Data Supplement for Rector et al., Outcomes of Citalopram Dosage Risk Mitigation in a Veteran Population. Am J Psychiatry (doi: 10.1176/appi.ajp.2016.15111444)

Table S1. Differences in All Baseline Characteristics of Subjects Whose Citalopram Dose Was or Wasn't Reduced to ≤ 40 mg/day.

Characteristic	Dose Not Reduced n = 17,441	Dose Decreased n = 18,407	Standardized Difference (%)[a]
Age (yrs)	58 ± 12	58 ± 11	4.6
Male (%)	92	92	1.3
Race (%)			
White	79	79	-0.3
Black	12	12	-
Other	1	1	-
Missing	8	7	-
Hispanic (%)			
Yes	5	5	-0.2
No	90	90	-
Missing	5	5	-
Married (%)	57	57	0.2
VA eligibility (%)			
Service connected disability > 50% (no prescription copay)	60	62	-
Service connected disability < 50% (prescription copay)	18	17	-
Economic Means Test (prescription copay)	22	20	-3.5
Other insurance (%)	55	56	2.8
VA health care			
Hospitalization (%)	14	15	2.1
Days with Outpatient Visit	14 ± 14	15 ± 15	11.3
Prescription classes	6.1 ± 3.0	6.3 ± 3.1	6.9
Electrocardiogram (%)	23	25	4.7
Internal cardiac defibrillator (%)	0.2	0.2	1.3
Diagnoses recorded (%)			
Depression	69	70	1.5
Post-traumatic stress disorder	51	54	5.6
Suicidal behavior	0.7	0.8	0.8
Anxiety	24	26	5.1
Psychosis	13	16	8.5
Substance abuse	22	22	0.7
Sleep disorder	11	11	0.3
Sleep apnea	20	19	-0.2
Tachycardia	1.9	1.8	-0.3
Atrial fibrillation	3.4	3.4	0.4
QT abnormality	0.03	0.04	0.5

Atrioventricular block	2.5	2.4	-0.7
Other arrhythmia	3.6	3.7	0.1
Hypertension	58	60	4.2
Ischemic heart disease	18	19	2.5
Heart failure	4.4	4.4	-0.1
Cardiac valve abnormality	2.1	2.4	1.8
Peripheral artery disease	11	12	3.6
Diabetes mellitus	32	32	-0.7
Pulmonary disease	17	17	1.9
Chronic kidney disease	5.1	5.1	-0.1
Hypothyroid	7.0	7.8	2.8
Liver disease	6.3	6.3	-0.3
Seizure disorder	3.5	3.8	2.0
Malignant cancer	0.5	0.4	-0.8
Other cancer (excluding basal skin)	7.9	8.0	0.4
Prescriptions (%)			
Other selective serotonin reuptake inhibitor	50	53	5.9
Tricyclic antidepressant	7.3	7.0	-1.2
Monoamine oxidase inhibitor	0.006	0.01	0.6
Sedative/hypnotic	40	44	7.6
Antipsychotic	24	29	10.9
Lithium	1.1	1.4	2.5
Dementia	3.1	3.3	0.9
Beta-adrenergic blocker	34	33	-0.9
Beta-adrenergic stimulant	0.3	0.4	0.2
Alpha-adrenergic blocker	29	29	-0.1
Angiotensin II antagonist	39	39	0.7
Calcium channel blocker	21	22	1.3
Nitrate	9.6	9.9	0.9
Digoxin	1.4	1.2	-1.7
Antiplatelet agent	25	27	4.8
Anticoagulant	4.9	5.0	0.6
Other antihypertensive	9.8	9.5	-0.9
Antiarrhythmic	0.8	0.8	-0.1
Diuretic (potassium-sparing)	4.5	4.6	0.4
Diuretic (other)	27	27	0.8
Cholesterol reducer	62	63	2.2
Others that can prolong QT-interval	22	24	3.3
Insulin	12	11	-2.5
Other glucose control	24	24	-1.0
Thyroid hormone replacement	9.2	9.4	0.8
Bone loss	8.6	9.0	1.4
Corticosteroid (systemic)	8.9	9.7	2.6
Testosterone replacement	4.3	4.4	0.5
Anticonvulsant	42	44	4.4
Migraine medication	3.3	2.9	-2.1
Parkinson’s disease	4.0	4.0	0.1
Nervous system	5.4	6.4	4.3

