Additional file 9

Analysis for the diagnosis 'any dementia'

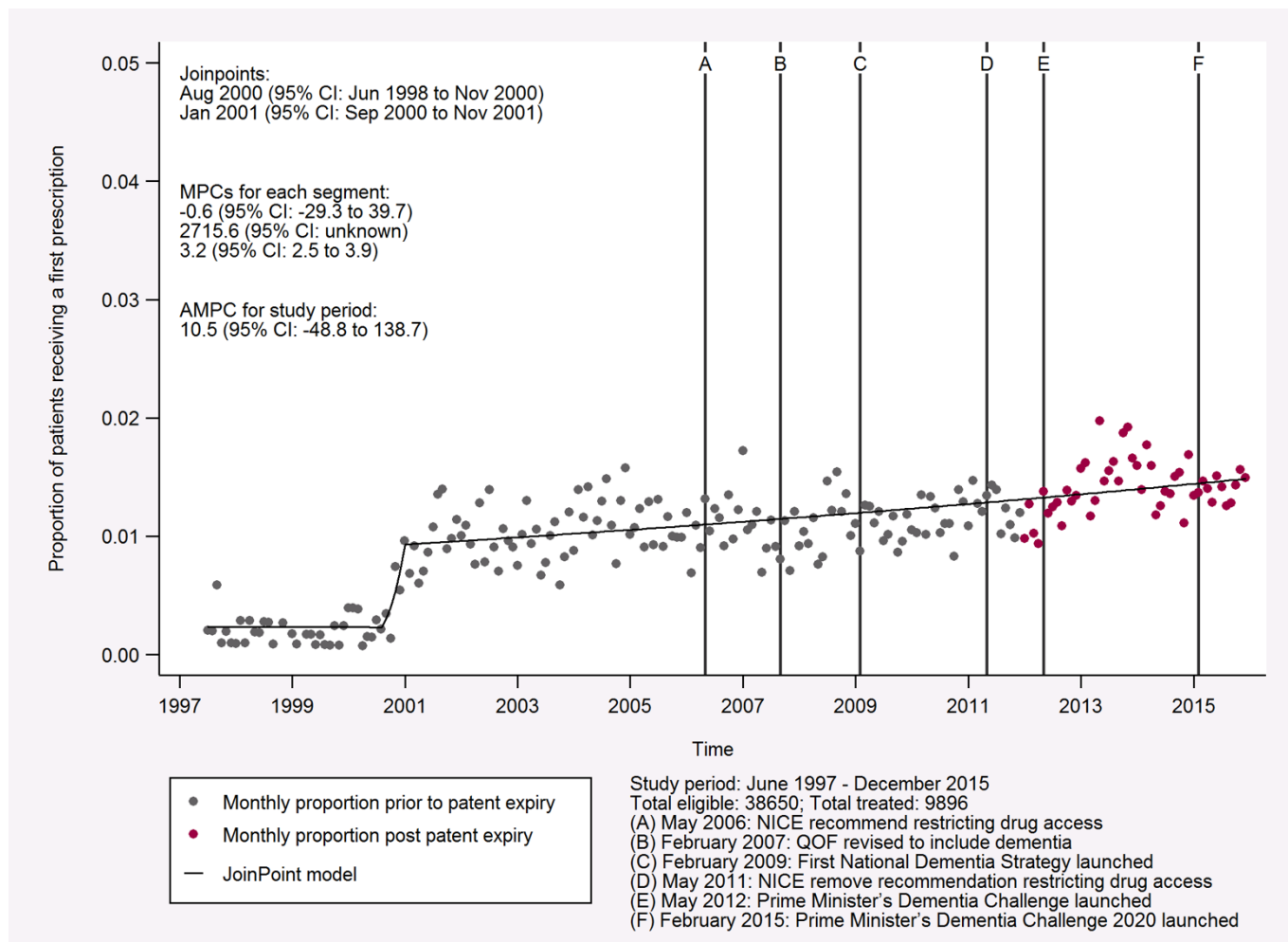This analysis considers patients with one of the following diagnoses:
- Probable Alzheimer's disease
- Possible Alzheimer's disease
- Vascular dementia
- Other dementia
- Mixed including probable Alzheimer's disease
- Mixed including possible Alzheimer's disease
- Mixed excluding Alzheimer's disease
- Undiagnosed dementia

