

# Supporting Information

## SUPPLEMENTARY TABLES

Table A. Criteria to determine the number of trajectories that best represent adherence patterns for the different therapeutic groups.

|               |                       | AIC             | BIC             | LMR-LRT<br>p-value | Entropy     | Minimum<br>size |
|---------------|-----------------------|-----------------|-----------------|--------------------|-------------|-----------------|
| Antiplatelet  | 1 trajectory          | 44674.64        | 44694.99        |                    |             |                 |
|               | 2 trajectories        | 34193.27        | 34240.74        | 0.00               | 0.93        | 0.16            |
|               | 3 trajectories        | 33145.46        | 33220.06        | 0.00               | 0.84        | 0.07            |
|               | 4 trajectories        | 32623.67        | 32725.39        | 0.00               | 0.86        | 0.06            |
|               | <b>5 trajectories</b> | <b>32258.50</b> | <b>32387.35</b> | <b>0.00</b>        | <b>0.83</b> | <b>0.05</b>     |
|               | 6 trajectories        | 32123.02        | 32279.00        | 0.15               | 0.73        | 0.04            |
|               | 7 trajectories        | 32019.33        | 32202.43        | 0.76               | 0.74        | 0.02            |
| Beta-blockers | 1 trajectory          | 49388.34        | 49407.90        |                    |             |                 |
|               | 2 trajectories        | 40104.29        | 40149.94        | 0.00               | 0.88        | 0.31            |
|               | 3 trajectories        | 39054.20        | 39125.93        | 0.00               | 0.85        | 0.09            |
|               | <b>4 trajectories</b> | <b>38763.30</b> | <b>38861.12</b> | <b>0.00</b>        | <b>0.83</b> | <b>0.06</b>     |
|               | 5 trajectories        | 38697.35        | 38821.25        | 0.00               | 0.69        | 0.06            |
|               | 6 trajectories        | 38441.08        | 38591.07        | 0.00               | 0.69        | 0.05            |
|               | 7 trajectories        | 38305.65        | 38481.72        | 0.00               | 0.69        | 0.04            |
| ACEI/ARB      | 1 trajectory          | 48741.65        | 48761.35        |                    |             |                 |
|               | 2 trajectories        | 37552.95        | 37598.91        | 0.00               | 0.91        | 0.24            |
|               | 3 trajectories        | 36223.22        | 36295.43        | 0.00               | 0.84        | 0.11            |
|               | <b>4 trajectories</b> | <b>35611.82</b> | <b>35710.29</b> | <b>0.00</b>        | <b>0.83</b> | <b>0.07</b>     |
|               | 5 trajectories        | 35380.51        | 35505.24        | 0.23               | 0.85        | 0.04            |
|               | 6 trajectories        | 35200.70        | 35351.68        | 0.00               | 0.81        | 0.03            |
|               | 7 trajectories        | 35043.57        | 35220.82        | 0.00               | 0.74        | 0.04            |
| Statins       | 1 trajectory          | 49039.28        | 49059.40        |                    |             |                 |
|               | 2 trajectories        | 39819.18        | 39866.11        | 0.00               | 0.91        | 0.18            |
|               | <b>3 trajectories</b> | <b>39003.50</b> | <b>39077.24</b> | <b>0.00</b>        | <b>0.84</b> | <b>0.08</b>     |
|               | 4 trajectories        | 38864.56        | 38965.13        | 0.00               | 0.66        | 0.06            |
|               | 5 trajectories        | 38441.97        | 38569.35        | 0.00               | 0.71        | 0.05            |
|               | 6 trajectories        | 38169.77        | 38323.97        | 0.16               | 0.64        | 0.06            |
|               | 7 trajectories        | 38005.69        | 38186.71        | 0.00               | 0.76        | 0.03            |

AIC: akaike information criterion; BIC: bayesian information criteria; LMR-LRT: Lo-Mendell-Rubin likelihood ratio test; ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blockers.

In bold the models selected after fulfilling all criteria. The criteria for rejecting k class models (and, thus, selecting k-1 class models) was the presence of some of the following criteria: BIC or AIC score higher; LMR-LRT p-value>0.5; entropy (minimum membership probability) <0.7; and minimum sample size <5%.