Muscle relaxant	23	24	1.0
Respiratory	25	26	2.4
Nonsteroidal anti-inflammatory	38	39	2.8
Gout	4.8	5.2	1.6
Immunosuppressant	1.0	0.9	-0.8
Antineoplastic agent	1.5	1.5	0.2
Cytochrome 2C19 enzyme inhibitor	47	48	2.1
Citalopram Prescriptions			
Days supplied for > 40 mg/day	232 ± 99	243 ± 98	11.9
Last prescribed daily dose (mg)	64 ± 8.6	63 ± 7.9	-12.9
Last Month (%)			
May	12	11	3.3
June	29	34	-11.4
July	59	55	8.6
Last Days Supply (%)			
≤ 34	36	43	-
35 to 89	7	7	-
90	57	50	-13.8
Carryover into follow-up period			
Zero (%)	51	59	16.8
Days , if not zero	28 ± 17	29 ± 16	-
Refill (%)	59	61	4.0
Mailed (%)	92	92	-0.2
Community-based outpatient clinic	41	42	3.0
Prescriber (%)			
Psychiatry	48	53	11.3
Physician, not psychiatry	30	24	-
Physician extender[b]	23	23	-
Veterans Integrated Service Network (%)			
1	4.4	4.0	-2.0
2	1.5	1.2	-2.6
3	1.4	2.0	4.9
4	4.1	3.6	-2.6
5	0.8	1.4	5.7
6	6.3	7.2	3.6
7	8.3	7.7	-2.2
8	5.6	8.9	12.5
9	3.5	9.1	23.2
10	2.7	4.3	8.7
11	4.9	5.3	2.0
12	2.7	3.6	4.9
15	5.5	4.5	-4.5
16	11	8.9	-6.5
17	8.2	5.8	-9.6
18	3.7	4.2	2.6
19	4.2	3.1	-5.8
20	6.3	4.0	-10.8
21	4.1	2.7	-7.9

22	5.0	4.4	-3.3
23	6.0	4.3	-7.7

[a]Reduced dose versus continued dose group difference in means or proportions expressed as a percentage of the pooled standard deviation or standard error for proportions. [b]Advanced practice nurse, physician's assistant, clinical pharmacist.

Table S2. Differences in All Baseline Characteristics in Propensity Model Used to Match Subjects Whose Citalopram Dose Was or Wasn't Reduced to ≤ 40 mg/day.

Characteristic	Dose Not Reduced n = 14,762	Dose Decreased n = 14,762	Standardized Difference (%)[a]
Patient Demographics			
Age (yrs)	58	58	6.0
Male (%)	92	92	1.3
White race (%)	84	86	4.6
Hispanic (%)	5.3	5.1	-0.9
Married (%)	57	58	2.4
VA eligibility by means test (%)	21	20	-1.7
Other insurance (%)	54	56	3.6
VA health care			
Hospitalization (%)	20	18	-4.5
Outpatient Visit Days	14	14	-0.6
Prescription classes	6.1	6.2	2.5
Electrocardiogram (%)	23	23	-0.2
ICD placement or check (%)	0.2	0.2	0.5
Diagnoses recorded (%)			
Mental health			
Depression	71	69	-3.2
Post-traumatic stress disorder	53	53	0.4
Suicidal behavior	0.1	0.1	-0.7
Anxiety	25	25	0.4
Psychosis	14	15	1.4
Substance abuse	23	22	-3.2
Sleep disorder	12	11	-1.4
Sleep apnea	20	19	-1.0
Cardiovascular			
Tachycardia	1.9	1.7	-1.5
Atrial fibrillation	3.4	3.2	-1.5
QT abnormality	0.0004	0.0003	-0.7
Atrioventricular block	2.5	2.4	-0.3
Other arrhythmia	3.7	3.5	-0.8
Hypertension	59	60	1.1
Ischemic heart disease	18	18	0.3
Heart failure	4.4	4.2	-0.8
Cardiac valve abnormality	2.2	2.2	0.1
Peripheral artery disease	11	12	1.1
Other			
Diabetes mellitus	32	32	-0.3
Pulmonary disease	17	17	-0.1
Chronic kidney disease	5.1	5.0	-0.6
Hypothyroid	7.0	7.8	2.8
Liver disease	6.4	6.1	-1.2
Seizure disorder	3.6	3.7	0.7
Malignant cancer	0.5	0.4	-2.1

