

**Prescriber variation in relation to prescribing trends within the Preferred Drugs Initiative in Ireland (2012-2015):
an interrupted time series study using latent curve models: Appendices**

Table A1: Model fitting steps: PPIs & statins

[illegible]

Medicine group	Model	Model fitted	No free parms	Log-likelihood	Correction factor for MLR	AIC	BIC	SSA-BIC	RMSEA (90%CI), p-value	CFI	TLI	SRMR	Satorra-Bentler test	Comments
	3a	2b + remove var(change of level)†	38	-82610.43	28.94	165296.86	165511.44	165390.71	0.02(0.02,0.03), p=1.00	0.97	0.97	0.04	3a v 2b: p=0.17	
	3b	2a + remove var(slope post-guidelines) †	38	-82561.14	27.70	165198.28	165412.86	165292.13	0.02(0.02,0.03), p=1.00	0.97	0.97	0.04	3b v 2b: p=0.53	Selected univariate model
	4a	3b+remove var(change of level)+	36	-82639.29	27.91	165350.59	165553.87	165439.50	0.02(0.02,0.03), p=1.00	0.97	0.97	0.04	4a v 3b: p=0.03	
PPIs & statins (bivariate model)	1	PPIs model 2b & statins model 3b: add time-specific correlations plus covariances between latent factors	101	-185853.52	16.55	371909.04	372481.09	372160.20	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03		
	2	1+ equality of time-specific correlations (2 nd quarter onwards)	87	-185896.76	18.25	371967.53	372460.28	372183.87	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03	2 v 1: p=0.42	
	3	2+ add autoregressive components among the residuals across both outcomes	117	-185754.84	15.01	374743.68	372406.36	372034.63	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03	2 v 3: p=0.01	
	4a	3+ add AR(1) structure to PPI residuals	103	-185904.83	15.80	372015.66	372599.04	372271.79	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03	4a v 3: p<0.001	
	4b	3+ add AR(1) structure to statin residuals	103	-186026.61	14.10	372259.21	378842.59	372515.35	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03	4b v 3: p=0.03	
	5a	3+ impose equality on autoregressive components from PPIs to statins	103	-185791.25	16.39	371788.50	372371.88	372044.64	0.02(0.02,0.02), p=1.00	0.98	0.98	0.03	5a v 3: p=0.38	Selected unconditional bivariate model
	5b	3+ impose equality on autoregressive components from statins to PPIs	103	-185838.55	16.38	371883.10	372466.48	372139.24	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03	5b v3: p=0.003	
	6	Conditional model (5a+no of patients/% of patients >=65 years Jan-Mar 2012)	119	-179168.51	13.69	358575.02	359245.56	358867.49	0.02(0.02,0.02), p=1.00	0.98	0.97	0.03		

No free parms: number of free parameters; MLR: maximum likelihood robust; AIC: aikake information criterion; BIC: bayesian information criterion; SSA-BIC: sample-size adjusted bayesian information criterion; RMSEA: root mean square error of approximation; CFI: comparative fit index; TLI: Tucker-Lewis index; SRMR: standardised root mean square residual; PPIs: proton pump inhibitors; LCM: latent curve model; LCM-SR: latent curve model with structured residuals; † removal of variance and associated covariance terms; IC: information criterion; AR(1): first order autoregressive

Medicine group	Model	Model fitted	No free parms	Log-likelihood	Correction factor for MLR	AIC	BIC	SSA-BIC	RMSEA (90%CI), p-value	CFI	TLI	SRMR	Satorra-Bentler test	Comments
ACEIs/ARB (bivariate model)	1	ACEI model 2a and ARB model 2a: add time-specific correlations plus covariances between latent factors	107	-206920.06	8.27	414054.12	414658.23	414318.28	0.01(0.01,0.02), p=1.00	0.99	0.99	0.02		
	2	1+ equality of time-specific correlations (2 nd quarter onwards)	93	-207002.77	8.95	414191.55	414716.62	414421.14	0.01(0.01,0.02), p=1.00	0.99	0.99	0.02	2 v 1: p<0.001	
	3	1+ add autoregressive components among the residuals across both outcomes	137	-206856.73	7.25	413986.85	414760.34	414325.08	0.01(0.01,0.02), p=1.00	0.99	0.99	0.02	1 v 3: p=0.24	
	4a	3+ add AR(1) structure to ACEI residuals	123	-206943.69	7.28	4141323.37	414827.82	414437.04	0.01(0.01,0.02), p=1.00	0.99	0.99	0.01	4a v 3: p=0.04	
	4b	3+ add AR(1) structure to ARB residuals	123	-206947.80	7.13	414141.60	414836.04	414445.26	0.01(0.01,0.02), p=1.00	0.99	0.99	0.01	4b v 3: p=0.09	
	5a	4b+ impose equality on autoregressive components from ACEIs to ARBs	109	-206982.39	7.54	414182.77	414798.18	414451.87	0.01(0.01,0.02), p=1.00	0.99	0.99	0.01	5a v 4b: p=0.22	
	5b	4b+ impose equality on autoregressive components from ARBs to ACEIs	109	-206987.49	7.51	414192.99	414808.39	414462.08	0.01(0.01,0.01), p=1.00	1.00	1.00	0.02	5b v 4b: p=0.17	
	5c	5a+ impose equality on autoregressive components from ARBs to ACEIs	95	-207006.25	8.13	414202.51	414738.86	414437.04	0.01(0.01,0.01), p=1.00	1.00	1.00	0.02	5c v 5a: p=0.49	Selected unconditional bivariate model
	6	Conditional model (5c+no of patients/% of patients >=65 years Jan-Mar 2012)	111	-198198.74	7.40	396619.49	397241.08	396888.43	0.01(0.01,0.01), p=1.00	1.00	1.00	0.02		

No free parms: number of free parameters; MLR: maximum likelihood robust; AIC: aikake information criterion; BIC: bayesian information criterion; SSA-BIC: sample-size adjusted bayesian information criterion; RMSEA: root= mean square error of approximation; CFI: comparative fit index; TLI: Tucker-Lewis index; SRMR: standardised root mean square residual; ACEIs: angiotensin-converting enzyme inhibitors; ARBs: angiotensin-II receptor blockers; LCM: latent curve model; LCM-SR: latent curve model with structured residuals; † removal of variance and associated covariance terms; AR(1): first order autoregressive

Table A3: Model fitting steps: SNRIs & SSRIs

[illegible]

Medicine group	Model	Model fitted	No free parms	Log-likelihood	Correction factor for MLR	AIC	BIC	SSA-BIC	RMSEA (90%CI), p-value	CFI	TLI	SRMR	Satorra-Bentler test	Comments
SSRIs (univariate model)	1a	LCM: variation between prescribers Jan-Mar12 only	21	-107499.06	8.55	215040.12	215158.46	215091.75	0.11(0.10,0.12), p<0.001	0.72	0.74	0.06		
	1b	LCM: all variance parameters estimated	30	-103436.67	7.38	206933.34	207102.40	207007.09	0.05(0.05,0.06), p=0.09	0.94	0.94	0.02	1a v 1b: p<0.001	
	1c	Baseline LCM-SR	45	-102432.87	7.44	204955.75	205209.34	205066.37	0.02(0.01,0.02), p=1.00	1.00	0.99	0.01	1b v 1c: p<0.001	Selected univariate model
	2a	1c+remove var(change of level-PDI guidelines)†	41	-102445.85	7.88	204973.70	205204.74	205074.48	0.02(0.01,0.02), p=1.00	1.00	0.99	0.01	2a v 1c: p=0.06	
	2b	1c+remove var(slope pre-guidelines) †	41	-102485.27	7.89	205052.54	205283.59	205153.33	0.02(0.02,0.03), p=1.00	0.99	0.99	0.02	2b v 1c: P<0.001	
	2c	1c+remove var(slope post-guidelines) †	41	-102495.39	7.94	205072.78	205303.83	205173.57	0.02(0.02,0.03), p=1.00	0.99	0.99	0.02	2c v 1c: P<0.001	
Medicine group	Model	Model fitted	No free parms	Log-likelihood	Correction factor for MLR	AIC	BIC	SSA-BIC	RMSEA (90%CI), p-value	CFI	TLI	SRMR	Satorra-Bentler test	Comments
SNRIs/SSRIs (bivariate model)	1	SNRI model 3d and SSRI model 1c: add time-specific correlations plus covariances between latent factors	124	-211420.17	4.93	423088.33	423788.36	423394.40	0.01(0.01,0.02), p=1.00	0.99	0.99	0.02		
	2	1+ equality of time-specific correlations (2 nd quarter onwards)	110	-211499.00	5.11	423118.00	423738.99	423389.52	0.01(0.01,0.02), p=1.00	0.99	0.99	0.02	2 v 1: p<0.001	
	3	1+ add autoregressive components among the residuals across both outcomes	154	-211378.57	4.54	423065.14	423934.53	423445.26	0.02(0.01,0.02) p=1.00	0.99	0.99	0.02	1 v 3: p=0.54	
	4a	3+ add AR(1) structure to SNRI residuals	140	-211456.95	4.69	423193.89	423954.25	423539.46	0.02(0.02,0.02), p=1.00	0.99	0.99	0.02	4a v 3: p<0.001	
	4b	3+ add AR(1) structure to SSRI residuals	140	-211445.44	4.36	423170.87	423961.23	423516.43	0.02(0.01,0.02) p=1.00	0.99	0.99	0.02	4b v 3: p=0.06	
	5a	3+ impose equality on autoregressive components from SNRIs to SSRIs	140	-211395.71	4.68	423071.42	423891.77	423416.98	0.02(0.01,0.02) P=1.00	0.99	0.99	0.02	5a v 3: p=0.69	
	5b	3+ impose equality on autoregressive	140	-211397.21	4.66	423074.42	423864.78	423419.98	0.02(0.01,0.02) P=1.00	0.99	0.99	0.02	5b v 3: p=0.68	

