

Supplementary tables and figure

Tables

Table S1. **Defined daily dose (DDD) of overactive bladder drugs**

Overactive bladder drugs	Defined daily dose (DDD)*
Darifenacin hydrobromide	7.5 mg
Fesoterodine fumarate	4 mg
Flavoxate hydrochloride	0.8 g
Oxybutynin hydrochloride	15 mg
Propiverine hydrochloride	30 mg
Solifenacin succinate	5 mg
Tolterodine tartrate	4 mg
Trospium chloride	40 mg
Mirabegron	50 mg

*DDD derived from the WHO collaborating centre for Drugs Statistics Methodology, is the assumed average maintenance dose per day for a drug used for its main indication in adults

Table S2. Non-OAB anticholinergic drugs and their Anticholinergic Effect on Cognition (AEC) score ^β

Anticholinergic medication class	AEC score 0	AEC score 1	AEC score 2	AEC score 3	AEC score unknown
Antipsychotics	Amisulpride Haloperidol Lurasidone Risperidone Sulpiride Ziprasidone	Aripiprazole Fluphenazine Iloperidone Perphenazine Sertindole Flupenthixol Paliperidone Zuclopentixol	Levomepromazine Olanzapine Pimozide Prochlorperazine Promazine Quetiapine Trifluoperazine Zotepine	Chlorpromazine Clozapine	
Antidepressants	Reboxetine Trazodone Venlafaxine Vortioxetine Bupropion Duloxetine Fluvoxamine Moclobemide	Citalopram Fluoxetine Lithium Mirtazapine Sertraline Buspirone Phenelzine Isocarboxazid	Desipramine Paroxetine	Amitriptyline Clomipramine Dothiepin Doxepin Imipramine Lofepamine Nortriptyline Trimipramine	
Gastrointestinal drugs (antiemetics and antispasmodics)	Alverine Cimetidine Docusate sodium Gaviscon Granisetron Lactulose Loperamide Macrogol Mebeverine Mesalazine Metoclopramide Omeprazole Ondansetron Peppermint oil Pantoprazole Rabeprazole Ranitidine Bisacodyl Senna Sulphasalazine	Hyoscine Pirenzepine Domperidone	Dicycloverine Propantheline Dimenhydrinate	Hyoscine Hydrobromide	Lansoprazole
Anti-epileptics	Gabapentin Lamotrigine Valproate	Carbamazepine			Levetiracetam Oxcarbazepine Pregabalin Phenytoin
Other anticholinergic drugs	Alendronic acid Alprazolam Amlodipine Amoxicillin Aspirin Atenolol Atorvastatin Cephalexin Cetirizine Chlordiazepoxide Ciprofloxacin Clopidogrel	Amiodarone Bromocriptine Diazepam Fentanyl Hydroxyzine Lithium Prednisolone Quinidine Temazepam	Amantadine Chlorphenamine Diphenhydramine Disopyramide Pethidine	Alimemazine Atropine Benztropine Clemastine Cyproheptadine Orphenadrine Procyclidine Promethazine Trihexyphenidryl (benzhexol)	Alendronic acid Allopurinol Anastrozole Apixaban Baclofen Bisoprolol Bumetanide Captopril Carbimazole Carvedilol Chlortalidone Clarithromycin

	Diclofenac Diltiazem Enalapril Entacapone Fexofenadine Furosemide Gliclazide Ibuprofen Ketorolac Levodopa Lisinopril Loratadine Lorazepam Losartan Lovastatin Meloxicam Metoprolol Morphine Naproxen Paracetamol Pravastatin Propranolol Rosiglitazone Simvastatin Theophylline Thyroxine Tramadol Trimethoprim Warfarin Zolpidem				Codeine Colchicine Dabigatran Dexamethasone Dextropropoxyphene Digoxin Erythromycin Hydrocodone Irbesartan Metformin Methocarbamol Methotrexate Nitrofurantoin Oxycodone Ramipril Rivaroxaban Rovustatin Spironolactone Tamoxifen Topiramate Tizanidine Verapamil Zopiclone
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^β Anticholinergic Effect on Cognition (AEC) score derived from Bishara et al. (22)

Table S3. Baseline characteristics of primary care patients in CPRD prescribed bladder anticholinergic drugs and Mirabegron