Table S9.1: The number of treated patients and relevant dates for the 'any dementia' analyses.

| Analysis | First record in CPRD | Analysis start date | Treated patients | Eligible patients |
|---|---|---|---|---|
| AChE inhibitors | 30/05/1997 | 01/06/1997 | 9896 | 38650 |
| NMDA receptor antagonists | 16/12/2002 | 01/01/2003 | 1961 | 35625 |
| Donepezil | 30/05/1997 | 01/06/1997 | 7611 | 38650 |
| Rivastigmine | 29/09/1998 | 01/10/1998 | 1621 | 38130 |
| Galantamine | 12/01/2001 | 01/02/2001 | 1188 | 36994 |

*Note that donepezil, rivastigmine and galantamine are acetylcholinesterase (AChE) inhibitors and memantine is an N-Methyl-D-aspartate (NMDA) receptor antagonist. The end date of the study is 31/12/2015.*

Figure S9.1: Indicative graph of acetylcholinesterase (AChE) inhibitor prescriptions in patients with any dementia.
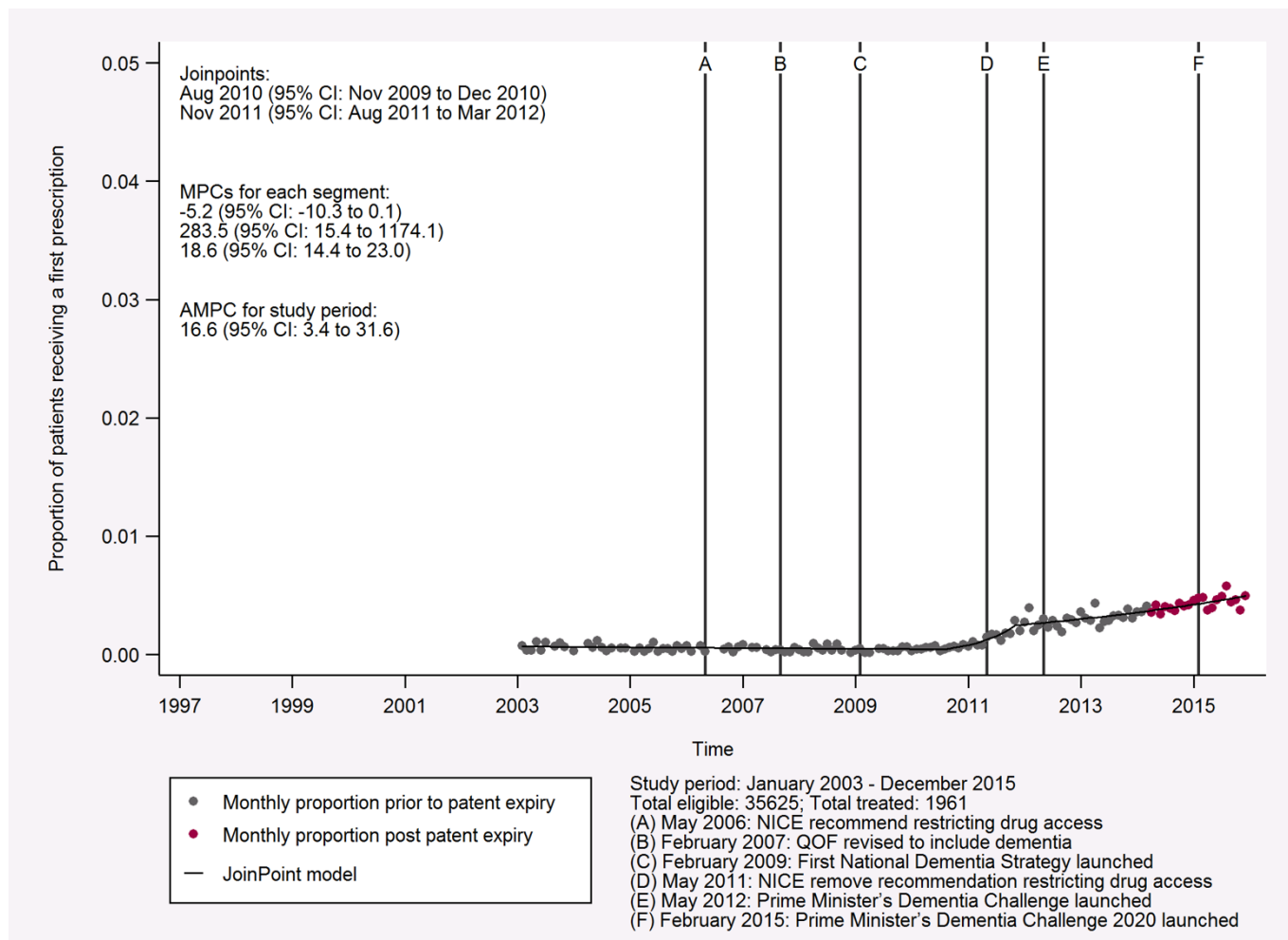