		components from SSRIs to SNRIs												
	5c	5a+ impose equality on autoregressive components from SSRIs to SNRIs	126	-211420.03	4.90	423092.06	423803.38	423403.07	0.01(0.01,0.02) p=1.00	0.99	0.99	0.02	5c v 5a: p=0.20	Selected unconditional bivariate model
	6	Conditional model (5c+no of patients/% of patients >=65 years Jan-Mar 2012)	146	-198519.64	4.32	397331.27	398143.42	397679.58	0.01(0.01,0.02) p=1.00	0.99	0.99	0.02		

No free parms: number of free parameters; MLR: maximum likelihood robust; AIC: aikake information criterion; BIC: bayesian information criterion; SSA-BIC: sample-size adjusted bayesian information criterion; RMSEA: root= mean square error of approximation; CFI: comparative fit index; TLI: Tucker-Lewis index; SRMR: standardised root mean square residual; SNRI: serotonin and noradrenaline reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; LCM: latent curve model; LCM-SR: latent curve model with structured residuals; † removal of variance and associated covariance terms; AR(1): first order autoregressive

Table A4: Model fitting steps: urology & beta-blockers

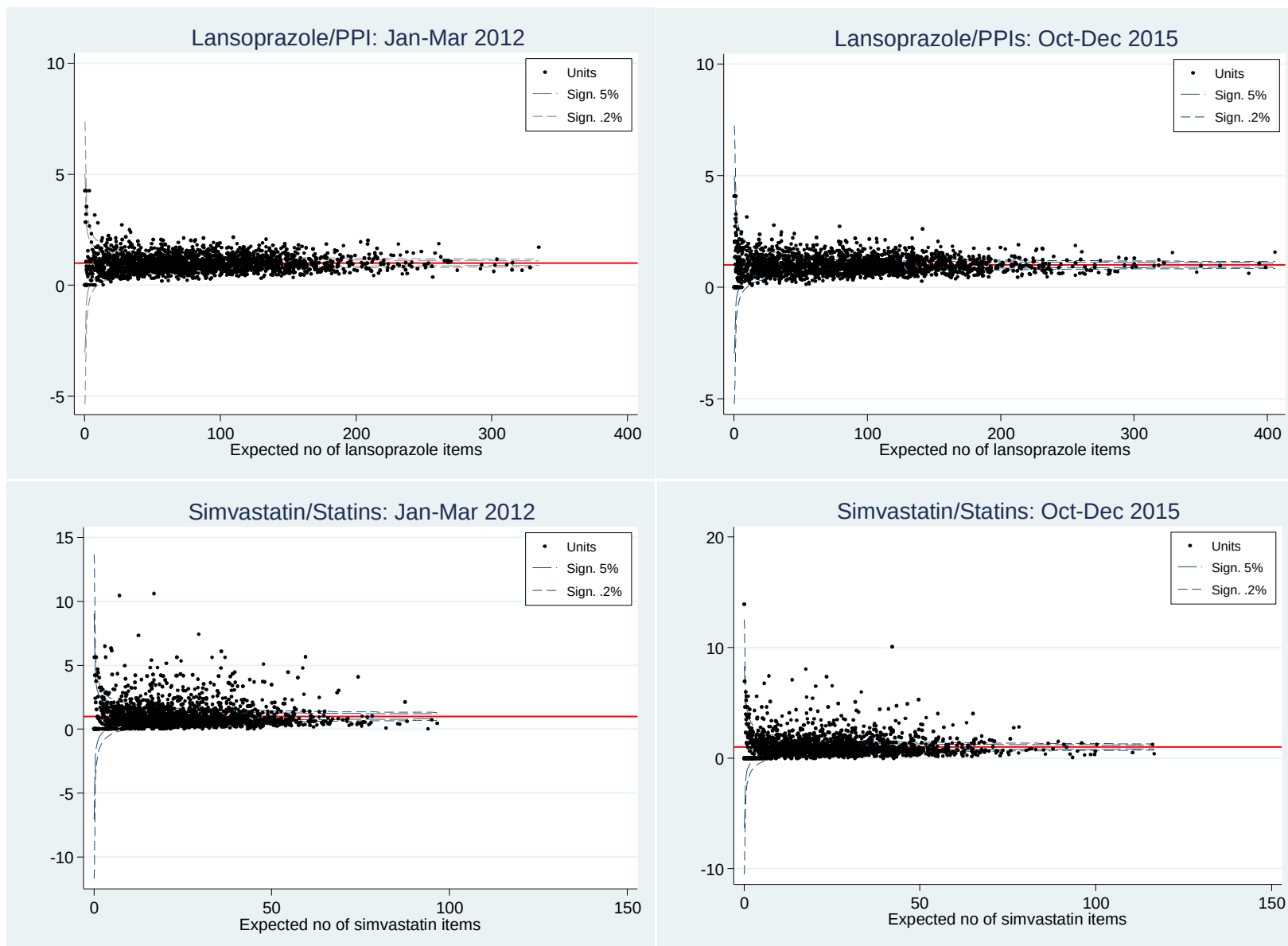
[illegible]

Medicine group	Model	Model fitted	No free parms	Log-likelihood	Correction factor for MLR	AIC	BIC	SSA-BIC	RMSEA (90%CI), p-value	CFI	TLI	SRMR	Satorra-Bentler test	Comments
beta-blockers (univariate model)	1a	LCM: variation between prescribers Jan-Mar12 only	23	-110650.37	7.07	221346.74	221476.58	221403.51	0.09(0.09,0.09), p<0.001	0.74	0.76	0.08		
	1b	LCM: all variance parameters estimated	43	-107036.16	7.35	214158.32	214401.07	214264.46	0.04(0.04,0.05), p=1.00	0.96	0.95	0.03	1a v 1b: p<0.001	
	1c	Baseline LCM-SR	58	-106441.46	7.26	212998.92	213326.36	213142.08	0.00(0.00,0.01), p=1.00	1.00	1.00	0.02	1b v 1c: p<0.001	
	2a	1c+remove var(change of level-PDI guidelines)†	52	-106471.65	7.81	213047.30	213340.86	213175.64	0.01(0.01,0.02), p=1.00	1.00	1.00	0.01		Negative variances
	2b	1c+remove var(slope pre-guidelines) †	52	-106459.72	7.68	213023.43	213316.99	213151.78	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01		Negative variances
	2c	1c+remove var(slope post-guidelines) †	52	-106457.79	7.71	213019.59	213313.15	213147.94	0.01(0.00,0.01), p=1.00	1.00	1.00	0.02	2c v 1c: p=0.14	Lowest IC of 2c, 2d
	2d	1c+remove var(change of level-licensing mirabegron)†	52	-106460.44	7.69	213024.88	213318.44	213153.24	0.01(0.00,0.01), p=1.00	1.00	1.00	0.03	2d v 1c: p=0.10	
	2e	1c+remove var(slope post-licensing mirabegron) †	52	-106510.62	8.01	213125.23	213418.79	213253.58	0.02(0.01,0.02), p=1.00	1.00	1.00	0.02	2e v 1c: p<0.001	
	3a	2c+ remove var (change of level-PDI guidelines)†	47	-106482.18	8.25	213058.36	213323.69	213174.37	0.01(0.01,0.01), p=1.00	1.00	1.00	0.02		Negative variances
	3b	2c+remove var(slope pre-guidelines) †	47	-106468.57	8.12	213031.15	213296.48	213147.16	0.00(0.00,0.01), p=1.00	1.00	1.00	0.02	3b c 2c: p=0.35	Lowest IC of 3b, 3c
	3c	2c+ remove var(change of level-licensing mirabegron)†	47	-106469.55	8.13	213033.10	213298.44	213149.11	0.00(0.00,0.01), p=1.00	1.00	1.00	0.02	3c v 2c: p=0.28	
	3d	2c+remove var(slope post-licensing mirabegron) †	47	-106570.62	8.34	213235.25	213500.58	213351.26	0.02(0.02,0.02), p=1.00	0.99	0.99	0.04		Negative variances
	4a	3b+ remove (change of level-PDI guidelines)†	43	-106488.89	8.54	213065.77	213306.53	213169.91	0.01(0.00,0.01), P=1.00	1.00	1.00	0.02	4a v 3b: p=0.02	
	4b	3b+ remove var(change of level-licensing mirabegron)†	43	-106477.68	8.59	213041.36	213284.12	213147.50	0.00(0.00,0.01), p1=1.00	1.00	1.00	0.02	4b v 3b: p=0.28	Selected univariate model
	4c	3b+ remove var(slope post-licensing mirabegron) †	43	-106646.04	8.56	213378.08	213620.83	213484.22	0.01(0.00,0.01), p=1.00	1.00	1.00	0.03	4c v 3b: p<0.001	Negative variances
	5a	4b+ remove (change of level-PDI guidelines)†	40	-106494.83	8.94	213069.65	213295.47	213168.38	0.01(0.00,0.01), p=1.00	1.00	1.00	0.02	5a v 4b: p=0.03	