Patient characteristics	Bladder anticholinergic drugs n(%)								
	Darifenacin (n=332)	Fesoterodine (n=2,646)	Flavoxate (n=2,599)	Oxybutynin (n=40,531)	Propiverine (n=2,193)	Solifenacin (n=23,836)	Tolterodine (n=35,240)	Trospium (n=7,320)	Mirabegron (n=1,826)
Age (years) at first prescription of drug, mean(SD)									
Overall	77.4 (6.6)	76.2 (7.3)	71.6 (8.7)	72.3 (8.9)	72.9 (8.0)	76.1 (7.4)	73.7 (8.1)	74.4 (7.8)	77.9 (6.8)
Patients with dementia (cases)	78.1 (6.4)	76.4 (7.3)	72.1 (9.0)	72.6 (9.0)	72.6 (8.0)	75.8 (7.7)	73.6 (8.3)	74.0 (8.1)	77.1 (7.1)
Patients without dementia (controls)	77.3 (6.7)	75.4 (7.5)	71.5 (8.7)	72.3 (8.8)	73.0 (8.0)	76.2 (7.3)	73.7 (8.0)	74.5 (7.7)	78.2 (6.7)
p-value [#]	0.3999	0.0059	0.1397	0.0290	0.2847	0.0020	0.1090	0.0290	0.0036
Sex									
Female	256 (77.1)	1,912 (72.3)	1,720 (66.2)	28,133 (69.4)	1,697 (77.4)	17,168 (72.0)	25,145 (71.4)	5,367 (73.3)	1,226 (67.1)
Male	76 (22.9)	734 (27.7)	879 (33.8)	12,398 (30.6)	496 (22.6)	6,668 (28.0)	10,095 (28.7)	1,953 (26.7)	600 (32.9)
p-value [~]	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005
Level of Practice deprivation (IMD) (N=447,483)									
	n=125 (100)	n=584 (100)	n=1,411 (100)	n=18,423	n=739	n=6,727	n=14,048	n=2,615	n=28
1 (least deprived)	31 (24.8)	73 (12.5)	241 (17.1)	2,701 (14.7)	99 (13.4)	1,069 (15.9)	2,459 (17.5)	355 (13.6)	28 (10.7)
2	10 (8.0)	86 (14.7)	281 (19.9)	3,676 (20.0)	150 (20.3)	1,485 (22.1)	3,071 (21.9)	584 (22.3)	65 (24.7)
3	18 (14.4)	100 (17.1)	230 (16.3)	3,302 (17.9)	138 (18.7)	1,204 (17.9)	2,377 (16.9)	425 (16.3)	41 (15.6)
4	31 (24.8)	144 (24.7)	289 (20.5)	4,195 (22.8)	169 (22.9)	1,319 (19.6)	2,889 (20.6)	443 (16.9)	43 (16.4)
5 (most deprived)	35 (28.0)	181 (31.0)	370 (26.2)	4,549 (24.7)	183 (24.8)	1,650 (24.5)	3,252 (23.2)	808 (30.9)	86 (32.7)
p-value (for trend) ⁺	0.001	<0.001	0.010	<0.001	0.091	<0.001	<0.001	<0.001	<0.001

[#]p-value for test of significance when comparing difference in age of first prescription of the OAB drug types in cases and controls

[~]p-value for test of significance when comparing difference in prescribing of the OAB drug types in males and females

⁺p-value for test of significance in difference in trends of prescribing of the OAB drug types by IMD groups

Table S4a. Crude and adjusted odds ratios for dementia[‡] by total cumulative use of different bladder anticholinergic drugs and mirabegron, in subgroup of patients aged 80 years and over (n=645,201)