*This graph shows the proportion of patients with any dementia receiving their first prescription for an AChE inhibitor (donepezil, rivastigmine, galantamine) each month from June 1997 to December 2015. The fixed lines indicate events with the potential to effect prescription rates during the study period. The joinpoints, monthly percent change (MPC) for each segment and the average monthly percent change (AMPC) for the entire study period are also presented.*

Table S9.2: Joinpoint analysis output for acetylcholinesterase (AChE) inhibitor prescriptions in patients with any dementia.

|  | Segment 1 | Segment 2 | Segment 3 |
|---|---|---|---|
| Joinpoint | Not applicable | August 2000 | January 2001 |
| Joinpoint 95% LCL | Not applicable | June 1998 | September 2000 |
| Joinpoint 95% UCL | Not applicable | November 2000 | November 2001 |
| Intercept estimate | 6.837 | -6683.509 | -67.325 |
| Intercept standard error | 345.577 | 34621.871 | 6.807 |
| Intercept test statistic | 0.020 | -0.193 | -9.890 |
| Intercept p-value | 0.984 | 0.847 | 0.000 |
| Slope estimate | -0.006 | 3.338 | 0.031 |
| Slope standard error | 0.173 | 17.305 | 0.003 |
| Slope test statistic | -0.037 | 0.193 | 9.248 |
| Slope p-value | 0.970 | 0.847 | 0.000 |
| Slope change estimate | Not applicable | 3.344 | -3.306 |
| Slope change standard error | Not applicable | 17.305 | 17.305 |
| Slope change test statistic | Not applicable | 0.193 | -0.191 |
| Slope change p-value | Not applicable | 0.847 | 0.849 |

*Output from the joinpoint analysis of the proportion of patients with any dementia receiving their first prescription for an AChE inhibitor (donepezil, rivastigmine, galantamine) each month from June 1997 to December 2015. Segments are the period between two join points and are numbered chronologically. Segment 1 begins in June 1997 and the remaining segments begin with each joinpoint. Segment 3 ends in December 2015.*