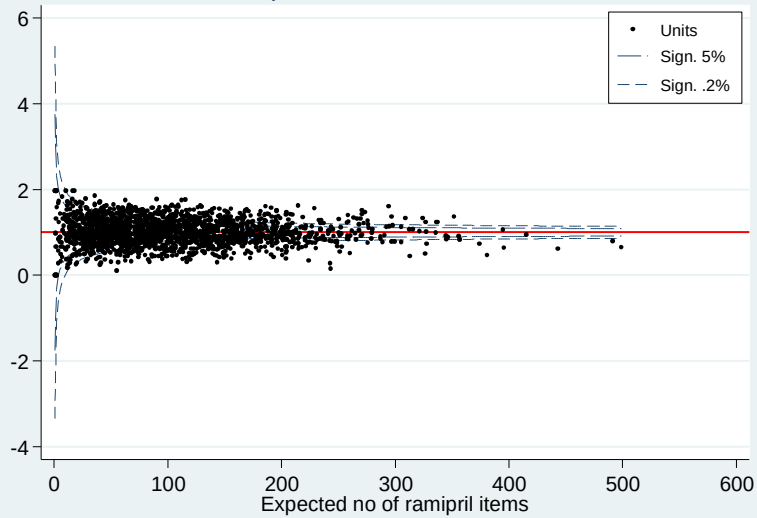
Medicine group	Model	Model fitted	No free parms	Log-likelihood	Correction factor for MLR	AIC	BIC	SSA-BIC	RMSEA (90%CI), p-value	CFI	TLI	SRMR	Satorra-Bentler test	Comments
	5b	4b+ remove var(slope post-licensing mirabegron) †	40	-106654.33	8.84	213388.66	213614.48	213487.39	0.02(0.02,0.03), p=1.00	0.98	0.98	0.02	5b v 4b: p<0.001	
urology/ beta-blockers (bivariate model)	1	urology model 2d and betablockers model 4b: add time-specific correlations plus covariances between latent factors	126	-213080.88	5.03	426413.76	427125.92	426725.61	0.01(0.00,0.01), p=1.00	1.00	1.00	0.02		
	2	1+ equality of time-specific correlations (2 nd quarter onwards)	112	-213100.74	5.23	426425.48	427058.51	426702.68	0.01(0.00,0.10), p=1.00	1.00	1.00	0.01	2 v 1: p=0.64	
	3	2+ add autoregressive components among the residuals across both outcomes	142	-213027.42	4.79	426338.83	427141.43	426690.28	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01	2 v 3: p=0.03	
	4a	3+ add AR(1) structure to tolterodine residuals	128	-213079.74	4.88	426415.48	427138.95	426732.28	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01	4a v 3: p=0.02	
	4b	3+ add AR(1) structure to bisoprolol residuals	128	-213093.27	4.35	426442.54	427166.00	426759.33	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01	4b v 3: p=0.38	
	5a	4b+ impose equality on autoregressive components from urology to beta-blockers	114	-213136.45	4.49	426500.89	427145.23	426783.04	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01	5a v 4b: p=0.02	
	5b	4b+ impose equality on autoregressive components from beta-blockers to urology	114	-213126.01	4.42	426480.03	427124.36	426762.17	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01	5b v 4b: p=0.24	Selected unconditional bivariate model
	6	Conditional model (5b+no of patients/% of patients >=65 years Jan-Mar 2012)	138	-199286.40	3.97	398848.79	399617.73	399179.30	0.01(0.00,0.01), p=1.00	1.00	1.00	0.01		

No free parms: number of free parameters; MLR: maximum likelihood robust; AIC: aikake information criterion; BIC: bayesian information criterion; SSA-BIC: sample-size adjusted bayesian information criterion; RMSEA: root= mean square error of approximation; CFI: comparative fit index; TLI: Tucker-Lewis index; SRMR: standardised root mean square residual; IC: information criterion; LCM: latent curve model; LCM-SR: latent curve model with structured residuals; † removal of variance and associated covariance terms; AR(1): first order autoregressive

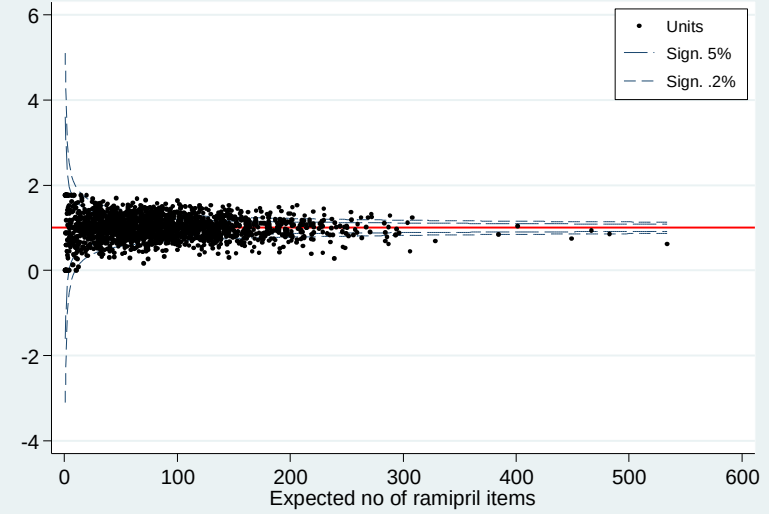
Fig A1 Funnelplots of standardised prescribing ratios plotted against expected number of preferred drug group items



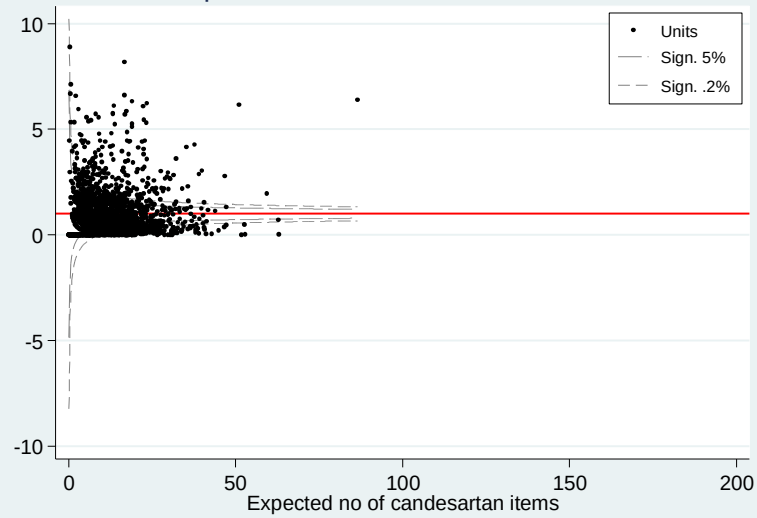
Ramipril/ACEIs: Jan-Mar 2012



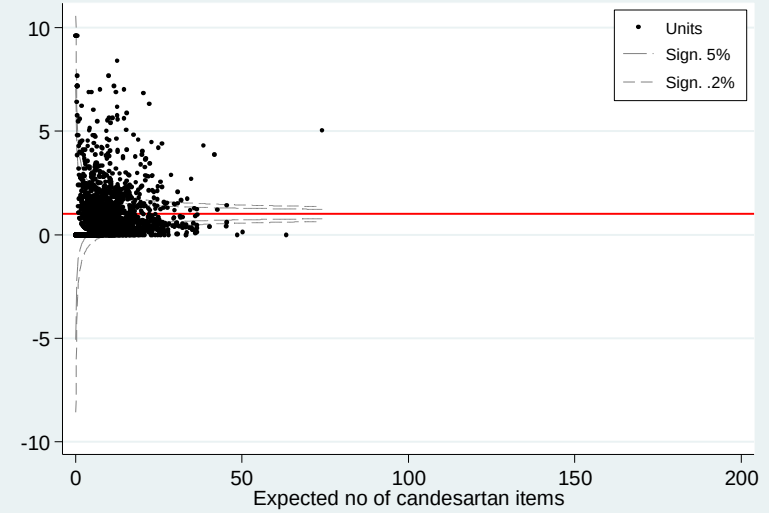
Ramipril/ACEIs: Oct-Dec 2015



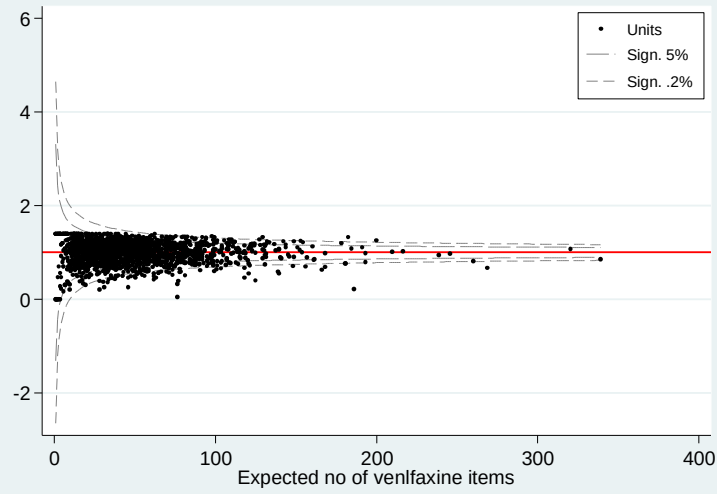
Funnel plot: Candesartan/ARBs: Jan-Mar 2012