Anticholinergic medication	Cumulative exposure to anticholinergic (TSDD)	Patients with dementia (Cases, n =115,369)	Patients without dementia (Controls, n = 529,832)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio** (95% CI)
Darifenacin hydrobromide	None	115,319 (99.96)	529,643 (99.96)	1.00 [Reference]	1.00 [Reference]
	1-90	26 (0.02)	92 (0.02)	1.32 (0.85-2.05)	1.16 (0.74-1.82)
	91-365	13 (0.01)	51 (0.01)	1.15 (0.62-2.12)	1.08 (0.58-2.02)
	366-1095	7 (0.01)	32 (0.01)	0.88 (0.38-2.04)	0.88 (0.38-2.05)
	>1095	4 (0.00)	14 (0.00)	1.43 (0.47-4.34)	1.58 (0.51-4.87)
Fesoterodine fumarate	None	115,045 (99.72)	528,385 (99.73)	1.00 [Reference]	1.00 [Reference]
	1-90	130 (0.11)	673 (0.13)	0.86 (0.71-1.04)	0.82 (0.67-0.99)
	91-365	90 (0.08)	363 (0.07)	1.16 (0.92-1.46)	1.06 (0.84-1.35)
	366-1095	64 (0.06)	242 (0.05)	1.17 (0.88-1.54)	1.07 (0.81-1.42)
	>1095	40 (0.03)	169 (0.03)	1.05 (0.74-1.48)	0.93 (0.65-1.32)
Flavoxate hydrochloride	None	114,996 (99.68)	528,220 (99.70)	1.00 [Reference]	1.00 [Reference]
	1-90	290 (0.25)	1,277 (0.24)	1.02 (0.90-1.17)	0.95 (0.83-1.08)
	91-365	48 (0.04)	194 (0.04)	1.13 (0.82-1.56)	1.04 (0.75-1.44)
	366-1095	24 (0.02)	108 (0.02)	1.01 (0.65-1.59)	0.98 (0.62-1.55)
	>1095	11 (0.01)	33 (0.01)	1.57 (0.79-3.11)	1.40 (0.70-2.82)
Oxybutynin hydrochloride	None	109,724 (95.11)	505,641 (95.43)	1.00 [Reference]	1.00 [Reference]
	1-90	3,775 (3.27)	16,728 (3.16)	1.03 (1.00-1.07)	1.03 (0.99-1.07)
	91-365	979 (0.85)	4,045 (0.76)	1.09 (1.02-1.17)	1.09 (1.01-1.17)
	366-1095	618 (0.54)	2,292 (0.43)	1.23 (1.12-1.34)	1.22 (1.12-1.34)
	>1095	273 (0.24)	1,126 (0.21)	1.11 (0.97-1.27)	1.09 (0.95-1.25)
Propiverine hydrochloride	None	115,058 (99.73)	528,588 (99.77)	1.00 [Reference]	1.00 [Reference]
	1-90	164 (0.14)	704 (0.13)	1.07 (0.90-1.27)	1.00 (0.84-1.19)
	91-365	53 (0.05)	209 (0.04)	1.13 (0.84-1.54)	1.02 (0.75-1.39)
	366-1095	50 (0.04)	180 (0.03)	1.29 (0.94-1.77)	1.16 (0.84-1.59)
	>1095	44 (0.04)	151 (0.03)	1.34 (0.96-1.88)	1.25 (0.89-1.77)
Solifenacin succinate	None	112,168 (97.23)	516,238 (97.43)	1.00 [Reference]	1.00 [Reference]
	1-90	1,238 (1.07)	5,747 (1.08)	0.98 (0.92-1.04)	0.99 (0.93-1.05)

	91-365	721 (0.62)	3,156 (0.60)	1.04 (0.96-1.13)	1.03 (0.95-1.12)
	366-1095	644 (0.56)	2,531 (0.48)	1.15 (1.05-1.25)	1.14 (1.04-1.25)
	>1095	598 (0.52)	2,160 (0.41)	1.26 (1.15-1.38)	1.24 (1.12-1.36)
Tolterodine tartrate	None	110,499 (95.87)	509,183 (96.10)	1.00 [Reference]	1.00 [Reference]
	1-90	2,275 (1.97)	10,228 (1.93)	1.01 (0.96-1.06)	1.02 (0.97-1.07)
	91-365	1,068 (0.93)	4,401 (0.83)	1.11 (1.04-1.19)	1.11 (1.03-1.19)
	366-1095	789 (0.68)	3,004 (0.57)	1.20 (1.11-1.30)	1.21 (1.11-1.31)
	>1095	738 (0.64)	3,016 (0.57)	1.11 (1.03-1.21)	1.13 (1.04-1.23)
Trospium chloride	None	114,335 (99.20)	525,609 (99.20)	1.00 [Reference]	1.00 [Reference]
	1-90	547 (0.47)	2,400 (0.45)	1.05 (0.96-1.16)	0.98 (0.89-1.08)
	91-365	241 (0.21)	913 (0.17)	1.21 (1.05-1.40)	1.13 (0.98-1.32)
	366-1095	165 (0.14)	556 (0.10)	1.36 (1.14-1.62)	1.25 (1.04-1.50)
	>1095	81 (0.07)	354 (0.07)	1.03 (0.81-1.32)	0.99 (0.77-1.27)
Mirabegron	None	115,096 (99.76)	528,838 (99.81)	1.00 [Reference]	1.00 [Reference]
	1-90	94 (0.08)	459 (0.09)	0.91 (0.73-1.14)	0.82 (0.66-1.04)
	91-365	95 (0.08)	309 (0.06)	1.36 (1.08-1.71)	1.27 (1.00-1.62)
	366-1095	76 (0.07)	191 (0.04)	1.82 (1.39-2.38)	1.66 (1.26-2.19)
	>1095	8 (0.01)	35 (0.01)	1.02 (0.47-2.22)	0.96 (0.44-2.10)