Table B. Predictors of poor or intermediate adherence trajectory groups for antiplatelet. Multinomial logistic regression analysis.

|                             |                       | Early gap   |                    | Occasional users |                    | Slow decline |                    | Fast decline |                    |
|-----------------------------|-----------------------|-------------|--------------------|------------------|--------------------|--------------|--------------------|--------------|--------------------|
|                             |                       | OR          | 95%CI              | OR               | 95%CI              | OR           | 95%CI              | OR           | 95%CI              |
| Age                         | <45 years             | <b>1.96</b> | <b>(1.29-2.97)</b> | 1.42             | (0.88-2.30)        | 1.34         | (0.67-2.67)        | 1.06         | (0.56-2.14)        |
|                             | 45 to 64              | 1.19        | (0.95-1.49)        | 0.94             | (0.72-1.27)        | 0.90         | (0.60-1.38)        | 0.83         | (0.58-1.30)        |
|                             | 65 to 79              | 1.00        |                    | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | 80 and over           | 1.08        | (0.80-1.33)        | 1.18             | (0.93-1.49)        | <b>1.56</b>  | <b>(1.13-2.15)</b> | <b>1.62</b>  | <b>(1.16-2.14)</b> |
| Gender                      | Male                  | 1.00        |                    | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | Female                | 1.11        | (0.94-1.32)        | 1.05             | (0.90-1.29)        | <b>1.34</b>  | <b>(1.01-1.75)</b> | 1.20         | (0.94-1.58)        |
| Country of birth            | Spain                 | 1.00        |                    | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | Other                 | 1.17        | (0.92-1.49)        | <b>1.38</b>      | <b>(1.07-1.81)</b> | <b>2.20</b>  | <b>(1.57-3.05)</b> | <b>2.14</b>  | <b>(1.53-2.87)</b> |
| Copayment                   | Yes                   | 0.97        | (0.76-1.20)        | <b>1.79</b>      | <b>(1.33-2.35)</b> | <b>1.74</b>  | <b>(1.33-2.35)</b> | <b>2.5</b>   | <b>(1.57-3.52)</b> |
|                             | No                    | 1.00        |                    | 1.00             |                    | 1.00         |                    | 1.00         |                    |
| Main diagnosis at discharge | AMI                   | 1.00        |                    | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | Unstable angina       | 1.06        | (0.85-1.32)        | <b>1.43</b>      | <b>(1.12-1.82)</b> | <b>1.67</b>  | <b>(1.12-1.82)</b> | 1.01         | (0.67-1.40)        |
|                             | Stable angina         | 1.23        | (0.98-1.56)        | <b>1.94</b>      | <b>(1.51-2.48)</b> | <b>2.47</b>  | <b>(1.74-3.43)</b> | <b>2.96</b>  | <b>(2.12-3.85)</b> |
|                             | Other CHD             | 1.12        | (0.92-1.37)        | 1.17             | (0.92-1.48)        | 1.21         | (0.92-1.48)        | 1.09         | (0.78-1.52)        |
| Comorbidities               | Hypertension          | 0.98        | (0.83-1.15)        | 1.03             | (0.86-1.24)        | 0.94         | (0.73-1.23)        | 0.97         | (0.77-1.26)        |
|                             | Hyperlipidemia        | 0.94        | (0.80-1.09)        | 0.90             | (0.75-1.07)        | 0.87         | (0.68-1.13)        | <b>0.75</b>  | <b>(0.61-0.98)</b> |
|                             | Diabetes              | 1.14        | (0.98-1.34)        | 1.08             | (0.90-1.29)        | <b>1.31</b>  | <b>(1.07-1.81)</b> | 1.05         | (0.82-1.36)        |
|                             | Smoking               | 0.94        | (0.77-1.14)        | 0.92             | (0.74-1.16)        | 1.27         | (0.90-1.72)        | 1.02         | (0.73-1.35)        |
|                             | Arrhythmias           | 1.11        | (0.92-1.34)        | 1.13             | (0.90-1.40)        | 1.26         | (0.93-1.70)        | <b>1.50</b>  | <b>(1.13-1.95)</b> |
|                             | Heart failure         | <b>1.39</b> | <b>(1.13-1.71)</b> | 1.26             | (0.99-1.63)        | <b>1.41</b>  | <b>(1.01-1.97)</b> | 1.07         | (0.81-1.58)        |
|                             | COPD                  | 1.23        | (0.93-1.62)        | 1.12             | (0.80-1.56)        | 1.03         | (0.64-1.68)        | 1.18         | (0.75-1.81)        |
|                             | Chronic renal failure | 0.88        | (0.61-1.26)        | 1.07             | (0.72-1.59)        | 1.25         | (0.74-2.10)        | 1.01         | (0.62-1.79)        |
|                             | Stroke                | 0.86        | (0.51-1.45)        | <b>1.64</b>      | <b>(1.01-2.60)</b> | 1.78         | (0.92-3.42)        | 1.83         | (0.94-3.33)        |

