

Appendix A The list of antidepressants filled and the percentage of off-label use by generic name and therapeutic class of drugs between 2000 and 2010

| Therapeutic Class (TC) | Sub-TC | Drug Name ^a (Genetic) | Number of Antidepressant Prescriptions Filled | Number of Off-label Use | Percentage of Off-label Use |
|------------------------|--------|----------------------------------|---|-------------------------|-----------------------------|
| Miscellaneous | 76 | Bupropion | 4,197 | 701 | 16.70 |
| | | Maprotiline | 14 | 14 | 100.00 |
| | | Mirtazapine | 946 | 190 | 20.08 |
| | | Nefazodone | 722 | 52 | 7.20 |
| | | Trazodone | 2,700 | 730 | 27.04 |
| | | Venlafaxine | 2,949 | 421 | 14.28 |
| | | Others | 4 | 1 | 25.00 |
| | | Sub-total | | 11,532 | 2,109 |
| SSRI ^b | 208 | Alprazolam | 3 | 0 | 0 |
| | | Citalopram | 14,494 | 1,939 | 13.38 |
| | | Escitalopram | 15,141 | 1,767 | 11.67 |
| | | Fluoxetine | 20,715 | 3,097 | 14.95 |
| | | Fluvoxamine | 672 | 95 | 14.14 |
| | | Lorazepam | 2 | 0 | 0 |
| | | Paroxetine | 20,380 | 2,640 | 12.95 |
| | | Sertraline | 26,664 | 3,439 | 12.90 |
| | | Trazodone | 9 | 9 | 100.00 |
| | | Others | 33 | 18 | 54.55 |
| Sub-total | | 98,113 | 13,004 | 13.25 | |
| Tricyclic | 209 | Amitriptyline | 13,881 | 6,651 | 47.91 |
| | | Amoxapine | 57 | 9 | 15.79 |
| | | Amoxicillin | 3 | 0 | 0 |
| | | Anafranil | 26 | 10 | 38.46 |
| | | Clomipramine | 475 | 101 | 21.26 |
| | | Desipramine | 345 | 128 | 37.10 |
| | | Imipramine | 1,573 | 612 | 38.90 |
| | | Nortriptyline | 2,713 | 1,368 | 50.42 |

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|-------------------|-----|-----------------|---------|--------|--------|
| | | Protriptyline | 45 | 5 | 11.11 |
| | | Trimipramine | 27 | 0 | 0 |
| | | Others | 20 | 20 | 100.00 |
| | | Sub-total | 19,165 | 8,904 | 46.46 |
| | | Phenelzine | 89 | 18 | 20.22 |
| MAOI ^c | 250 | Tranylcypromine | 51 | 0 | 0 |
| | | Sub-total | 140 | 18 | 12.86 |
| | | Nefazodone | 511 | 73 | 14.29 |
| Phenylpiperazine | 306 | Trazodone | 11,251 | 2,852 | 25.35 |
| | | Sub-total | 11,762 | 2,925 | 24.87 |
| | | Maprotiline | 7 | 0 | 0 |
| Tetracyclic | 307 | Mirtazapine | 3,616 | 827 | 22.87 |
| | | Sub-total | 3,623 | 827 | 22.83 |
| | | Desvenlafaxine | 315 | 14 | 4.44 |
| | | Duloxetine | 6,291 | 993 | 15.78 |
| | | Milnacipran | 77 | 30 | 38.96 |
| SNRI ^d | 308 | Venlafaxine | 11,709 | 1,589 | 13.57 |
| | | Others | 6 | 0 | 0 |
| | | Sub-total | 18,398 | 2,626 | 14.27 |
| Total | | | 162,733 | 30,413 | 18.69 |

^a Some drugs are classified into multiple therapeutic classes.

^b SSRI stands for Selective Serotonin Reuptake Inhibitor.

^c MAOI stands for Monoamine Oxidase Inhibitors.

^d SNRI stands for Serotonin-Norepinephrine Reuptake Inhibitor.

Appendix B The list of medical conditions reported by ICD-9-CM codes for which antidepressant drugs were frequently prescribed off-label

| ICD-9-CM Codes | | | Number of Off-Label Prescriptions Filled (N=30,413) | Share of Off-Label Use (%) |
|---------------------------------------|----------------|-----------------------------|--|----------------------------|
| First 3-digit (Medical conditions) | Sub-categories | Description | | |
| 780 | 780.0 | Alteration of consciousness | 4,164 | 13.69 |
| (General symptoms) | 780.1 | Hallucinations | | |
| | 780.2 | Syncope and collapse | | |

