



# The Open Rheumatology Journal

## Supplementary Material

Content list available at: [www.benthamopen.com/TORJ/](http://www.benthamopen.com/TORJ/)

DOI: 10.2174/1874312901711012345



## RESEARCH ARTICLE

## Dose Escalation and Co-therapy Intensification Between Etanercept, Adalimumab, and Infliximab: The CADURA Study

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## APPENDIX A

Supplementary Table A. Generalized linear model base case and sensitivity analysis cost ratios for total cost over 12 months.

| Independent Variables                          | Total Cost over 12-month Follow-up <sup>1</sup> |              |              |         | Total Cost over 12-month Follow-up Sensitivity Analysis <sup>2</sup> |              |              |         |
|--|---|--------------|--------------|---------|--|--------------|--------------|---------|
|  | Cost Ratio                                      | Lower 95% CI | Upper 95% CI | P-value | Cost Ratio   | Lower 95% CI | Upper 95% CI | P-value |
| <b>Index Medication</b>                        |   |              |              |         |  |              |              |         |
| Etanercept                                     | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| Adalimumab                                     | 0.988   | 0.958        | 1.018        | 0.413   | 0.978  | 0.951        | 1.006        | 0.125   |
| Infliximab                                     | 1.240   | 1.181        | 1.302        | <0.001  | 1.214  | 1.159        | 1.271        | <0.001  |
| <b>Charlson Comorbidity Score (continuous)</b> | 0.975   | 0.943        | 1.008        | 0.137   | 0.972  | 0.946        | 1.000        | 0.051   |
| <b>RA Duration (in years)</b>                  |   |              |              |         |  |              |              |         |
| 0-10   | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| 11-15  | 1.030   | 0.992        | 1.070        | 0.122   | 1.027  | 0.984        | 1.073        | 0.226   |
| 16+  | 1.024   | 0.976        | 1.073        | 0.335   | 1.008  | 0.954        | 1.066        | 0.772   |
| <b>Age (continuous)</b>                        | 1.000   | 0.999        | 1.002        | 0.445   | 1.000  | 0.999        | 1.001        | 0.770   |
| <b>Gender</b>                                  |   |              |              |         |  |              |              |         |
| Male   | 0.994   | 0.961        | 1.027        | 0.706   | 1.000  | 0.969        | 1.031        | 0.976   |
| Female   | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| <b>Medication Insurance at Index Date</b>      |   |              |              |         |  |              |              |         |
| Government                                     | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| Private  | 1.012   | 0.980        | 1.045        | 0.471   | 1.003  | 0.972        | 1.034        | 0.868   |
| None   | 1.001   | 0.905        | 1.106        | 0.989   | 0.899  | 0.836        | 0.967        | 0.004   |
| Not government but unknown if private or none  | 1.018   | 0.880        | 1.178        | 0.813   | 1.008  | 0.893        | 1.139        | 0.895   |
| Unknown  | 1.029   | 0.950        | 1.115        | 0.485   | 1.009  | 0.942        | 1.081        | 0.789   |
| <b>Prior 3-month DMARD Use</b>                 |   |              |              |         |  |              |              |         |
| One  | 1.021   | 0.951        | 1.097        | 0.568   | 1.032  | 0.974        | 1.093        | 0.283   |

Uwrr#Table 1 contd.....

| Independent Variables         | Total Cost over 12-month Follow-up <sup>1</sup> |              |              |         | Total Cost over 12-month Follow-up Sensitivity Analysis <sup>2</sup> |              |              |         |
|-------------------------------|---|--------------|--------------|---------|--|--------------|--------------|---------|
|                               | Cost Ratio                                      | Lower 95% CI | Upper 95% CI | P-value | Cost Ratio   | Lower 95% CI | Upper 95% CI | P-value |
| More than one                 | 1.071   | 0.996        | 1.151        | 0.063   | 1.082  | 1.022        | 1.145        | 0.007   |
| None                          | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| <b>Initiation of Anti-TNF</b> |   |              |              |         |  |              |              |         |
| Monotherapy                   | 1.022   | 0.955        | 1.094        | 0.532   | 1.043  | 0.984        | 1.105        | 0.157   |
| Concomitant DMARD             | ref.  | –            | –            | –       | ref.   | –            | –            | –       |