AMI: acute myocardial infarction; CI: confidence interval; COPD: chronic obstructive pulmonary disease; IHD: ischemic heart disease, pulmonary disease; OR: odds ratio.

The reference category is the nearly-always adherent trajectory group. In bold significant covariates ( $p < 0.05$ ) are marked. Estimates for peripheral vascular disease, cancer and dementia were not included due to their high random error.

Table C. Predictors of poor or intermediate adherence trajectory groups for beta-blocker. Multinomial logistic regression analysis.

|                             |                       | Occasional users |                    | Slow decline |                    | Fast decline |                    |
|-----------------------------|-----------------------|------------------|--------------------|--------------|--------------------|--------------|--------------------|
|                             |                       | OR               | 95%CI              | OR           | 95%CI              | OR           | 95%CI              |
| Age                         | <45 years             | 1.05             | (0.70-1.58)        | 1.79         | (0.96-3.36)        | 1.08         | (0.62-1.93)        |
|                             | 45 to 64              | 0.93             | (0.75-1.16)        | 1.02         | (0.67-1.55)        | 0.92         | (0.68-1.29)        |
|                             | 65 to 79              | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | 80 and over           | 1.00             | (0.82-1.23)        | 1.40         | (0.98-2.00)        | <b>1.51</b>  | <b>(1.17-1.95)</b> |
| Gender                      | Male                  | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | Female                | 0.96             | (0.81-1.13)        | 1.18         | (0.89-1.57)        | 0.94         | (0.75-1.17)        |
| Country of birth            | Spain                 | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | Other                 | 1.21             | (0.97-1.51)        | 1.95         | (0.86-2.64)        | <b>1.46</b>  | <b>(1.09-1.94)</b> |
| Copayment                   | Yes                   | <b>1.45</b>      | <b>(1.16-1.82)</b> | <b>2.25</b>  | <b>(1.49-3.37)</b> | <b>1.84</b>  | <b>(1.32-2.53)</b> |
|                             | No                    | 1.00             |                    | 1.00         |                    | 1.00         |                    |
| Main diagnosis at discharge | AMI                   | 1.00             |                    | 1.00         |                    | 1.00         |                    |
|                             | Unstable angina       | 1.02             | (0.83-1.27)        | <b>1.45</b>  | <b>(1.02-2.06)</b> | 0.99         | (0.73-1.32)        |
|                             | Stable angina         | 1.23             | (0.99-1.52)        | 0.86         | (0.55-1.33)        | <b>1.55</b>  | <b>(1.17-2.01)</b> |
|                             | Other CHD             | <b>1.23</b>      | <b>(1.03-1.48)</b> | 1.34         | (0.96-1.85)        | <b>0.72</b>  | <b>(0.53-0.95)</b> |
| Comorbidities               | Hypertension          | <b>1.24</b>      | <b>(1.07-1.45)</b> | 1.09         | (0.83-1.42)        | 1.16         | (0.95-1.44)        |
|                             | Hyperlipidemia        | 1.00             | (0.87-1.16)        | 0.88         | (0.68-1.14)        | <b>0.81</b>  | <b>(0.67-0.99)</b> |
|                             | Diabetes              | 0.96             | (0.83-1.12)        | 0.94         | (0.71-1.23)        | 0.94         | (0.77-1.17)        |
|                             | Smoking               | <b>1.24</b>      | <b>(1.04-1.49)</b> | 1.03         | (0.75-1.43)        | 0.93         | (0.71-1.20)        |
|                             | Arrhythmias           | 1.09             | (0.90-1.31)        | <b>1.60</b>  | <b>(1.18-2.17)</b> | 1.23         | (0.96-1.56)        |
|                             | Heart failure         | 1.00             | (0.81-1.23)        | 1.07         | (0.74-1.53)        | <b>1.37</b>  | <b>(1.07-1.80)</b> |
|                             | COPD                  | 1.16             | (0.82-1.62)        | 0.72         | (0.34-1.52)        | 1.36         | (0.87-2.11)        |
|                             | Chronic renal failure | 1.30             | (0.93-1.82)        | 1.51         | (0.86-2.64)        | 1.29         | (0.83-1.98)        |
|                             | Stroke                | 1.17             | (0.73-1.86)        | 1.39         | (0.64-3.00)        | 1.54         | (0.88-2.69)        |