Figure S9.2: Indicative graph N-Methyl-D-aspartate (NMDA) receptor antagonist prescriptions in patients with probable Alzheimer's disease.
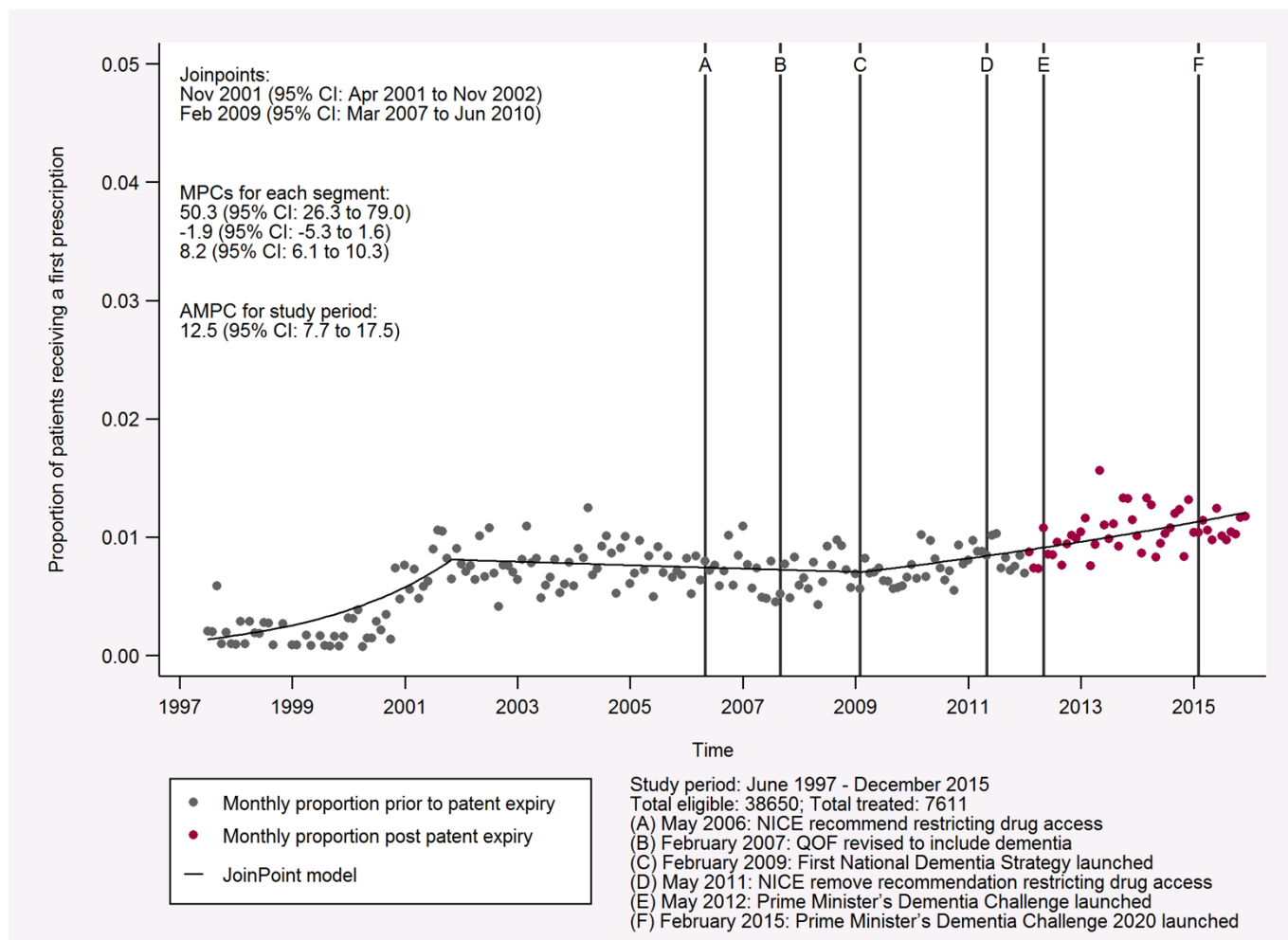