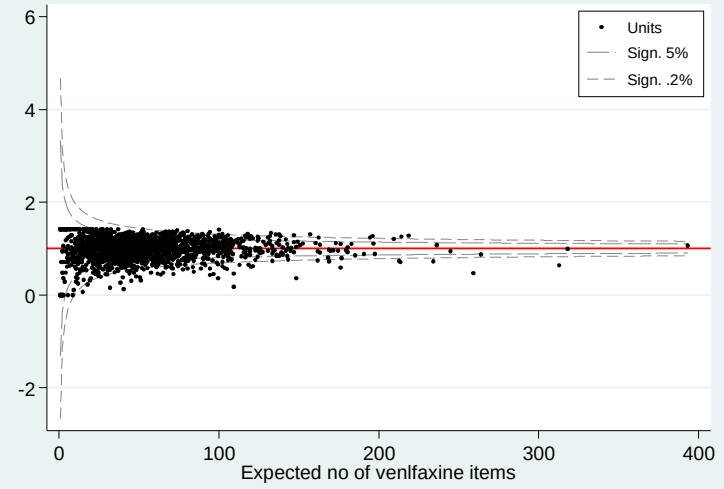
Funnel plot: Candesartan/ARBs: Oct-Dec 2015



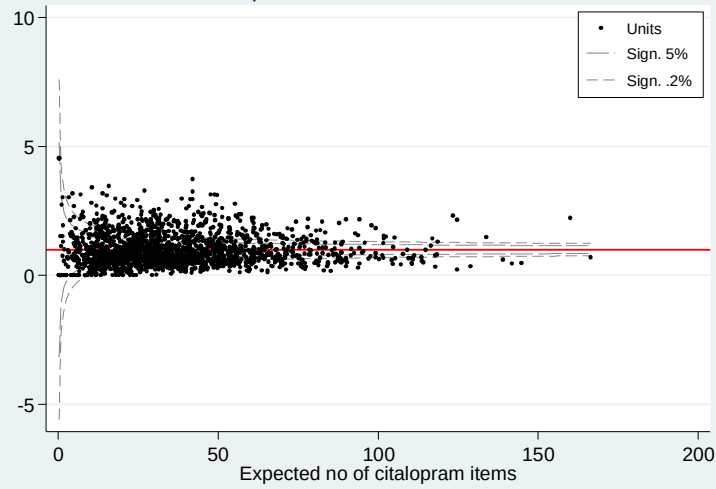
Venlafaxine/SNRI: Jan-Mar 2012



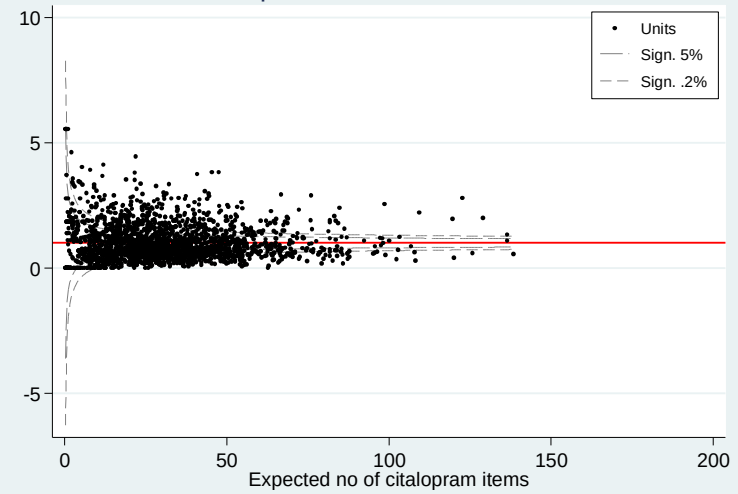
Venlafaxine/SNRI: Oct-Dec 2015



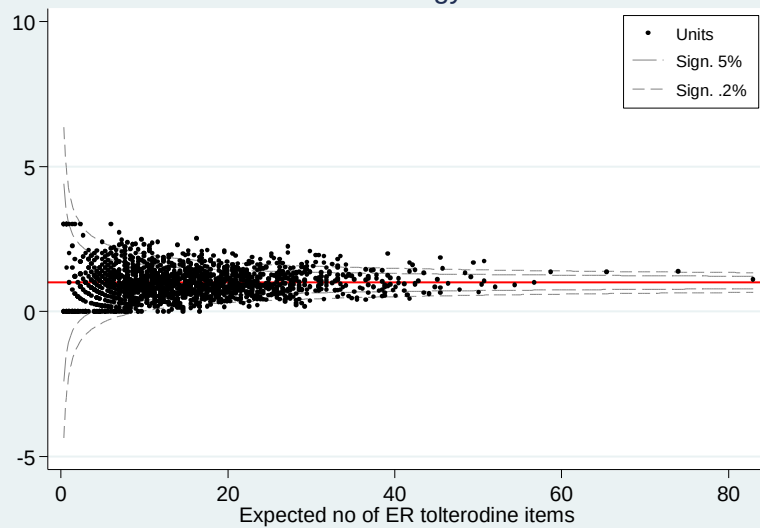
Citalopram/SSRIs: Jan-Mar 2012



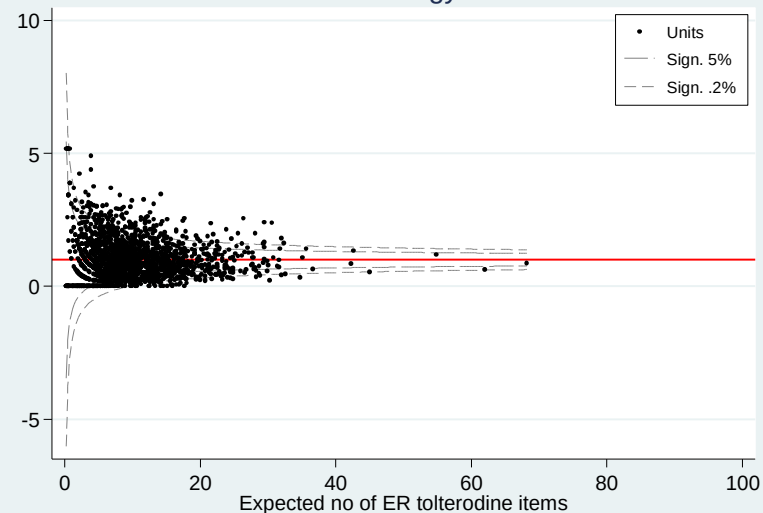
Citalopram/SSRIs: Oct-Dec 2015



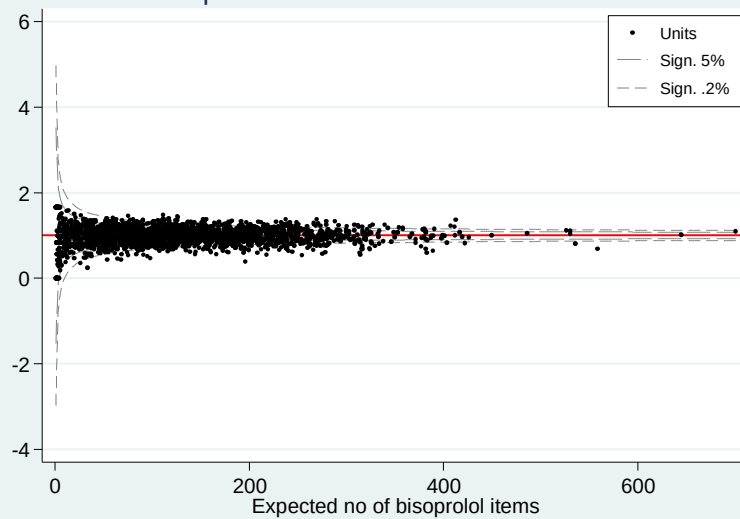
ER Tolterodine/Urology: Jan-Mar 2012



ER Tolterodine/Urology: Oct-Dec 2015



bisoprolol/beta-blockers: Oct-Dec 2015



bisoprolol/beta-blockers: Jan-Mar 2012

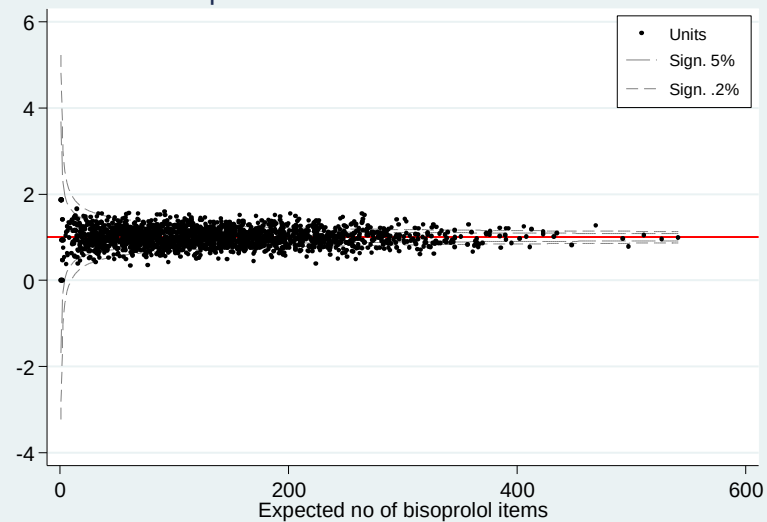


Fig A2 Average prescribing trends in issuing of PDI preferred drugs (2012-2015): adjusted analyses

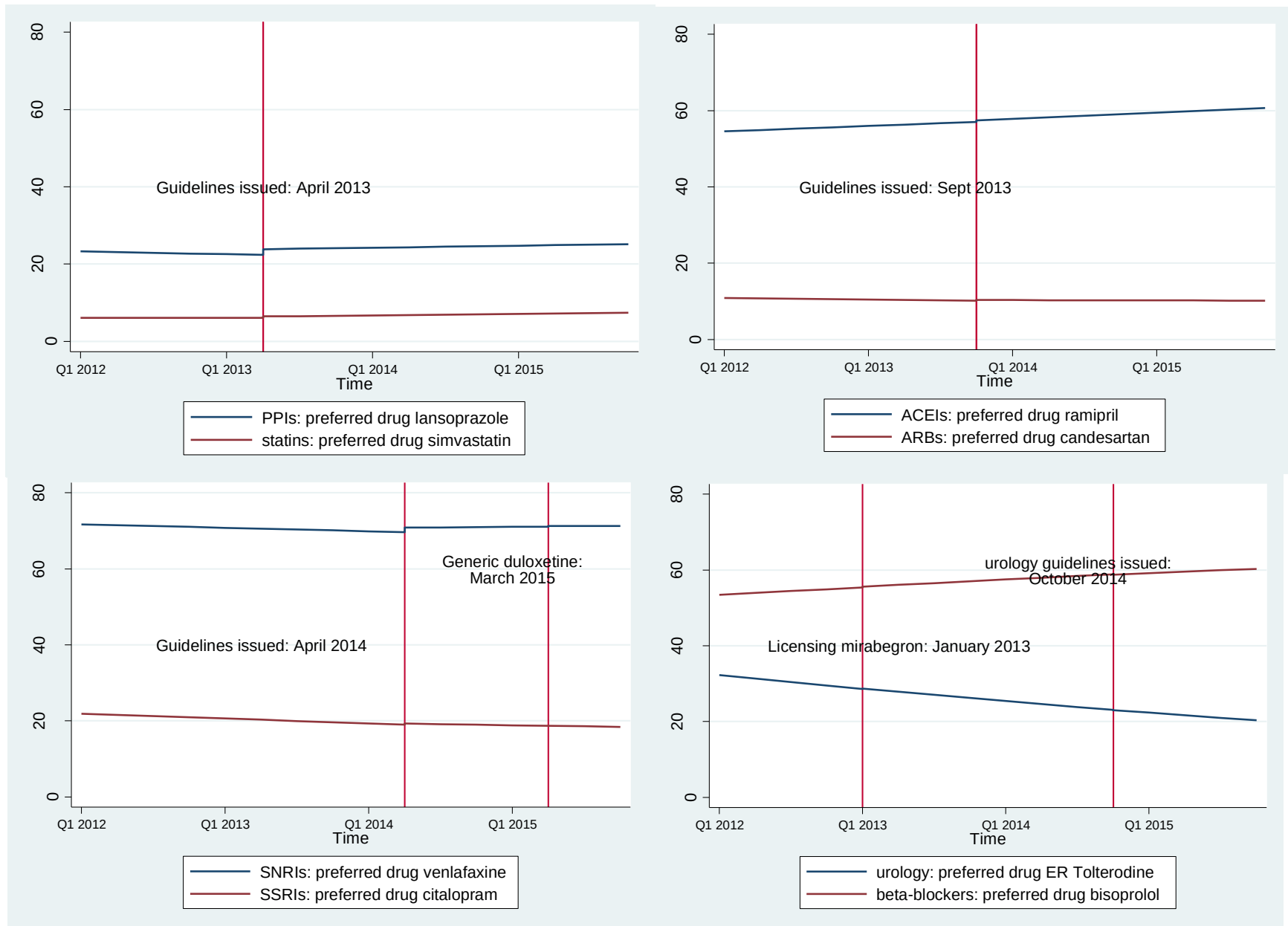


Table A5: Residual variances and correlations of random effects: adjusted analyses for PPIs/statins

		PPIs				statins			
		Intercept (Jan-Mar 2012)	Slope1 (Slope pre- PDI guidelines)	Change of level calendar quarter following PDI guidelines	Slope2 (Slope post- PDI guidelines)	Intercept (Jan-Mar 2012)	Slope1 (Slope pre- PDI guidelines)	Change of level calendar quarter following PDI guidelines	Slope2 (Slope post - PDI guidelines)
PPIs	Intercept	65.99 (4.04) ***							
	Slope1	-	-						
	Change of level	0.06 (0.11)	-	10.77 (3.74) ***					
	Slope2	-0.23 (0.03) ***	-	-0.29 (0.11)**	0.74 (0.13)***				
Statins	Intercept	0.02 (0.03)	-	0.04 (0.05)	0.08 (0.03)**	29.91 (2.96)***			