‡Dementia outcome includes all dementia subtypes.

**Multivariable model adjusted for ethnicity, patient level of deprivation, smoking status, alcohol consumption, body mass index, records of anxiety, asthma, atrial fibrillation, bipolar disorder, chronic kidney disease, chronic obstructive pulmonary disease (COPD), coronary heart disease, depression, down syndrome, head injury, heart failure, hyperlipidaemia, hypertension, learning disability, schizophrenia, stroke, subarachnoid haemorrhage, transient ischaemic attack (TIA), type 1 diabetes, type 2 diabetes, mean anticholinergic effect of cognition (AEC) score of other prescribed non-bladder anticholinergic medication, prescription of other commonly prescribed bladder anticholinergic medication (oxybutynin, solifenacin, tolterodine); with case-control matching by age, sex and general practice.

Table S4b. Crude and adjusted odds ratios for dementia[‡] by total cumulative use of different bladder anticholinergic drugs and mirabegron, in subgroup of patients < 80 years (n=329,926)

Anticholinergic medication	Cumulative exposure to anticholinergic (TSDD)	Patients with dementia (Cases, n =55,373)	Patients without dementia (Controls, n = 274,553)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio** (95% CI)
Darifenacin hydrobromide	None	55,357 (99.97)	274,476 (99.97)	1.00 [Reference]	1.00 [Reference]
	1-90	10 (0.02)	35 (0.01)	1.40 (0.69-2.83)	0.93 (0.44-1.94)
	91-365	2 (0.00)	19 (0.01)	0.53 (0.12-2.26)	0.38 (0.09-1.67)
	366-1095	3 (0.01)	19 (0.01)	0.75 (0.22-2.57)	0.60 (0.17-2.12)
	>1095	1 (0.00)	4 (0.00)	1.27 (1.14-11.36)	0.41 (0.04-4.07)
Fesoterodine fumarate	None	55,169 (99.63)	273,882 (99.76)	1.00 [Reference]	1.00 [Reference]
	1-90	90 (0.16)	324 (0.12)	1.37 (1.09-1.74)	1.03 (0.80-1.32)
	91-365	48 (0.09)	167 (0.06)	1.43 (1.04-1.98)	1.12 (0.80-1.57)
	366-1095	35 (0.06)	107 (0.04)	1.64 (1.12-2.40)	1.16 (0.78-1.74)
	>1095	31 (0.06)	73 (0.03)	2.15 (1.41-3.28)	1.68 (1.07-2.63)
Flavoxate hydrochloride	None	55,253 (99.78)	274,059 (99.82)	1.00 [Reference]	1.00 [Reference]
	1-90	89 (0.16)	398 (0.14)	1.11 (0.88-1.40)	0.84 (0.66-1.07)
	91-365	14 (0.03)	62 (0.02)	1.13 (0.63-2.01)	0.84 (0.46-1.53)
	366-1095	8 (0.01)	22 (0.01)	1.82 (0.81-4.09)	1.58 (0.68-3.70)
	>1095	9 (0.02)	12 (0.00)	3.71 (1.56-8.81)	2.72 (1.07-6.97)
Oxybutynin hydrochloride	None	53,066 (95.83)	266,165 (96.94)	1.00 [Reference]	1.00 [Reference]
	1-90	1,435 (2.59)	5,938 (2.16)	1.22 (1.15-1.29)	1.07 (1.01-1.14)
	91-365	414 (0.75)	1,316 (0.48)	1.59 (1.42-1.77)	1.32 (1.17-1.49)
	366-1095	283 (0.51)	739 (0.27)	1.93 (1.68-2.21)	1.60 (1.38-1.85)
	>1095	175 (0.32)	395 (0.14)	2.23 (1.87-2.67)	1.86 (1.53-2.25)
Propiverine hydrochloride	None	55,216 (99.72)	274,072 (99.82)	1.00 [Reference]	1.00 [Reference]
	1-90	77 (0.14)	270 (0.10)	1.42 (1.10-1.83)	1.07 (0.82-1.40)
	91-365	39 (0.07)	96 (0.03)	2.02 (1.39-2.93)	1.47 (0.99-2.19)
	366-1095	26 (0.05)	66 (0.02)	1.96 (1.24-3.08)	1.16 (0.71-1.89)
	>1095	15 (0.03)	49 (0.02)	1.54 (0.86-2.74)	1.08 (0.58-1.99)
Solifenacin succinate	None	53,796 (97.15)	269,089 (98.01)	1.00 [Reference]	1.00 [Reference]
	1-90	551 (1.00)	2,163 (0.79)	1.28 (1.17-1.41)	1.12 (1.01-1.24)