*This graph shows the proportion of patients with any dementia receiving their first prescription for an NMDA receptor antagonist (memantine) each month from January 2003 to December 2015. The fixed lines indicate events with the potential to effect prescription rates during the study period. The joinpoints, monthly percent change (MPC) for each segment and the average monthly percent change (AMPC) for the entire study period are also presented.*

Table S9.3: Joinpoint analysis output for N-Methyl-D-aspartate (NMDA) receptor antagonist prescriptions in patients with any dementia.

|  | Segment 1 | Segment 2 | Segment 3 |
|---|---|---|---|
| Joinpoint | Not applicable | August 2010 | November 2011 |
| Joinpoint 95% LCL | Not applicable | November 2009 | August 2011 |
| Joinpoint 95% UCL | Not applicable | December 2010 | March 2012 |
| Intercept estimate | 100.313 | -2710.001 | -349.231 |
| Intercept standard error | 55.359 | 1219.196 | 36.632 |
| Intercept test statistic | 1.812 | -2.223 | -9.534 |
| Intercept p-value | 0.073 | 0.028 | 0.000 |
| Slope estimate | -0.054 | 1.344 | 0.171 |
| Slope standard error | 0.028 | 0.606 | 0.018 |
| Slope test statistic | -1.947 | 2.217 | 9.382 |
| Slope p-value | 0.054 | 0.029 | 0.000 |
| Slope change estimate | Not applicable | 1.398 | -1.173 |
| Slope change standard error | Not applicable | 0.607 | 0.606 |
| Slope change test statistic | Not applicable | 2.303 | -1.935 |
| Slope change p-value | Not applicable | 0.023 | 0.055 |

*Output from the joinpoint analysis of the proportion of patients with any dementia receiving their first prescription for an NMDA receptor antagonist (memantine) each month from January 2003 to December 2015 Segments are the period between two join points and are numbered chronologically. Segment 1 begins in January 2003 and the remaining segments begin with each joinpoint. Segment 3 ends in December 2015.*

Figure S9.3: Indicative graph of donepezil prescriptions in patients with any dementia.
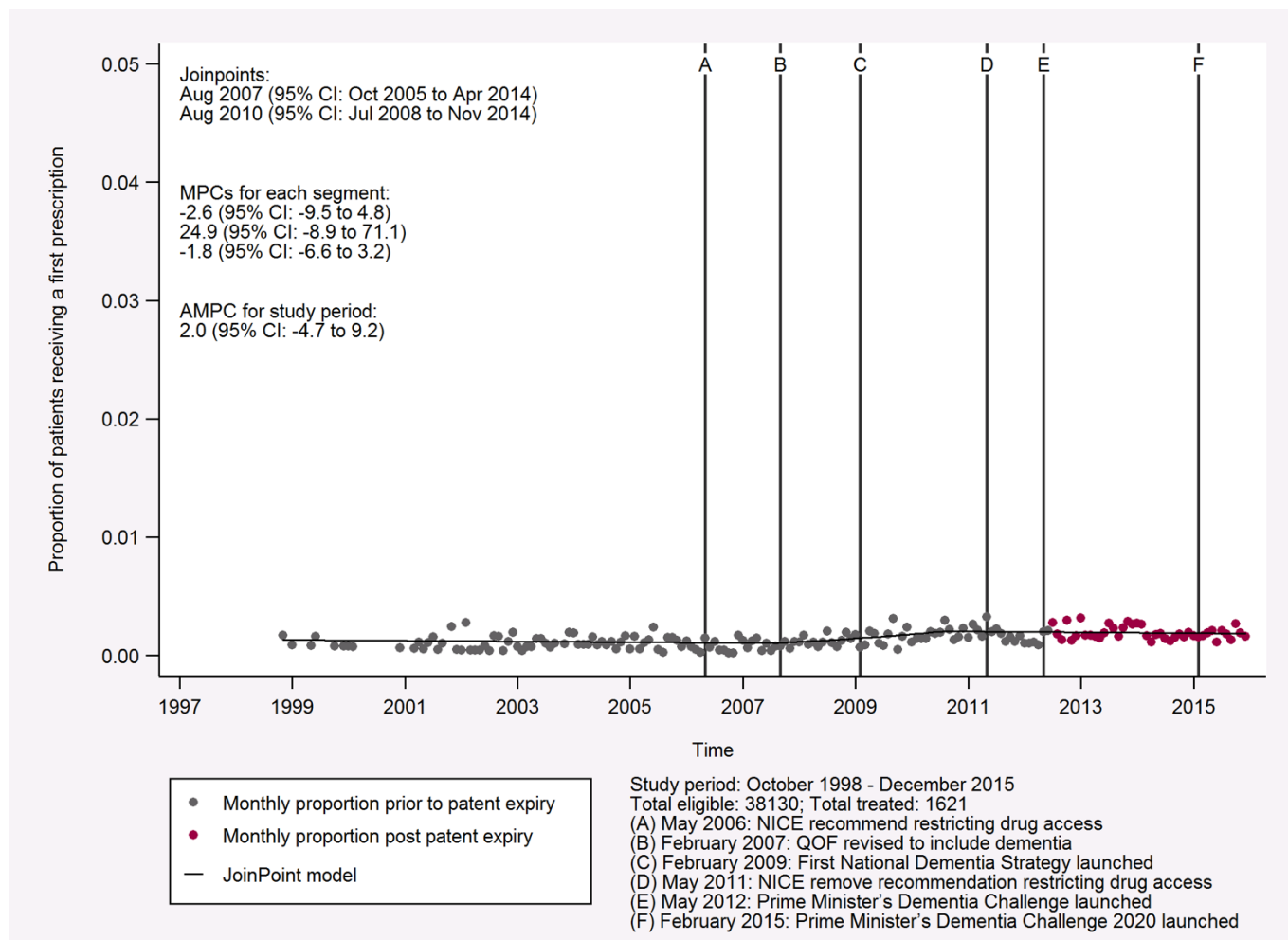