	Slope1	-	-	-	-	-	-		
	Change of level	0.04 (0.05)	-	0.47 (0.13)***	-0.08 (0.05)	-0.02 (0.04)	-	3.77 (0.96) ***	
	Slope2	-	-	-	-	-	-	-	-

p<0.05; ** p<0.01; *** p<0.001; PPI: proton pump inhibitor; - random effects not estimated due to lack of statistical significance (Satorra-Bentler test)

Table A6: Residual variances and correlations of random effects: adjusted analyses for ACEIs/ARBs

		ACEIs				ARBs			
		Intercept (Jan-Mar 2012)	Slope1 (Slope pre-PDI guidelines)	Change of level calendar quarter following PDI guidelines	Slope2 (Slope post- PDI guidelines)	Intercept (Jan-Mar 2012)	Slope1 (Slope pre- PDI guidelines)	Change of level calendar quarter following PDI guidelines	Slope2 (Slope post - PDI guidelines)
ACEIs	Intercept	219.67 (9.19) ***							
	Slope1	-0.31 (0.04) ***	1.17 (0.21) ***						
	Change of level	-	-	-					
	Slope2	-0.13 (0.03) ***	-0.05 (0.07)	-	1.58 (0.22) ***				
ARBs	Intercept	0.10 (0.03) ***	0.01 (0.04)	-	-0.05 (0.04)	133.89 (9.94) ***			
	Slope1	-0.003 (0.04)	-0.14 (0.12)	-	0.17 (0.10)	-0.25 (0.04)***	0.67 (0.18) ***		
	Change of level	-	-	-	-	-	-	-	
	Slope2	-0.05 (0.04)	0.07 (0.07)	-	-0.13 (0.10)	-0.15 (0.05)***	-0.10 (0.10)	-	0.65 (0.11) ***

p<0.05; ** p<0.01; *** p<0.001; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin-II receptor blocker; -: not estimated due to lack of statistical significance (Satorra-Bentler test)

Table A7: Residual variances and correlations of random effects: adjusted analyses for SNRIs/SSRIs