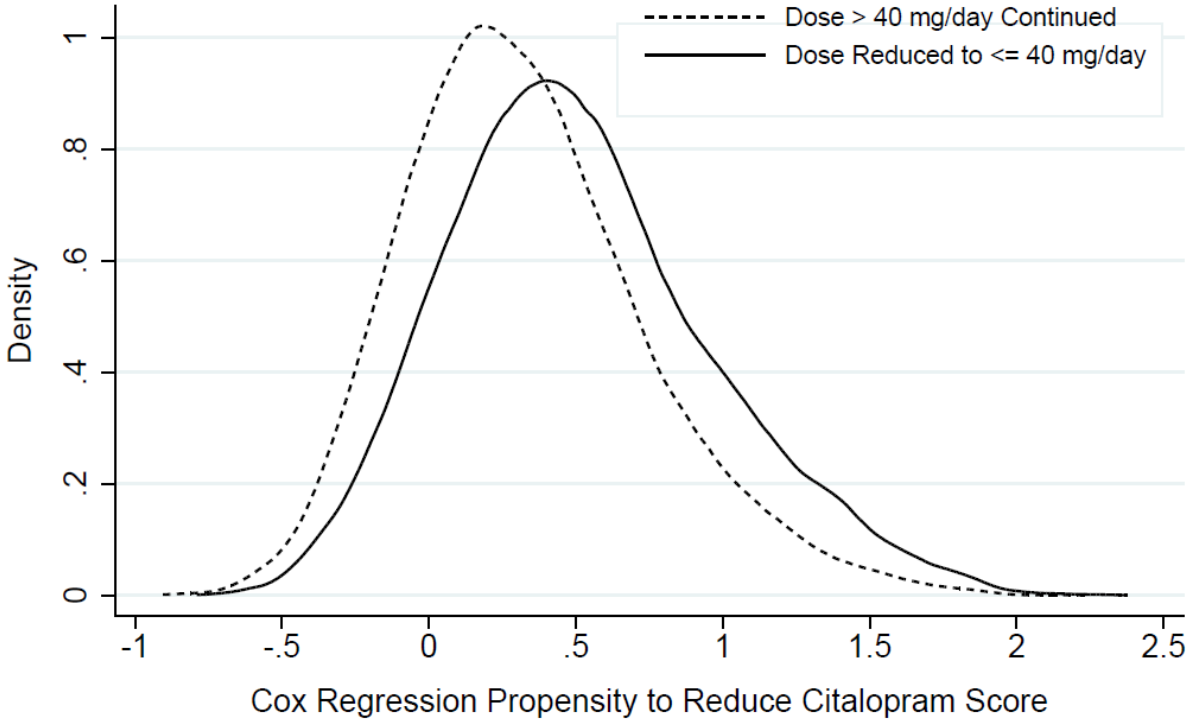
Other cancer (excluding basal skin)	8.0	7.8	-0.6
Prescriptions (%)			
Mental health			
Other selective serotonin receptor inhibitor	52	51	-1.4
Tricyclic antidepressant	7.4	7.0	-1.7
Monoamine oxidase inhibitor	0.00	0.00	-0.7
Sedative/hypnotic	41	42	2.1
Antipsychotic	26	27	2.8
Lithium	1.2	1.2	0.2
Dementia	3.1	3.3	1.5
Cardiovascular			
Beta-adrenergic blocker	33	34	0.3
Beta-adrenergic stimulant	0.4	0.4	0.1
Alpha-adrenergic blocker	28	29	1.2
Angiotensin II antagonist	38	39	0.6
Calcium channel blocker	21	22	0.5
Nitrate	9.7	9.8	0.6
Digoxin	1.3	1.2	-1.3
Antiplatelet agent	25	26	3.2
Anticoagulant	5.0	4.7	-1.6
Other antihypertensive	9.8	10	0.6
Antiarrhythmic	0.8	0.7	-1.7
Diuretic (potassium-sparing)	4.5	4.6	-0.2
Diuretic (other)	27	27	0.3
Cholesterol reducer	61	63	3.3
Others that prolong QT interval	23	23	-0.1
Other			
Insulin	12	11	-0.8
Other glucose control	24	24	0.5
Thyroid hormone replacement	9.0	9.4	1.2
Bone loss	8.3	9.1	2.7
Corticosteroid (systemic)	9.3	8.9	-1.2
Testosterone replacement	4.1	4.4	1.5
Anticonvulsant	43	44	1.0
Migraine medication	3.3	3.0	-1.7
Parkinson's disease	4.0	4.2	1.1
Nervous system	5.6	6.0	1.5
Muscle relaxant	24	24	-0.1
Respiratory	26	26	0.8
Nonsteroidal anti-inflammatory	39	39	0.3
Gout	4.8	4.9	0.7
Immunosuppressant	0.9	0.9	-0.2
Antineoplastic agent	1.4	1.5	0.4
Cytochrome 2C19 enzyme inhibitor	46	47	1.4
Citalopram Prescriptions			
Days supplied for > 40 mg/day	228	249	20
Mean index dose over 40 mg/day	23	23	-1.1