*This graph shows the proportion of patients with any dementia receiving their first prescription for donepezil each month from June 1997 to December 2015. The fixed lines indicate events with the potential to effect prescription rates during the study period. The joinpoints, monthly percent change (MPC) for each segment and the average monthly percent change (AMPC) for the entire study period are also presented.*

Table S9.4: Joinpoint analysis output for donepezil prescriptions in patients with any dementia.

|  | Segment 1 | Segment 2 | Segment 3 |
|---|---|---|---|
| Joinpoint | Not applicable | November 2001 | February 2009 |
| Joinpoint 95% LCL | Not applicable | April 2001 | March 2007 |
| Joinpoint 95% UCL | Not applicable | November 2002 | June 2010 |
| Intercept estimate | -821.143 | 33.594 | -163.100 |
| Intercept standard error | 177.033 | 36.026 | 19.951 |
| Intercept test statistic | -4.638 | 0.932 | -8.175 |
| Intercept p-value | 0.000 | 0.352 | 0.000 |
| Slope estimate | 0.408 | -0.019 | 0.079 |
| Slope standard error | 0.089 | 0.018 | 0.010 |
| Slope test statistic | 4.606 | -1.068 | 7.944 |
| Slope p-value | 0.000 | 0.287 | 0.000 |
| Slope change estimate | Not applicable | -0.427 | 0.098 |
| Slope change standard error | Not applicable | 0.090 | 0.021 |
| Slope change test statistic | Not applicable | -4.727 | 4.773 |
| Slope change p-value | Not applicable | 0.000 | 0.000 |

*Output from the joinpoint analysis of the proportion of patients with any dementia receiving their first prescription for donepezil each month from June 1997 to December 2015. Segments are the period between two join points and are numbered chronologically. Segment 1 begins in June 1997 and the remaining segments begin with each joinpoint. Segment 3 ends in December 2015.*