		SNRIs						SSRIs			
		Intercept (Jan-Mar 2012)	Slope1 (Slope pre- PDI guidelines)	Change of level 1: calendar quarter following PDI guidelines	Slope2 (Slope post- PDI guidelines)	Change of level 2: calendar quarter following licensing of generic duloxetine	Slope3 (Slope following licensing of generic duloxetine)	Intercept (Jan-Mar 2012)	Slope1 (Slope pre- PDI guidelines)	Change of level calendar quarter following PDI guidelines	Slope2 (Slope post- PDI guidelines)
SNRIs	Intercept	218.42 (12.43) ***									
	Slope1	-0.33 (0.05) ***	1.93 (0.26) ***								
	Change of level 1	0.001 (0.05)	-0.31 ** (0.10)	36.04 (12.95) **							
	Slope2	-0.14 (0.04) ***	-0.14 (0.06)*	-0.19 (0.16)	5.73 (1.08) ***						
	Change of level 2	-	-	-	-	-					
	Slope3	-	-	-	-	-	-				
SSRIs	Intercept	0.03 (0.03)	0.06 (0.04)	0.02 (0.04)	-0.06 (0.03)	-	-	150.85 (7.88) ***			
	Slope1	-0.02 (0.06)	-0.03 (0.09)	-0.09 (0.09)	0.06 (0.06)	-	-	-0.37 (0.04) ***	0.56 (0.12) ***		
	Change of level 1	-0.02 (0.08)	-0.15 (0.15)	0.21 (0.25)	-0.01 (0.14)	-	-	0.04 (0.07)	-0.11 (0.24)	4.49 (4.48)	
	Slope2	0.01 (0.04)	-0.06 (0.07)	0.20 (0.11)	0.03 (0.09)	-	-	-0.10 (0.04) **	-0.14 (0.07)*	-0.08 (0.28)	1.86 (0.46) ***

p<0.05; ** p<0.01; *** p<0.001; SNRI: serotonin noradrenaline reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; -: not estimated due to lack of statistical significance (Satorra-Bentler test)

Table A8: Residual variances and correlations of random effects: adjusted analyses for urology/beta-blockers

		Urology						Beta blockers					
		Intercept (Jan-Mar 2012)	Slope1 (Slope pre licensing of Mirabegron)	Change of level 1: licensing of mirabegron	Slope2 (Slope post- licensing of mirabegron)	Change of level 2: PDI guidelines	Slope3 (Slope post- PDI guidelines)	Intercept (Jan-Mar 2012)	Slope1 (Slope pre licensing of Mirabegron)	Change of level 1: licensing of mirabegron	Slope 2 (Slope post- licensing of mirabegron)	Change of level 2: PDI guidelines	Slope3 (Slope post- PDI guidelines)
Urology	Intercept	214.36 (10.24)***											
	Slope1	-	-										
	Change of level 1	-0.11 (0.07)		20.93 (6.38)***									
	Slope 2	-0.36 (0.04) ***	-	-0.15 (0.12)	2.94 (0.39) ***								
	Change of level 2	0.02 (0.05)	-	-0.06 (0.10)	-0.34 (0.08) ***	38.11 (11.50) ***							
	Slope 3	-0.17 (0.04) ***	-	-0.01 (0.08)	-0.14 (0.06) *	-0.21 (0.14)	7.26 (1.63) ***						
Beta blockers	Intercept	0.03 (0.03)	-	0.02 (0.06)	-0.04 (0.04)	-0.02 (0.05)	-0.02 (0.04)	103.08 (4.01) ***					
	Slope 1	-	-	-	-	-	-	-	-	-			
	Change of level 1	-	-	-	-		-	-	-	-			
	Slope 2	-0.03 (0.05)	-	0.08 (0.12)	-0.04 (0.08)	0.14 (0.11)	-0.08 (0.08)	-0.21 (0.04) ***	-	-	0.71 (0.14)***		
	Change of level 2	0.09 (0.09)	-	-0.18 (0.17)	0.11 (0.15)	0.18 (0.23)	0.02 (0.20)	-0.08 (0.06)	-	-	-0.05 (0.19)	7.25 (3.64) *	
	Slope 3	-	-		-	--	-	-	-	-	-	-	-

p<0.05; ** p<0.01; *** p<0.001; ER: extended release; -: not estimated due to lack of statistical significance (Satorra-Bentler test)

Table A9: Effects associated with increase of 100 patients at baseline (Jan-Mar 2012)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Change in average % of preferred drug (Jan- Mar 2012) (SE) , p- value	Change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug following licensing of mirabegron (Jan 2013) (SE), p-value	Average change in % of preferred drug per quarter following licensing of mirabegron (SE), p-value,	Average change in % of preferred drug following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug following licensing of generic duloxetine (SE), p-value	Average change in % of preferred drug per quarter post- guidelines (SE), p-value,
PPIs/ lansoprazole (April 2013)	2,105	0.06 (0.07) p=0.41	0.00 (0.01), p=0.98	-	-	-0.06 (0.05), p=0.22	0.00 (0.01), p=0.47	-	-
statins/ simvastatin (April 2013)	2,094	-0.06 (0.03), p=0.06	0.01 (0.01), p=0.54	-	-	-0.04 (0.03), p=-0.16	0.00 (0.00), p=0.96	-	-
ACEs/ ramipril (Sept 2013)	1,999	-0.04 (0.11), p=0.72	-0.01 (0.01), p=0.64	-	-	0.09 (0.06), p=0.12	-0.02 (0.01), p=0.06	-	-
ARBs/ candesartan (Sept 2013)	2,043	-0.07 (0.08), p=0.38	0.00 (0.01), p=0.82	-	-	-0.01 (0.03), p=0.68	0.00 (0.01), p=0.98	-	-
SNRIs/ venlafaxine (April 2014)	1,875	-0.15 (0.12), p=0.22	0.00 (0.02), p=0.98	-	-	-0.09 (0.08), p=0.26	0.02 (0.03), p=0.56	0.01 (0.08), p=0.87	0.07 (0.04), p=0.11
SSRIs/ duloxetine (April 2014)	2,070	-0.11 (0.08), p=0.18	-0.01 (0.01), p=0.17	-	-	0.05 (0.04), p=0.18	-0.01 (0.01), p=0.56	-	-
urology (ER tolterodine) (October 2014)	1,861	0.08 (0.14), p=0.59	0.01 (0.03), p=0.81	0.00 (0.08), p=0.99	-0.03 (0.06), p=0.60	-0.03 (0.06), p=0.60	-0.01 (0.02), p=0.58	-	-
betablockers/ bisoprolol (reference group)	2,092	0.03 (0.08), p=0.72	0.01 (0.02), p=0.70	-0.07 (0.04), p=0.09	0.00 (0.01), p=0.90	0.07 (0.04), p=0.11	-0.01 (0.01), p=0.59	-	-

Table A10: Effects associated with increase of 5% of patients aged 65 years and over at baseline (Jan-Mar 2012)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Change in average % of preferred drug (Jan- Mar 2012) per 100 patient increase (SE)	Change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug following licensing of mirabegron (Jan 2013) (SE), p-value	Average change in % of preferred drug per quarter following licensing of mirabegron (SE), p-value,	Average change in % of preferred drug following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug following licensing of generic duloxetine (SE), p-value	Average change in % of preferred drug per quarter post- guidelines (SE), p-value,
PPIs/ lansoprazole (April 2013)	2,105	-0.03 (0.11), p=0.80	-0.02(0.02), p=0.23			-0.02(0.06), p=0.70	-0.01(0.01), p=0.60	-	-
statins/ simvastatin (April 2013)	2,094	0.04 (0.04), p=0.33	0.00 (0.01), p=0.69			0.01 (0.03), p=0.83	-0.01(0.00), p=0.18	-	-
ACEs/ ramipril (Sept 2013)	1,999	-0.21 (0.14), p=0.15	-0.04 (0.02), p=0.03			-0.02 (0.07), p=0.84	-0.0 (0.01), p=0.74	-	-
ARBs/ candesartan (Sept 2013)	2,043	-0.04 (0.11), p=0.74	0.02 (0.01), p=0.24			-0.07 (0.05), p=0.11	-0.01 (0.01), p=0.37	-	-
SNRIs/ venlafaxine (April 2014)	1,875	0.55 (0.17) p=0.001	-0.03 (0.02), p=0.14	-	-	-0.07 (0.09), p=0.49	0.05 (0.04), p=0.22	-0.045 0.10), p=0.59	0.05 (0.05), p=0.37
SSRIs/ duloxetine (April 2014)	2,070	0.89 (0.14), p<0.001	-0.02 (0.01), p=0.16	-	-	-0.06 (0.05), p=0.23	0.02 (0.02), p=0.28		
urology (ER tolterodine) (October 2014)	1,861	0.08 (0.03), p=0.03	0.00 (0.01), p=0.67	0.03 (0.02), p=0.27	-0.01 0.01), p=0.02	0.02 (0.02), p=0.22	0.00 (0.01), p=0.82	-	-
betablockers/ bisoprolol (reference group)	2,092	0.81 (0.11), p<0.001	0.05 (0.07), p=0.52	-0.08 (0.06), p=0.19	-0.01 (0.01), p=0.60	0.05 (0.07), p=0.52	-0.03 (0.02), p=0.22	-	-

