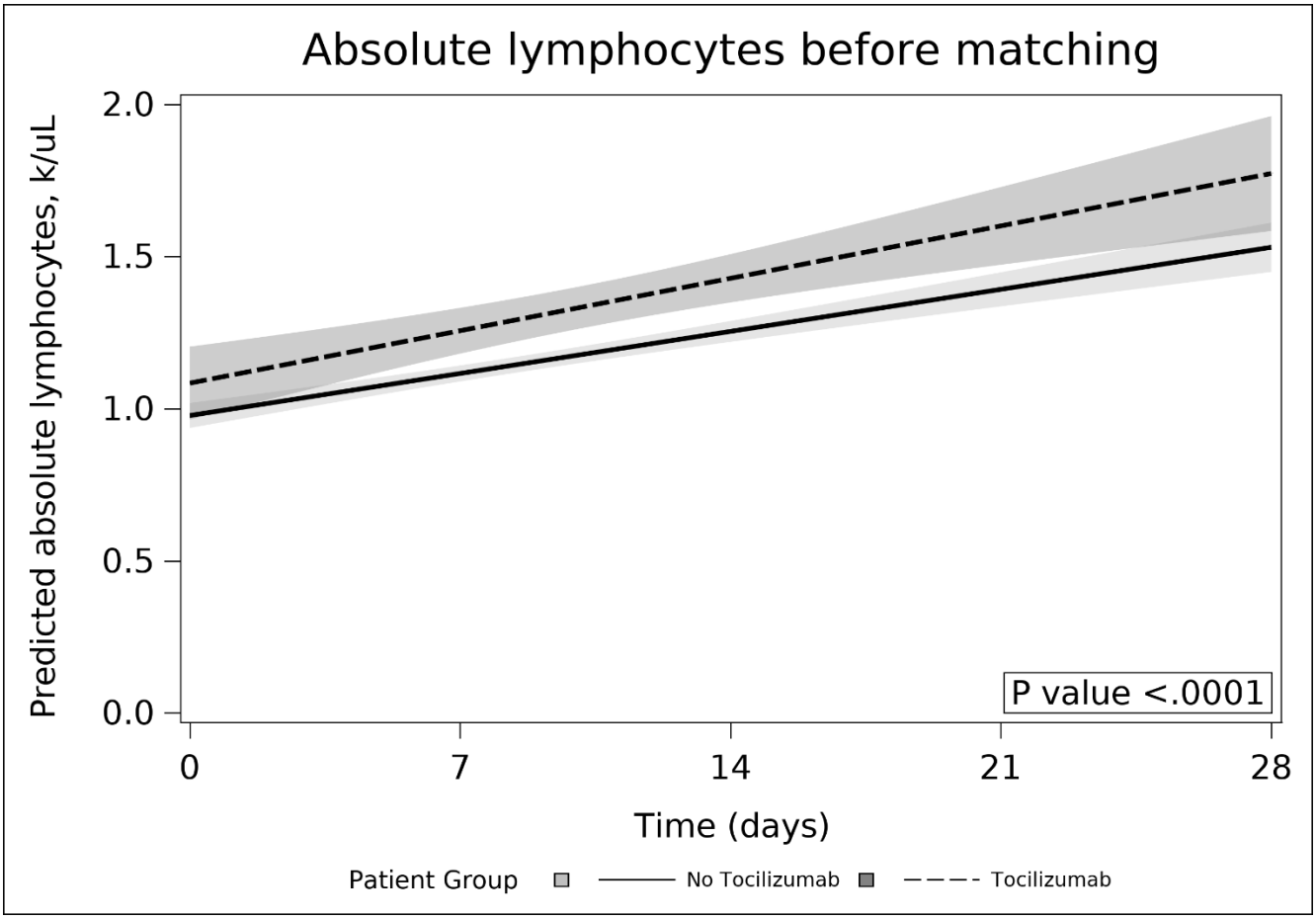
eFigure 3: Biomarker Trend Graphs Before Matching






Ferritin before matching
Predicted ferritin, ng/mL
4000
3000
2000
1000
0
-1000
0
7
14
21
28
Time (days)
P value 0.0945
Patient Group
No Tocilizumab
Tocilizumab


IL-6 before matching
Predicted interleukin-6, pg/mL
400
300
200
100
0
-100
0
7
14
21
28
Time (days)
P value 0.0023
Patient Group
No Tocilizumab
Tocilizumab



Each figure depicts each specific biomarker in all included patients before matching over time from baseline until 28 days after baseline. Baseline in patients who received tocilizumab is the time of tocilizumab initiation and baseline in patients who did not receive tocilizumab is the time of ICU admission. The solid line in each graph represents the predicted slope of each biomarker (with 95% confidence interval in light gray shaded area) in patients who did not receive tocilizumab; the dashed line represents the predicted slope of each biomarker (with 95% confidence interval in dark gray shaded area) in patients who received tocilizumab. A comparison of the 95% CI slopes of the predicted slopes in patients who received tocilizuamb and those who did not receive tocilizumab was conducted for each biomarker.

Figure A: Before matching, a comparison in the predicted slopes revealed a significant difference between the predicted slope of C-reactive protein in those who received tocilizumab compared to those who did not receive tocilizumab ($p<0.0001$).

Figure B: Before matching, a comparison in the predicted slopes revealed a significant difference between the predicted slope of d Dimer in those who received tocilizumab compared to those who did not receive tocilizumab ($p=0.0007$).

Figure C: Before matching, a comparison in the predicted slopes revealed no significant difference between the predicted slope of ferritin in those who received tocilizumab compared to those who did not receive tocilizumab ($p=0.095$).

Figure D: Before matching, a comparison in the predicted slopes revealed a significant difference between the predicted slope of interleukin-6 in those who received tocilizumab compared to those who did not receive tocilizumab ($p=0.002$).

Figure E: Before matching, a comparison in the predicted slopes revealed a significant difference between the predicted slope of absolute lymphocyte count in those who received tocilizumab compared to those who did not receive tocilizumab ($p<0.0001$).