	91-365	388 (0.70)	1,288 (0.47)	1.52 (1.36-1.70)	1.32 (1.17-1.49)
	366-1095	308 (0.56)	1,027 (0.37)	1.51 (1.33-1.72)	1.23 (1.07-1.41)
	>1095	330 (0.60)	986 (0.36)	1.69 (1.49-1.92)	1.37 (1.19-1.56)
Tolterodine tartrate	None	53,183 (96.05)	267,022 (97.26)	1.00 [Reference]	1.00 [Reference]
	1-90	961 (1.74)	3,823 (1.39)	1.26 (1.18-1.36)	1.14 (1.06-1.23)
	91-365	497 (0.90)	1,665 (0.61)	1.51 (1.36-1.67)	1.26 (1.13-1.40)
	366-1095	364 (0.66)	1,050 (0.38)	1.74 (1.54-1.96)	1.49 (1.31-1.70)
	>1095	368 (0.66)	993 (0.36)	1.87 (1.66-2.11)	1.60 (1.41-1.82)
Trospium chloride	None	54,889 (99.13)	272,974 (99.42)	1.00 [Reference]	1.00 [Reference]
	1-90	234 (0.42)	892 (0.32)	1.30 (1.13-1.51)	1.02 (0.88-1.19)
	91-365	115 (0.21)	363 (0.13)	1.57 (1.27-1.93)	1.09 (0.87-1.36)
	366-1095	79 (0.14)	179 (0.07)	2.20 (1.69-2.87)	1.53 (1.16-2.03)
	>1095	56 (0.10)	145 (0.05)	1.89 (1.39-2.58)	1.37 (0.99-1.90)
Mirabegron	None	55,230 (99.74)	274,137 (99.85)	1.00 [Reference]	1.00 [Reference]
	1-90	58 (0.10)	188 (0.07)	1.54 (1.14-2.06)	1.14 (0.83-1.56)
	91-365	40 (0.07)	111 (0.04)	1.76 (1.23-2.53)	1.26 (0.86-1.85)
	366-1095	40 (0.07)	97 (0.04)	2.05 (1.42-2.96)	1.52 (1.04-2.24)
	>1095	5 (0.01)	20 (0.01)	1.26 (0.47-3.36)	0.71 (0.25-2.02)

‡Dementia outcome includes all dementia subtypes.

**Multivariable model adjusted for ethnicity, patient level of deprivation, smoking status, alcohol consumption, body mass index, records of anxiety, asthma, atrial fibrillation, bipolar disorder, chronic kidney disease, chronic obstructive pulmonary disease (COPD), coronary heart disease, depression, down syndrome, head injury, heart failure, hyperlipidaemia, hypertension, learning disability, schizophrenia, stroke, subarachnoid haemorrhage, transient ischaemic attack (TIA), type 1 diabetes, type 2 diabetes, mean anticholinergic effect of cognition (AEC) score of other prescribed non-bladder anticholinergic medication, prescription of other commonly prescribed bladder anticholinergic medication (oxybutynin, solifenacin, tolterodine); with case-control matching by age, sex and general practice.