AMI: acute myocardial infarction; CI: confidence interval; COPD: chronic obstructive pulmonary disease; IHD: ischemic heart disease, pulmonary disease; OR: odds ratio.

The reference category is the nearly-always adherent trajectory group. . In bold significant covariates ( $p < 0.05$ ) are marked. Estimates for peripheral vascular disease, cancer and dementia were not included due to their high random error.

Table D. Predictors of poor or intermediate adherence trajectory groups for ACEI/ARB.  
Multinomial logistic regression analysis.

|                             |                       | Occasional users |                    | Slow decline       |                    | Fast decline |                    |
|-----------------------------|-----------------------|------------------|--------------------|--------------------|--------------------|--------------|--------------------|
|                             |                       | OR               | 95%CI              | OR                 | 95%CI              | OR           | 95%CI              |
| Age                         | <45 years             | 1.47             | (0.93-2.30)        | 1.59               | (0.81-3.08)        | 1.05         | (0.58-1.94)        |
|                             | 45 to 64              | 0.98             | (0.77-1.25)        | 1.08               | (0.74-1.57)        | 0.79         | (0.57-1.13)        |
|                             | 65 to 79              | 1.00             |                    | 1.00               |                    | 1.00         |                    |
|                             | 80 and over           | 0.95             | (0.77-1.17)        | <b>1.62</b>        | <b>(1.21-2.19)</b> | <b>1.48</b>  | <b>(1.14-1.87)</b> |
| Gender                      | Male                  | 1.00             |                    | 1.00               |                    | 1.00         |                    |
|                             | Female                | 1.13             | (0.95-1.34)        | 0.85               | (0.65-1.11)        | 1.12         | (0.90-1.39)        |
| Country of birth            | Spain                 | 1.00             |                    | 1.00               |                    | 1.00         |                    |
|                             | Other                 | <b>1.28</b>      | <b>(1.01-1.62)</b> | <b>1.45</b>        | <b>(1.03-2.03)</b> | <b>1.64</b>  | <b>(1.23-2.17)</b> |
| Copayment                   | Yes                   | <b>1.52</b>      | <b>(1.18-1.96)</b> | <b>1.79</b>        | <b>(1.23-2.67)</b> | <b>2.46</b>  | <b>(1.70-3.42)</b> |
|                             | No                    | 1.00             |                    | 1.00               |                    | 1.00         |                    |
| Main diagnosis at discharge | AMI                   | 1.00             |                    | 1.00               |                    | 1.00         |                    |
|                             | Unstable angina       | 1.07             | (0.85-1.34)        | 1.16               | (0.84-1.59)        | 0.92         | (0.68-1.22)        |
|                             | Stable angina         | 1.21             | (0.98-1.52)        | 0.97               | (0.67-1.38)        | 1.12         | (0.83-1.47)        |
|                             | Other CHD             | 1.32             | (1.08-1.62)        | 1.09               | (0.79-1.47)        | 1.11         | (0.85-1.45)        |
| Comorbidities               | Hypertension          | 0.84             | (0.71-0.99)        | 0.88               | (0.69-1.13)        | 1.15         | (0.93-1.44)        |
|                             | Hyperlipidemia        | 0.89             | (0.77-1.05)        | 0.99               | (0.79-1.25)        | 0.95         | (0.79-1.17)        |
|                             | Diabetes              | 0.98             | (0.84-1.15)        | <b>1.31</b>        | <b>(1.04-1.66)</b> | 0.92         | (0.76-1.14)        |
|                             | Smoking               | 1.12             | (0.91-1.37)        | 0.95               | (0.69-1.28)        | 0.97         | (0.74-1.26)        |
|                             | Arrhythmias           | 0.92             | (0.76-1.12)        | 0.84               | (0.62-1.12)        | 1.09         | (0.87-1.38)        |
|                             | Heart failure         | <b>1.26</b>      | <b>(1.18-1.96)</b> | 1.07               | (0.78-1.46)        | 1.23         | (0.97-1.62)        |
|                             | COPD                  | 1.22             | (0.91-1.64)        | 0.99               | (0.62-1.57)        | <b>1.52</b>  | <b>(1.06-2.14)</b> |
|                             | Chronic renal failure | 1.16             | (0.81-1.67)        | 1.20               | (0.71-2.03)        | 1.82         | (1.23-2.63)        |
| Stroke                      | 1.19                  | (0.72-1.94)      | <b>2.60</b>        | <b>(1.51-4.46)</b> | 1.75               | (1.01-2.97)  |                    |