Figure S9.4: Indicative graph of rivastigmine prescriptions in patients with any dementia.
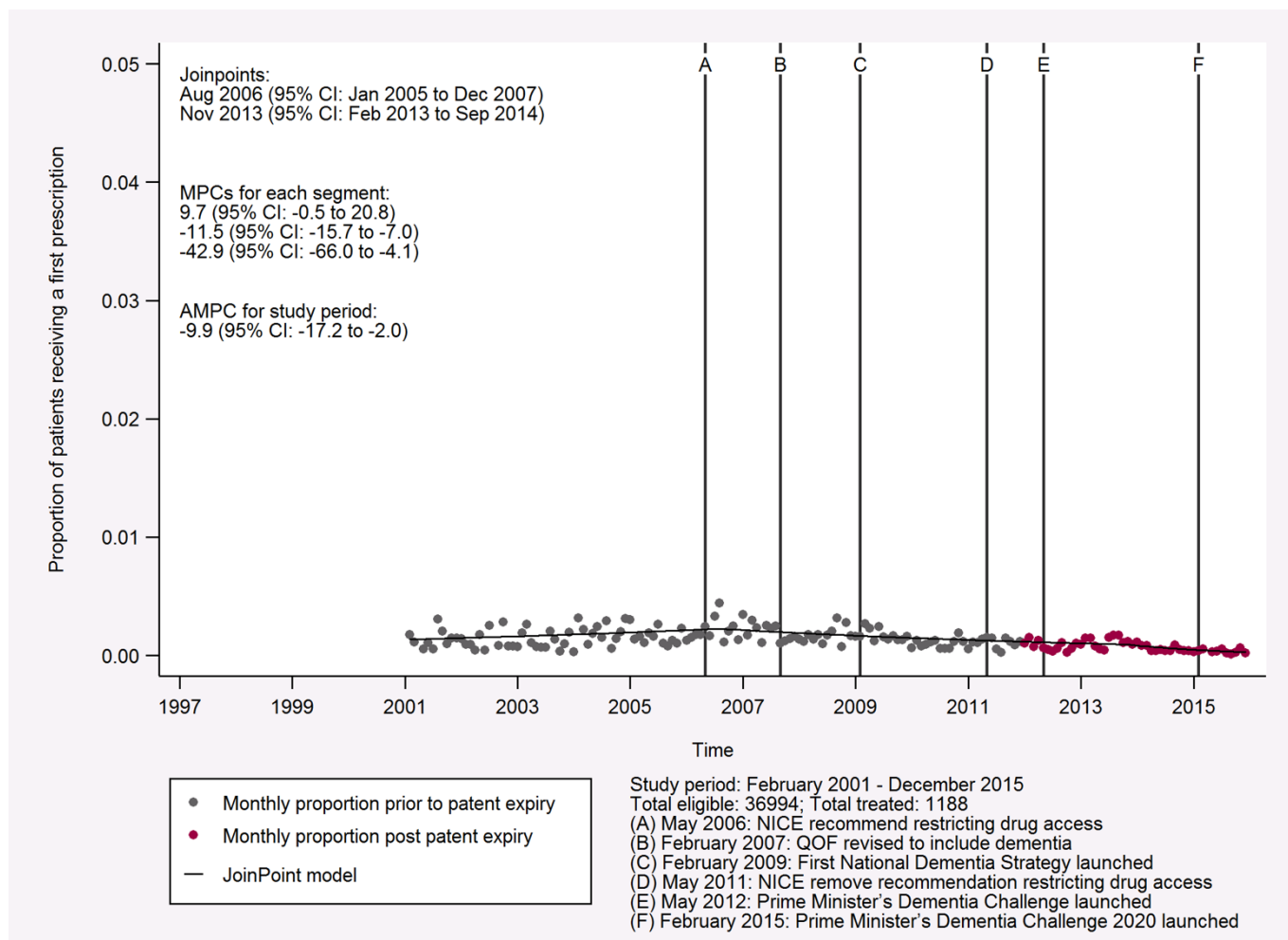


This graph shows the proportion of patients with any dementia receiving their first prescription for rivastigmine each month from October 1998 to December 2015. The fixed lines indicate events with the potential to effect prescription rates during the study period. The joinpoints, monthly percent change (MPC) for each segment and the average monthly percent change (AMPC) for the entire study period are also presented.