Last Month (%)			
May	10	12	9.1
June	33	30	-8.6
July	57	58	2.3
Last prescription supply 90 days (%)	53	54	2.0
Mean carryover into follow-up (days)	13	13	0.3
Refill (%)	59	62	6.7
Mailed (%)	91	92	4.2
Community-based outpatient clinic	42	42	0.2
Prescriber Psychiatry (%)	51	51	0.2
VA Integrated Service Network (%)[b]			
1	4.1	4.7	2.8
2	1.3	1.4	0.9
3	1.6	1.6	-0.4
4	4.1	4.2	0.4
5	1.0	1.0	0.2
6	7.2	6.4	-3.2
7	8.6	8.8	0.8
8	6.6	6.6	-0.2
9	4.1	3.9	-0.8
10	3.1	3.2	0.1
11	5.3	5.6	1.6
12	3.1	3.2	0.7
15	5.1	5.4	1.0
16	11	10	-0.8
17	7.1	7.0	-0.3
18	3.8	4.6	3.9
19	4.0	3.7	-5.8
20	5.2	4.9	-1.4
21	3.3	3.3	0.3
22	5.2	5.0	-3.3
23	5.5	5.2	-1.3

[a]Standardized differences of $\leq$ 10% are unlikely to lead to differences in outcome when baseline variables are not strongly related to a study outcome. ICD – internal cardiac defibrillator.
[b]Geographical organization of VA health care systems.

Figure S1. Density Distributions of Propensity Scores for Citalopram Dose Reductions.

The distribution of the propensity scores estimated by Cox regression of times to citalopram dose reductions in relation to all baseline characteristics listed in Table ST2 was higher in subjects whose dose was reduced to ≤ 40 mg/day, but overlapped extensively with the distribution of propensity scores in the group whose doses were not reduced to ≤ 40 mg/day. One-to-one matching selected the nearest neighbor from these distributions.



Citalopram prescriptions from specific Veterans Integrated Service Networks, VA community-based outpatient clinics or psychiatrists were independently associated with shorter times to dose reductions in the propensity model as were the presence of a diagnosis of depression, post-traumatic stress disorder, psychosis or anxiety along with corresponding medication classes. Patients that were older and those with ischemic heart disease, hypothyroidism, or an internal cardiac defibrillator also were more likely to have a dose reduction. Higher baseline citalopram doses and number of days > 40 mg/day during the baseline year decreased the likelihood of a prescription for ≤ 40mg/day.