AMI: acute myocardial infarction; CI: confidence interval; COPD: chronic obstructive pulmonary disease; IHD: ischemic heart disease, pulmonary disease; OR: odds ratio; ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blockers.

The reference category is the nearly-always adherent trajectory group. . In bold significant covariates ( $p < 0.05$ ) are marked. Estimates for peripheral vascular disease, cancer and dementia were not included due to their high random error.

Table E. Predictors of poor or intermediate adherence trajectory groups for statins.  
Multinomial logistic regression analysis.

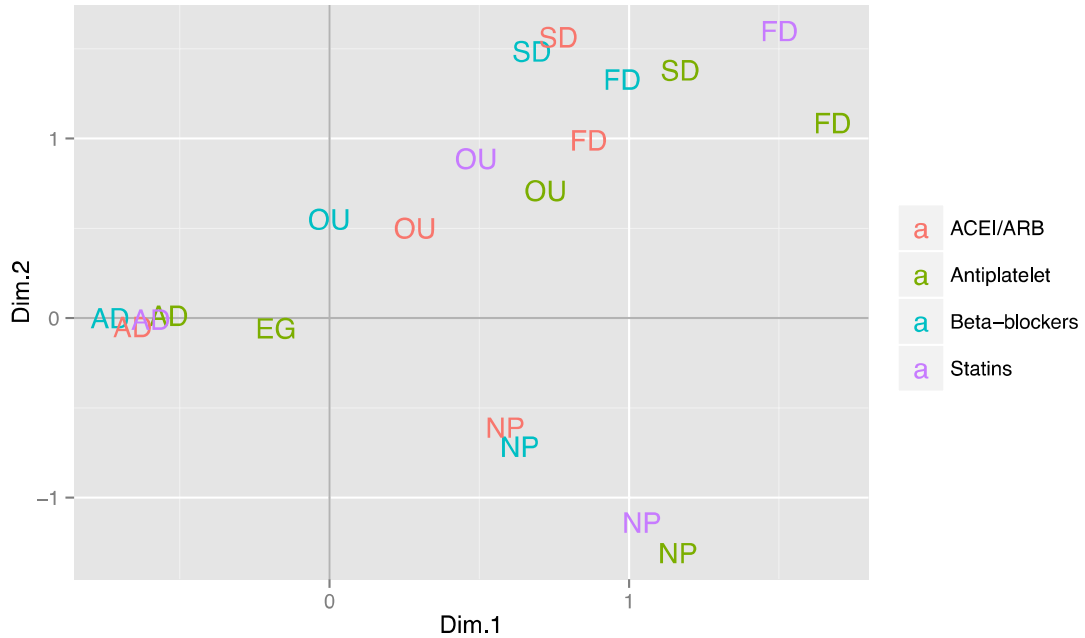
|                             |                       | Occasional users |                    | Fast decline |                    |
|-----------------------------|-----------------------|------------------|--------------------|--------------|--------------------|
|                             |                       | OR               | 95%CI              | OR           | 95%CI              |
| Age                         | <45 years             | <b>1.79</b>      | <b>(1.22-2.58)</b> | 1.55         | (0.92-2.64)        |
|                             | 45 to 64              | 1.11             | (0.89-1.40)        | 0.92         | (0.66-1.32)        |
|                             | 65 to 79              | 1.00             |                    | 1.00         |                    |
|                             | 80 and over           | <b>1.25</b>      | <b>(1.02-1.53)</b> | <b>1.45</b>  | <b>(1.09-1.91)</b> |
| Gender                      | Male                  | 1.00             |                    | 1.00         |                    |
|                             | Female                | 1.1              | (0.93-1.29)        | 1.12         | (0.89-1.42)        |
| Country of birth            | Spain                 | 1.00             |                    | 1.00         |                    |
|                             | Other                 | 1.18             | (0.95-1.46)        | <b>1.79</b>  | <b>(1.34-2.32)</b> |
| Copayment                   | Yes                   | <b>2.02</b>      | <b>(1.61-2.52)</b> | <b>2.85</b>  | <b>(2.00-3.95)</b> |
|                             | No                    | 1.00             |                    | 1.00         |                    |
| Main diagnosis at discharge | AMI                   | 1.00             |                    | 1.00         |                    |
|                             | Unstable angina       | <b>1.57</b>      | <b>(1.29-1.91)</b> | 1.23         | (0.89-1.64)        |