<sup>1</sup> Observations read=314, observations used=183, Pearson chi-square=1.541, DF=168

<sup>2</sup> Includes patients with RA duration missing, observations read=314, observations used=314, Pearson chi-square=4.190, DF=299

**APPENDIX B**

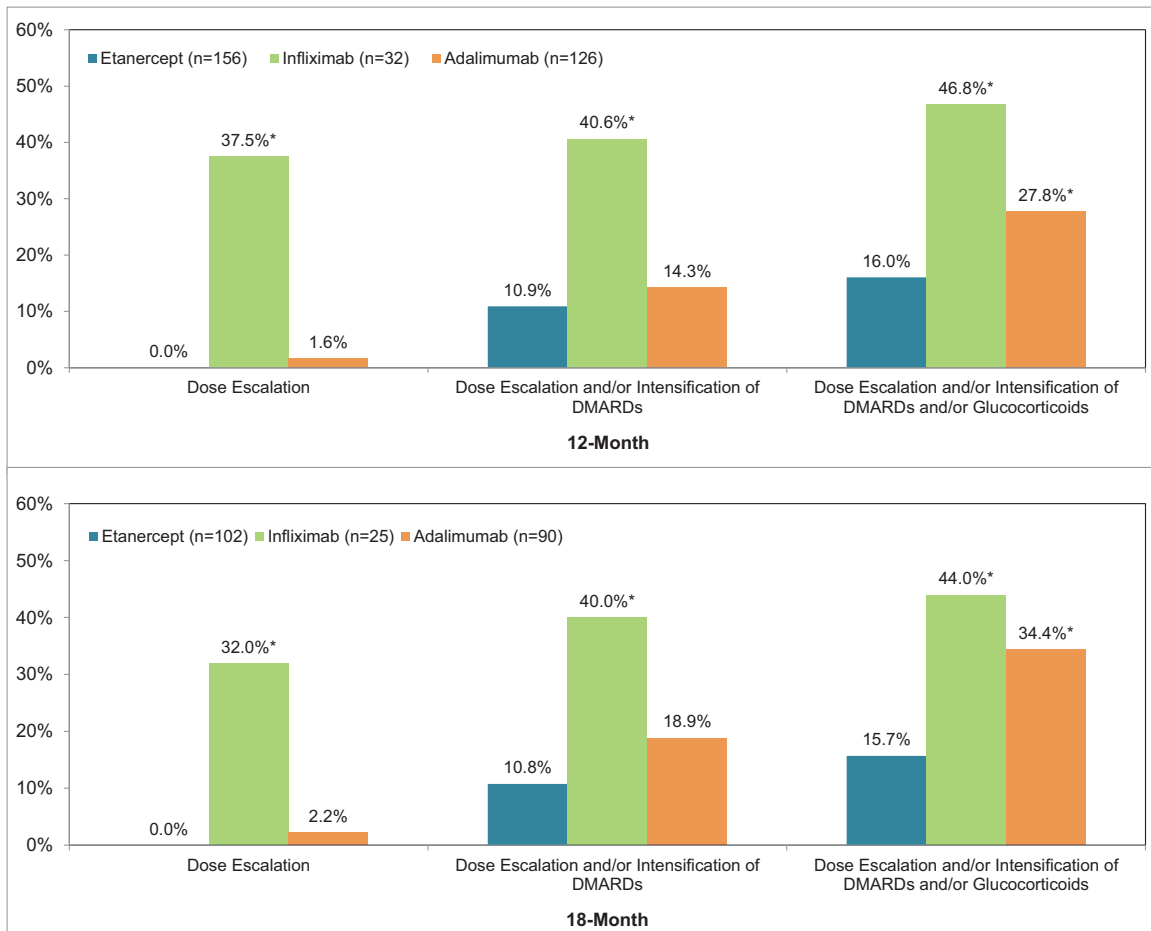
**Supplementary Table B. Generalized linear model base case and sensitivity analysis cost ratios for total cost over 18 months.**