Table S5. Adjusted odds ratios for dementia associated with different bladder anticholinergic drugs and mirabegron, in males and females

Anticholinergic medication	Cumulative exposure to anticholinergic (TSDD)	Adjusted odds ratio** (95% CI) in males (n=363,213)	Adjusted odds ratio** (95% CI) in females (n=611,914)
		Cases = 63,865 Controls = 299,348	Cases = 106,877 Controls = 505,037
All bladder anticholinergic medications		1.22 (1.18-1.26)	1.16 (1.13-1.19)
Darifenacin hydrobromide	None	1.00	1.00
	1-90	1.41 (0.69-2.89)	0.99 (0.63-1.56)
	91-365	0.33 (0.04-2.61)	0.99 (0.55-1.81)
	366-1095	2.29 (0.80-6.57)	0.40 (0.14-1.15)
	>1095	1.36 (0.10-17.9)	1.25 (0.41-3.80)
Fesoterodine fumarate	None	1.00	1.00
	1-90	1.07 (0.82-1.41)	0.84 (0.70-1.01)
	91-365	1.36 (0.98-1.90)	0.96 (0.76-1.22)
	366-1095	1.11 (0.72-1.72)	1.10 (0.84-1.45)
	>1095	1.42 (0.87-2.32)	1.06 (0.76-1.48)
Flavoxate hydrochloride	None	1.00	1.00
	1-90	0.87 (0.71-1.06)	0.93 (0.80-1.07)
	91-365	1.14 (0.72-1.82)	0.87 (0.61-1.25)
	366-1095	1.36 (0.75-2.46)	0.88 (0.51-1.53)
	>1095	1.94 (0.75-5.03)	1.62 (0.83-3.17)
Oxybutynin hydrochloride	None	1.00	1.00
	1-90	1.03 (0.97-1.09)	1.05 (1.01-1.09)
	91-365	1.14 (1.02-1.27)	1.14 (1.06-1.23)
	366-1095	1.24 (1.08-1.42)	1.35 (1.23-1.48)
	>1095	1.28 (1.06-1.55)	1.29 (1.13-1.47)
Propiverine hydrochloride	None	1.00	1.00
	1-90	1.12 (0.84-1.48)	0.99 (0.84-1.18)
	91-365	1.27 (0.79-2.05)	1.14 (0.87-1.51)
	366-1095	1.21 (0.63-2.32)	1.19 (0.89-1.59)
	>1095	1.24 (0.63-2.42)	1.17 (0.83-1.64)
Solifenacin succinate	None	1.00	1.00
	1-90	1.12 (1.01-1.24)	0.99 (0.93-1.05)
	91-365	1.27 (1.12-1.43)	1.05 (0.97-1.15)
	366-1095	1.32 (1.16-1.51)	1.11 (1.02-1.22)
	>1095	1.49 (1.30-1.72)	1.20 (1.10-1.32)
Tolterodine tartrate	None	1.00	1.00
	1-90	1.09 (1.01-1.17)	1.03 (0.98-1.08)
	91-365	1.33 (1.20-1.47)	1.08 (1.00-1.16)
	366-1095	1.45 (1.28-1.64)	1.21 (1.12-1.32)
	>1095	1.23 (1.08-1.40)	1.26 (1.16-1.37)
Trospium chloride	None	1.00	1.00
	1-90	1.13 (0.97-1.32)	0.94 (0.86-1.04)
	91-365	1.63 (1.33-2.01)	0.93 (0.80-1.09)
	366-1095	1.26 (0.94-1.69)	1.33 (1.11-1.59)
	>1095	1.49 (1.03-2.15)	1.002 (0.81-1.28)
Mirabegron	None	1.00	1.00
	1-90	1.28 (0.94-1.76)	0.78 (0.62-0.99)

	91-365	1.53 (1.12-2.09)	1.10 (0.84-1.44)
	366-1095	1.46 (1.00-2.13)	1.72 (1.30-2.27)
	>1095	0.55 (0.16-1.87)	1.13 (0.54-2.34)

**Multivariable model adjusted for ethnicity, patient level of deprivation, smoking status, alcohol consumption, body mass index, records of anxiety, asthma, atrial fibrillation, bipolar disorder, chronic kidney disease, chronic obstructive pulmonary disease (COPD), coronary heart disease, depression, down syndrome, head injury, heart failure, hyperlipidaemia, hypertension, learning disability, schizophrenia, stroke, subarachnoid haemorrhage, transient ischaemic attack (TIA), type 1 diabetes, type 2 diabetes, mean anticholinergic effect of cognition (AEC) score of other prescribed non-bladder anticholinergic medication, prescription of other commonly prescribed bladder anticholinergic medication (oxybutynin, solifenacin, tolterodine); with case-control matching by age, sex and general practice.