Table A11: Results from uadjusted segmented regression models

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug following licensing of mirabegron (Jan 2013) (SE), p-value	Average change in % of preferred drug per quarter following licensing of mirabegron (SE), p-value,	Average change in % of preferred drug in calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug following licensing of generic duloxetine (SE), p-value	Average change in % of preferred drug per quarter following licensing of generic duloxetine (SE), p-value,
PPIs/ lansoprazole (April 2013)	2,105	23.29 (0.23)	-0.20 (0.04) p<0.001	-	-	1.52 (0.13), p<0.001	0.12 (0.02), p<0.001	-	-
statins/ simvastatin (April 2013)	2,094	6.01 (0.13)	0.01 (0.02), p=0.47	-	-	0.34 (0.06), p<0.001	0.10 (0.01), p<0.001	-	-
ACEIs/ ramipril (Sept 2013)	1,999	51.67 (0.36)	0.32 (0.04), p<0.001	-	-	0.18 (0.16), p=0.26	0.40 (0.04) p<0.001	-	-
ARBs/ candesartan (Sept 2013)	2,043	10.84 (0.28)	-0.08 (0.03), p=0.006	-	-	0.25 (0.12), p=0.03	-0.02 (0.03), p=0.38	-	-
SNRIs/ venlafaxine (April 2014)	1,875	71.52 (0.40)	-0.21(0.05), p<0.001	-	-	0.97 (0.24), p<0.001	0.09 (0.10), p=0.33	0.09 (0.27), p=0.74	-0.05 (0.13), p=0.72
SSRIs/ citalopram (April 2014)	2,070	21.67 (0.30)	-0.31 (0.03), p<0.001	-	-	0.21 (0.13), p=0.11	-0.12 (0.04) p=0.004	-	-
urology (ER tolterodine) (October 2014)	1,861	32.35 (0.42)	-0.91 (0.11), p<0.001	0.08 (0.28), p=0.79	-0.86 (0.06), p<0.001	0.01 (0.23), p=0.98	-0.69 (0.08), p<0.001	-	-
betablockers/ bisoprolol (reference group)	2,092	53.41 (0.27)	0.48 (0.06), p<0.001	0.28 (0.16), p=0.10	0.47 (0.03), p<0.001	-0.21 (0.15), p=0.16	0.37 (0.05), p<0.001	-	-

Table A12: Sensitivity analyses

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms (and associated covariances) constrained to zero	Autoregressive terms constrained equal	Cross-lagged residuals constrained equal
PPIs/ lansoprazole (April 2013)	2,352	Trim lower 5% prescribers: retain prescribers with average ≥ 5 PPIs per quarter	23.51 (0.24)	-0.22 (0.05), p<0.001	1.56 (0.18), p<0.001	0.10 (0.03), p<0.001	change of level following PDI guidelines	-	PPI->statin (0.08 (SE 0.05), p=0.11)
PPIs/ lansoprazole (April 2013)	2,105	Trim lower 15% prescribers: retain prescribers with average ≥ 38 PPIs per quarter	23.33 (0.24)	-0.20 (0.05) p<0.001	1.50 (0.15), p<0.001	0.13 (0.02), p<0.001	slope pre PDI guidelines	-	PPI->statin (0.08 (SE 0.05), p=0.11)
PPIs/ lansoprazole (April 2013)	1,859	Trim lower 25% prescribers: retain prescribers with average ≥ 106 PPIs per quarter	23.11 (0.23)	-0.16 (0.04), p<0.001	1.39 (0.15), p<0.001	0.11 (0.03), p<0.001	-	-	-
PPIs/ lansoprazole (April 2013)	2,173	Central limit theorem: retain prescribers with average ≥ 21 PPIs per quarter	23.22 (0.23)	-0.21 (0.05), p<0.001	1.60 (0.16), p<0.001	0.11 (0.03), p<0.001	slope pre PDI guidelines	-	-

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms (and associated covariances) constrained to zero	Autoregressive terms constrained equal	Cross-lagged residuals constrained equal
Statins/ simvatstatin (April 2013)	2,348	Trim lower 5% prescribers: retain prescribers with average >=5 statins per quarter	5.97 (0.14)	0.01 (0.03), p=0.58	0.37 (0.09), p<0.001	0.10 (0.02), p<0.001	slope pre PDI guidelines	-	PPI->statin (0.08 (SE 0.05), p=0.11)
Statins/ simvatstatin (April 2013)	2,094	Trim lower 15% prescribers: retain prescribers with average >=38 statins per quarter	6.06 (0.13)	0.01 (0.02), p=0.50	0.32 (0.06), p<0.001	0.10 (0.01), p<0.001	slope pre PDI guidelines; slope post PDI guidelines	-	PPI->statin (0.08 (SE 0.05), p=0.11)
Statins/ simvatstatin (April 2013)	1,847	Trim lower 25% prescribers: retain prescribers with average >=118 statins per quarter	6.08 (0.14)	0.01 (0.02), p=0.59	0.29 (0.06), p<0.001	0.10 (0.01), p<0.001	slope pre PDI guidelines	-	-
Statins/ simvatstatin (April 2013)	1,977	Central limit theorm: retain prescribers with >=75 statins per quarter	6.08 (0.14)	0.01 (0.02), p=0.42	0.32 (0.07), p<0.001	0.11 (0.01), p<0.001	slope pre PDI guidelines	-	-