| Independent Variables                          | Total Cost over 18-month Follow-up <sup>1</sup> |              |              |         | Total Cost over 18-month Follow-up Sensitivity Analysis <sup>2</sup> |              |              |         |
|--|---|--------------|--------------|---------|--|--------------|--------------|---------|
|  | Cost Ratio                                      | Lower 95% CI | Upper 95% CI | P-value | Cost Ratio   | Lower 95% CI | Upper 95% CI | P-value |
| <b>Index Medication</b>                        |   |              |              |         |  |              |              |         |
| Etanercept                                     | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| Adalimumab                                     | 0.965   | 0.927        | 1.006        | 0.090   | 0.958  | 0.917        | 1.002        | 0.059   |
| Infliximab                                     | 1.197   | 1.125        | 1.275        | <0.001  | 1.160  | 1.082        | 1.243        | <0.001  |
| <b>Charlson Comorbidity Score (continuous)</b> | 0.927   | 0.885        | 0.970        | 0.001   | 0.941  | 0.901        | 0.981        | 0.005   |
| <b>RA Duration (in years)</b>                  |   |              |              |         |  |              |              |         |
| 0-10   | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| 11-15  | 1.020   | 0.968        | 1.075        | 0.455   | 1.022  | 0.954        | 1.096        | 0.528   |
| 16+  | 1.002   | 0.944        | 1.064        | 0.941   | 0.978  | 0.901        | 1.062        | 0.595   |
| <b>Age (continuous)</b>                        | 1.000   | 0.999        | 1.002        | 0.885   | 0.999  | 0.997        | 1.001        | 0.289   |
| <b>Gender</b>                                  |   |              |              |         |  |              |              |         |
| Male   | 0.995   | 0.950        | 1.042        | 0.826   | 1.017  | 0.966        | 1.070        | 0.527   |
| Female   | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| <b>Medication Insurance at Index Date</b>      |   |              |              |         |  |              |              |         |
| Government                                     | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| Private  | 1.012   | 0.966        | 1.059        | 0.618   | 1.003  | 0.954        | 1.054        | 0.920   |
| None   | 1.004   | 0.882        | 1.143        | 0.947   | 0.901  | 0.804        | 1.010        | 0.075   |
| Not government but unknown if private or none  | 1.024   | 0.868        | 1.208        | 0.781   | 0.994  | 0.848        | 1.166        | 0.944   |
| Unknown  | 1.051   | 0.955        | 1.157        | 0.306   | 1.019  | 0.927        | 1.119        | 0.701   |
| <b>Prior 3-month DMARD Use</b>                 |   |              |              |         |  |              |              |         |
| One  | 1.003   | 0.916        | 1.098        | 0.949   | 1.065  | 0.977        | 1.162        | 0.151   |
| More than one                                  | 1.034   | 0.942        | 1.135        | 0.485   | 1.093  | 1.002        | 1.192        | 0.045   |
| None   | ref.  | –            | –            | –       | ref.   | –            | –            | –       |
| <b>Initiation of Anti-TNF</b>                  |   |              |              |         |  |              |              |         |
| Monotherapy                                    | 0.991   | 0.910        | 1.079        | 0.838   | 1.064  | 0.977        | 1.159        | 0.156   |
| Concomitant DMARD                              | ref.  | –            | –            | –       | ref.   | –            | –            | –       |

<sup>1</sup> Observations read=217, observations used=124, Pearson chi-square=1.205, DF=109

<sup>2</sup> Includes patients with missing RA duration, observations read=217, observations used=217, Pearson chi-square=4.717, DF=202

APPENDIX C



**Supplementary Fig. (A).** Percentage of Patients with anti-TNF dose escalation and DMARD and/or glucocorticoid intensification.

Abbreviations: DMARD=disease-modifying anti-rheumatic drug, TNF=tumor necrosis factor.

\* p<0.05