Table S6.

Crude and adjusted odds ratios for dementia[‡] by total cumulative use of mirabegron in patients with no bladder anticholinergic drug exposure, 3-16 years before dementia[‡] diagnosis

Anticholinergic medication	Cumulative exposure to anticholinergic (TSDD)	Cases (n =170,376)	Controls (n = 803,158)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio** (95% CI)
Mirabegron	None	170,317 (99.97)	802,965 (99.98)	1.00 [Reference]	1.00 [Reference]
	1-90	22 (0.01)	98 (0.01)	1.06 (0.67-1.69)	1.09 (0.68-1.76)
	91-365	22 (0.01)	54 (0.01)	1.93 (1.17-3.18)	1.99 (1.19-3.31)
	366->1095***	15 (0.01)	41 (0.01)	1.73 (0.95-3.13)	1.81 (0.98-3.33)

[‡]Dementia outcome includes all dementia subtypes.

**Multivariable model adjusted for ethnicity, patient level of deprivation, smoking status, alcohol consumption, body mass index, records of anxiety, asthma, atrial fibrillation, bipolar disorder, chronic kidney disease, chronic obstructive pulmonary disease (COPD), coronary heart disease, depression, down syndrome, head injury, heart failure, hyperlipidaemia, hypertension, learning disability, schizophrenia, stroke, subarachnoid haemorrhage, transient ischaemic attack (TIA), type 1 diabetes, type 2 diabetes, mean anticholinergic effect of cognition (AEC) score of other prescribed non-bladder anticholinergic medication; with case-control matching by age, sex and general practice.

***last row for TSDD >1095 has been suppressed and merged with TSDD category 366-1095 due to small cell count with fewer than 5 observations

Supplementary figures

Figure S1.

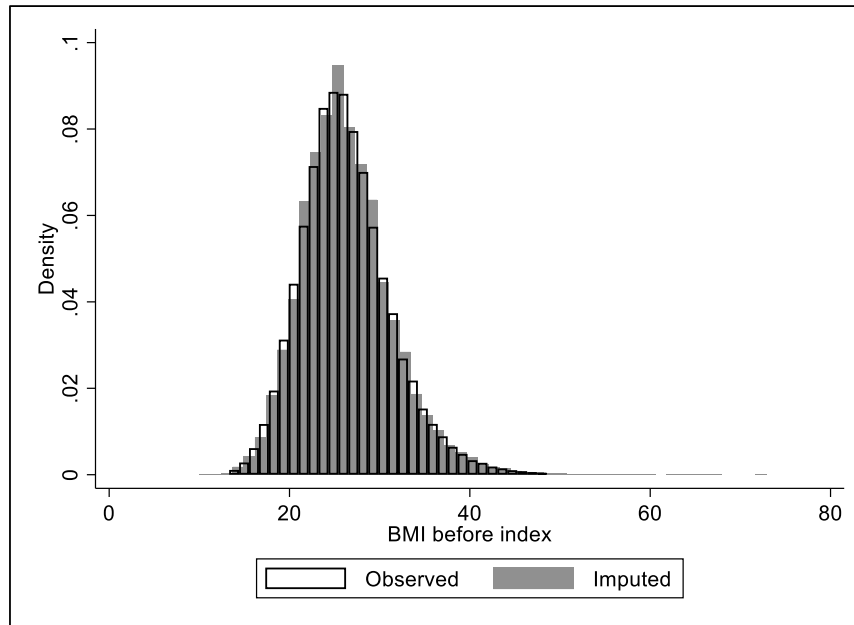


Figure S1. Kernel density plot showing the distribution of observed BMI records superimposed on the plot of BMI records after data imputation.