Table S9.5: Joinpoint analysis output for rivastigmine prescriptions in patients with any dementia.

|  | Segment 1 | Segment 2 | Segment 3 |
|---|---|---|---|
| Joinpoint | Not applicable | August 2007 | August 2010 |
| Joinpoint 95% LCL | Not applicable | October 2005 | July 2008 |
| Joinpoint 95% UCL | Not applicable | April 2014 | November 2014 |
| Intercept estimate | 46.011 | -452.677 | 30.805 |
| Intercept standard error | 74.337 | 320.359 | 50.930 |
| Intercept test statistic | 0.619 | -1.413 | 0.605 |
| Intercept p-value | 0.537 | 0.160 | 0.546 |
| Slope estimate | -0.026 | 0.222 | -0.018 |
| Slope standard error | 0.037 | 0.159 | 0.025 |
| Slope test statistic | -0.710 | 1.393 | -0.727 |
| Slope p-value | 0.479 | 0.166 | 0.468 |
| Slope change estimate | Not applicable | 0.248 | -0.240 |
| Slope change standard error | Not applicable | 0.164 | 0.161 |
| Slope change test statistic | Not applicable | 1.517 | -1.490 |
| Slope change p-value | Not applicable | 0.131 | 0.138 |

*Output from the joinpoint analysis of the proportion of patients with any dementia receiving their first prescription for rivastigmine each month from October 1998 to December 2015 Segments are the period between two join points and are numbered chronologically. Segment 1 begins in October 1998 and the remaining segments begin with each joinpoint. Segment 3 ends in December 2015.*

Figure S9.5: Indicative graph of galantamine prescriptions in patients with any dementia.



*This graph shows the proportion of patients with any dementia receiving their first prescription for galantamine each month from February 2001 to December 2015. The fixed lines indicate events with the potential to effect prescription rates during the study period. The joinpoints, monthly percent change (MPC) for each segment and the average monthly percent change (AMPC) for the entire study period are also presented.*

Table S9.6: Joinpoint analysis output for galantamine prescriptions in patients with any dementia.

| | Segment 1 | Segment 2 | Segment 3 |
|---|---|---|---|
| Joinpoint | Not applicable | August 2006 | November 2013 |
| Joinpoint 95% LCL | Not applicable | January 2005 | February 2013 |
| Joinpoint 95% UCL | Not applicable | December 2007 | September 2014 |
| Intercept estimate | -191.240 | 238.361 | 1122.422 |
| Intercept standard error | 98.265 | 50.315 | 528.582 |
| Intercept test statistic | -1.946 | 4.737 | 2.123 |
| Intercept p-value | 0.054 | 0.000 | 0.035 |
| Slope estimate | 0.092 | -0.122 | -0.561 |
| Slope standard error | 0.049 | 0.025 | 0.262 |
| Slope test statistic | 1.882 | -4.867 | -2.138 |
| Slope p-value | 0.062 | 0.000 | 0.034 |
| Slope change estimate | Not applicable | -0.214 | -0.439 |
| Slope change standard error | Not applicable | 0.055 | 0.263 |
| Slope change test statistic | Not applicable | -3.889 | -1.666 |
| Slope change p-value | Not applicable | 0.000 | 0.098 |

*Output from the joinpoint analysis of the proportion of patients with any dementia receiving their first prescription for galantamine each month from February 2001 to December 2015. Segments are the period between two join points and are numbered chronologically. Segment 1 begins in February 2001 and the remaining segments begin with each joinpoint. Segment 3 ends in December 2015.*