|                             | Stable angina         | <b>1.49</b>      | <b>(1.20-1.84)</b> | <b>1.76</b>  | <b>(1.30-2.31)</b> |
|                             | Other CHD             | <b>1.33</b>      | <b>(1.10-1.60)</b> | 1.15         | (0.87-1.51)        |
| Comorbidities               | Hypertension          | 0.97             | (0.84-1.13)        | 0.95         | (0.77-1.18)        |
|                             | Hyperlipidemia        | 0.91             | (0.79-1.05)        | 0.81         | (0.67-1.01)        |
|                             | Diabetes              | <b>1.28</b>      | <b>(1.10-1.48)</b> | 1.07         | (0.87-1.35)        |
|                             | Smoking               | <b>1.30</b>      | <b>(1.09-1.55)</b> | 1.11         | (0.85-1.42)        |
|                             | Arrhythmias           | 1.07             | (0.89-1.28)        | 1.21         | (0.95-1.57)        |
|                             | Heart failure         | <b>1.24</b>      | <b>(1.01-1.52)</b> | <b>1.33</b>  | <b>(1.02-1.78)</b> |
|                             | COPD                  | 1.51             | (0.80-1.41)        | <b>1.06</b>  | <b>(1.04-2.18)</b> |
|                             | Chronic renal failure | 1.63             | (0.88-1.69)        | <b>1.22</b>  | <b>(1.07-2.46)</b> |
| Stroke                      | 1.33                  | (0.64-1.64)      | 1.03               | (0.72-2.42)  |                    |

AMI: acute myocardial infarction; CI: confidence interval; COPD: chronic obstructive pulmonary disease; IHD: ischemic heart disease, pulmonary disease; OR: odds ratio.

The reference category is the nearly-always adherent trajectory group. . In bold significant covariates ( $p < 0.05$ ) are marked. Estimates for peripheral vascular disease, cancer and dementia were not included due to their high random error.

SUPPORTING FIGURES

**Figure A. Multiple correspondence analysis (MCA) plot for the adherence trajectories of the four therapeutic groups (N=7,462).** AD: adherent; EG: early gap; OU: occasional users; SD: slow decline; FD: fast decline, NP: no prescription; ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blockers. The relative position of the categories indicates the level of association between the categories. The closer the categories are, the stronger is the relationship between the categories. Cumulative variance: 22.8 % for the 2 dimensions plotted.



**Figure B. Adherence trajectory patterns to three or more therapeutic groups (N= 5,717).** AD: adherent; EG: early gap; SD: slow decline; FD: fast decline.