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms (and associated covariances) constrained to zero	Autoregressive terms constrained equal	Cross-lagged residuals constrained equal
ACEIs/ ramipril (Sept 2013)	2,239	Trim lower 5% prescribers: retain prescribers with average >=6 ACEIs per quarter	51.29 (0.38)	0.37 (0.05), p<0.001	0.20 (0.22), p=0.38	0.38 (0.04), p<0.001	change of level following PDI guidelines	ACEIs: (0.52 (SE 0.03), p<0.001)	ACEI->ARB (-0.02 (SE 0.06), p=0.78) ARB->ACEI: (-0.02 (SE 0.02), p=0.52)
ACEIs/ ramipril (Sept 2013)	1,999	Trim lower 15% prescribers: retain prescribers with average >=30 ACEIs per quarter	54.56 (0.38)	0.35 (0.04), p<0.001	0.08 (0.17), p=0.65	0.41 (0.04) p<0.001	change of level following PDI guidelines		ACEI->ARB: (0.01 (SE 0.05), p=0.89) ARB->ACEI: (0.00 (SE 0.02) p=0.98)
ACEIs/ ramipril (Sept 2013)	1,771	Trim lower 25% prescribers: retain prescribers with average >=59 ACEIs per quarter	51.61 (0.41)	0.32 (0.04), p<0.001	0.21 (0.15), p=0.16	0.41 (0.04), p<0.001	change of level following PDI guidelines	-	-
ACEIs/ ramipril (Sept 2013)	2,086	Central limit theorm: retain prescribers with average >=21 ACEIs per quarter	51.52 (0.38)	0.33 (0.05), p<0.001	0.21 (0.18), p=0.29	0.39 (0.04), p<0.001	change of level following PDI guidelines	ACEIs: (0.49 (SE 0.03), p<0.001)	ACE->ARB: (0.07 (SE 0.10), p=0.52) ARB-ACEI: (0.01 (SE 0.02), p=0.72)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms (and associated covariances) constrained to zero	Autoregressive terms constrained equal	Cross-lagged residuals constrained equal
ARBs/ candesartan (Sept 2013)	2,253	Trim lower 5% prescribers: retain prescribers with average ≥ 2 ARBs per quarter	10.83 (0.30)	-0.06 (0.03), p=0.06	0.11 (0.14), p=0.40	0.01 (0.03), p=0.83	change of level following PDI guidelines	-	ACEI->ARB (-0.02 (SE 0.06), p=0.78) ARB->ACEI: (-0.02 (SE 0.02), p=0.52)
ARBs/ candesartan (Sept 2013)	2,043	Trim lower 15% prescribers: retain prescribers with average ≥ 14 ARBs per quarter	10.87 (0.29)	-0.11 (0.03), p=0.001	0.34 (0.12), p=0.01	-0.02 (0.03), p=0.42	change of level following PDI guidelines	ARBs: (0.47 (SE 0.04), p<0.001)	ACEI->ARB: (0.01 (SE 0.05), p=0.89) ARB->ACEI: (0.00 (SE 0.02) p=0.98)
ARBs/ candesartan (Sept 2013)	1,695	Trim lower 25% prescribers: retain prescribers with average ≥ 40 ARBs per quarter	10.99 (0.34)	-0.09 (0.03), p=0.004	0.16 (0.11), p=0.17	0.00 (0.03), p=0.93	-	-	-
ARBs/ candesartan (Sept 2013)	1,623	Central limit theorem: retain prescribers with average ≥ 45 ARBs per quarter	10.96 (0.36)	-0.08 (0.02), p<0.001	0.13 (0.12), p=0.28	0.00 (0.03), p=0.88	change of level following PDI guidelines	ARBs: (0.40 (SE 0.04), p<0.001)	ACE->ARB: (0.07 (SE 0.10), p=0.52) ARB-ACEI: (0.01 (SE 0.02), p=0.72)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug calendar quarter following licensing of generic duloxetine (SE), p-value	Average change in % of preferred drug per quarter following licensing of generic duloxetine (SE),p-value	Variance terms (and associated covariances) constrained to zero	Auto- regressive terms constrained equal	Cross-lagged residuals constrained equal
SNRIs/ venlafaxine (April 2014)	2,090	Trim lower 5% prescribers: retain prescribers with average >=9 SNRIs per quarter	71.31 (0.43)	-0.25 (0.05), p<0.001	1.17 (0.27), p<0.001	0.15 (0.11), p=0.20	-0.02 (0.31), p=0.94	0.13 (0.17), p=0.43	change of level & slope following licensing of generic duloxetine	SNRIs: (0.39 (SE 0.02), p<0.001)	SNRI->SSRI: (0.00 (SE 0.04), p=0.99); SSRI->SNRI: (-0.01 (SE 0.01), p=0.45)
SNRIs/ venlafaxine (April 2014)	1,875	Trim lower 15% prescribers: retain prescribers with average >= 19 SNRIs per quarter	71.72 (0.44)	-0.23 (0.05), p<0.001	1.17 (0.26), p<0.001	0.07 (0.10), p=0.53	0.19 (0.28), p=0.50	-0.06 (0.15), p=0.68	change of level & slope following licensing of generic duloxetine	-	SNRI->SSRI: (-0.04 (SE 0.04), p=0.39); SNRI->SSRI: (-0.01 (SE 0.01), p=0.41)
SNRIs/ venlafaxine (April 2014)	1,661	Trim lower 25% prescribers: retain prescribers with average >=28 SNRIs per quarter	71.77 (0.46)	-0.25 (0.05), p<0.001	0.86 (0.27), p<0.001	0.21 (0.11), p=0.04	0.11 (0.27), p=0.68	-0.03 (0.15), p=0.86	change of level & slope following licensing of generic duloxetine	-	SNRI->SSRI: (-0.03 (SE 0.04), p=0.94) SSRI->SNRI: (0.01 (SE 0.02), p=0.63)
SNRIs/ venlafaxine (April 2014)	1,924	Central limit theroem: retain prescribers with average >=16 SNRIs per quarter	71.72(0.40)	-0.25 (0.05), p<0.001	1.26 (0.27), p<0.001	0.08 (0.10), p=0.44	0.12 (0.29), p=0.67	-0.03 (0.15), p=0.84	change of level & slope following licensing of generic duloxetine	-	SNRI->SSRI: (-0.03 (SE 0.04), p=0.46) SSRI->SNRI: (0.01 (SE 0.01),p=0.63)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms (and associated covariances) constrained to zero	Autoregressive terms constrained equal	Cross-lagged residuals constrained equal
SSRIs/ citalopram (April 2014)	2,300	Trim lower 5% prescribers: retain prescribers with average ≥10 SSRIs per quarter	21.77(0.30),	-0.33 (0.03), p<0.001	0.31 (0.15), p=0.04	-0.11 (0.05), p=0.03	-	-	SNRI->SSRI: (0.00 (SE 0.04), p=0.99); SSRI->SNRI: (-0.01 (SE 0.01), p=0.45)
SSRIs/ citalopram (April 2014)	2,070	Trim lower 15% prescribers: retain prescribers with average ≥37 SSRIs per quarter	21.89 (0.32)	-0.32 (0.03), p<0.001	0.26 (0.13), p=0.05	-0.14 (0.05), p=0.003	-	-	SNRI->SSRI: (-0.04 (SE 0.04), p=0.39); SNRI->SSRI: (-0.01 (SE 0.01), p=0.41)
SSRIs/ citalopram (April 2014)	1,824	Trim lower 25% prescribers: retain prescribers with average ≥64 SSRIs per quarter	22.01 (0.35)	-0.32 (0.03), p<0.001	0.32 (0.13), p=0.01	-0.19 (0.04), p<0.001	-	-	SNRI->SSRI: (-0.03 (SE 0.04), p=0.94) SSRI->SNRI: (0.01 (SE 0.02), p=0.63)
SSRIs/ citalopram (April 2014)	2,172	Central limit theroem: retain prescribers with average ≥25 SSRIs per quarter	21.86 (0.32)	-0.32 (0.03), p<0.001	0.23 (0.14), p=0.09	-0.12 (0.05), p=0.01	-	-	SNRI->SSRI: (-0.03 (SE 0.04), p=0.46) SSRI->SNRI: (0.01 (SE 0.01),p=0.63)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan-Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p-value	Average change in % of preferred drug calendar quarter following licensing of mirabegron (Jan 2013) (SE), p-value	Average change in % of preferred drug per quarter following licensing of mirabegron (SE), p-value,	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms and associated covariances constrained to zero	Auto-regressive terms constrained equal	Cross-lagged residuals constrained equal
Urology (ER tolterodine) (October 2014)	2,092	Trim lower 5% prescribers: retain prescribers with average >=6 urology items per quarter	32.24 (0.49)	-0.91 (0.12), p<0.001	0.11 (0.30), p=0.70	-0.81 (0.06), p<0.001	-0.04 (0.26), p=0.89	-0.67 (0.09), p<0.001	slope pre licensing of mirabegron	-	bb->urol: (0.01 (SE 0.02), p=0.66)
Urology (ER tolterodine) (October 2014)	1,861	Trim lower 15% prescribers: retain prescribers with average >=13 urology items per quarter	32.24 (0.49)	-0.91 (0.12), p<0.001	0.11 (0.30), p=0.70	-0.81 (0.06), p<0.001	-0.04 (0.26), p=0.89	-0.67 (0.09), p<0.001	slope pre licensing of mirabegron	-	bb->urol: (0.01 (SE 0.02), p=0.66)
Urology (ER tolterodine) (October 2014)	1,632	Trim lower 25% prescribers: retain prescribers with average >=20 urology items per quarter	32.42 (0.50)	-0.86 (0.12), p<0.001	0.33 (0.29), p=0.26	-0.89 (0.06), p<0.001	-0.08 (0.25), p=0.75	-0.71 (0.09), p<0.001	change of level following PDI guidelines	-	urol->bb: (0.01 (SE 0.03), p=0.86); bb->urol: (0.01 (SE 0.01), p=0.62)
Urology (ER tolterodine) (October 2014)	1,632	Central limit theroem: retain prescribers with >=20 urology items per quarter	32.38 (0.49)	-0.84 (0.12), p<0.001	0.29 (0.30), p=0.32	-0.88 (0.06), p<0.001	-0.07 (0.26), p=0.78	-0.72 (0.09), p<0.001	slope pre licensing of mirabegron	-	urol->bb: (0.07 (SE 0.06), p=0.19)

Medication class/ Preferred Drug (Guidelines introduced)	Number of GMS prescribers included	Sample	Average % of preferred drug (Jan- Mar 2012) (SE)	Average change in % of preferred drug per quarter (SE), p- value	Average change in % of preferred drug calendar quarter following licensing of mirabegron (Jan 2013) (SE), p-value	Average change in % of preferred drug per quarter following licensing of mirabegron (SE), p-value,	Average change in % of preferred drug calendar quarter following PDI guidelines (SE), p-value	Average change in % of preferred drug per quarter following PDI guidelines (SE), p-value	Variance terms and associated covariances constrained to zero	Auto- regressive terms constrained equal	Cross- lagged residuals constrained equal
Betablockers/ bisoprolol (reference)	2,350	Trim lower 5% prescribers: retain prescribers with average >=7 beta-blockers per quarter	53.15 (0.29)	0.51 (0.07), p<0.001	0.18 (0.16), p=0.27	0.48 (0.04), p<0.001	-0.26 (0.17), p=0.12	0.40 (0.06), p<0.001	slope pre mirabegron licensing; change of level following mirabegron licensing; change of level following PDI; slope following PDI	0.41 (0.03), p<0.001	bb->urol: (0.01 (SE 0.02), p=0.66)
Betablockers/ bisoprolol (reference)	2,091	Trim lower 15% prescribers: retain prescribers with average >=42 beta-blockers per quarter	53.15 (0.29)	0.51 (0.07), p<0.001	0.18 (0.16), p=0.27	0.48 (0.04), p<0.001	-0.26 (0.17), p=0.12	0.40 (0.06), p<0.001	slope pre mirabegron licensing; change of level following mirabegron licensing; slope following PDI	0.41 (0.03), p<0.001	bb->urol: (0.01 (SE 0.02), p=0.66)
Betablockers/ bisoprolol (reference)	1,851	Trim lower 25% prescribers: retain prescribers with average >=77 beta-blockers per quarter	53.22 (0.31)	0.48 (0.07), p<0.001	0.18 (0.16), p=0.27	0.49 (0.03), p<0.001	-0.28 (0.14), p=0.05	0.42 (0.05), p<0.001	slope pre mirabegron licensing; change of level following mirabegron licensing; slope following PDI	0.43 (0.03), p<0.001	urol->bb: (0.01 (SE 0.03), p=0.86); bb->urol: (0.01 (SE 0.01), p=0.62)

Betablockers/ bisoprolol (reference)	2,316	Central limit theorem: retain prescribers with average >=11 beta-blockers per quarter	52.89 (0.30)	0.57 (0.08), p<0.001	0.16 (0.20), p=0.41	0.49 (0.04), p<0.001	-0.37 (0.18), p=0.04	0.41 (0.06), p<0.001	slope pre mirabegron licensing; change of level following mirabegron licensing; slope following PDI	0.50 (0.02), p<0.001	urol->bb: (0.07 (SE 0.06), p=0.19)
---	-------	--	--------------	-------------------------	------------------------	-------------------------	-------------------------	-------------------------	---	-------------------------	---