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|--|-------|--|-------|------|
| | 780.3 | Convulsions | | |
| | 780.4 | Dizziness and giddiness | | |
| | 780.5 | Sleep disturbances | | |
| | 780.6 | Fever and other physiologic disturbances of temperature regulation | | |
| | 780.7 | Malaise and fatigue | | |
| | 780.8 | Generalized hyperhidrosis | | |
| | 780.9 | Other general symptoms | | |
| | V68.0 | Issue of medical certificates | | |
| V68 | V68.1 | Issue of repeat prescriptions | | |
| (Encounters for administrative purposes) | V68.2 | Request for expert evidence | 2,870 | 9.44 |
| | V68.8 | Encounters for other specified administrative purpose | | |
| | V68.9 | Encounters for unspecified administrative purpose | | |
| | 308.0 | Predominant disturbance of emotions | | |
| | 308.1 | Predominant disturbance of consciousness | | |
| 308 | 308.2 | Predominant psychomotor disturbance | | |
| (Acute reaction to stress) | 308.3 | Other acute reactions to stress | 1,900 | 6.25 |
| | 308.4 | Mixed disorders as reaction to stress | | |
| | 308.9 | Unspecified acute reaction to stress | | |
| | 346.0 | Migraine with aura | | |
| | 346.1 | Migraine without aura | | |
| | 346.2 | Variants of migraine, not elsewhere classified | | |
| | 346.3 | Hemiplegic migraine | | |
| 346 | 346.4 | Menstrual migraine | | |
| (Migraine) | 346.5 | Persistent migraine aura without cerebral infarction | 1,626 | 5.35 |
| | 346.6 | Persistent migraine aura with cerebral infarction | | |
| | 346.7 | Chronic migraine without aura | | |
| | 346.8 | Other forms of migraine | | |
| | 346.9 | Migraine unspecified | | |
| 729 | 729.0 | Rheumatism unspecified and fibrositis | 1,426 | 4.69 |
| (Other disorders of soft tissues) | 729.1 | Myalgia and myositis unspecified | | |
| | 729.2 | Neuralgia neuritis and radiculitis unspecified | | |

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|---|-------|--|-------|------|
| | 729.3 | Panniculitis unspecified | | |
| | 729.4 | Fasciitis unspecified | | |
| | 729.5 | Pain in limb | | |
| | 729.6 | Residual foreign body in soft tissue | | |
| | 729.7 | Nontraumatic compartment syndrome | | |
| | 729.8 | Other musculoskeletal symptoms referable to limbs | | |
| | 729.9 | Other and unspecified disorders of soft tissue | | |
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| | 314.0 | Attention deficit disorder of childhood | | |
| 314 | 314.1 | Hyperkinesis of childhood with developmental delay | | |
| (Hyperkinetic syndrome of childhood) | 314.2 | Hyperkinetic conduct disorder of childhood | 1,094 | 3.60 |
| | 314.8 | Other specified manifestations of hyperkinetic syndrome of childhood | | |
| | 314.9 | Unspecified hyperkinetic syndrome of childhood | | |
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| | 627.0 | Premenopausal menorrhagia | | |
| | 627.1 | Postmenopausal bleeding | | |
| 627 | 627.2 | Symptomatic menopausal or female climacteric states | | |
| (Menopausal and postmenopausal disorders) | 627.3 | Postmenopausal atrophic vaginitis | 881 | 2.90 |
| | 627.4 | Symptomatic states associated with artificial menopause | | |
| | 627.8 | Other specified menopausal and postmenopausal disorders | | |
| | 627.9 | Unspecified menopausal and postmenopausal disorder | | |
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| 401 | 401.0 | Malignant essential hypertension | | |
| (Essential hypertension) | 401.1 | Benign essential hypertension | 875 | 2.88 |
| | 401.9 | Unspecified essential hypertension | | |
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| | 799.0 | Asphyxia and hypoxemia | | |
| | 799.1 | Respiratory arrest | | |
| 799 | 799.2 | Nervousness | | |
| (Other ill-defined and unknown causes of morbidity and mortality) | 799.3 | Debility unspecified | 732 | 2.41 |
| | 799.4 | Cachexia | | |
| | 799.8 | Other ill-defined conditions | | |
| | 799.9 | Other unknown and unspecified cause of morbidity or mortality | | |
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| 295 | 295.0 | Simple type schizophrenia | 723 | 2.38 |
| (Schizophrenic) | 295.1 | Disorganized type schizophrenia | | |

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|---------------------|-------|--|--------|-------|
| disorders) | 295.2 | Catatonic type schizophrenia | | |
| | 295.3 | Paranoid type schizophrenia | | |
| | 295.4 | Schizophreniform disorder | | |
| | 295.5 | Latent schizophrenia | | |
| | 295.6 | Residual type schizophrenia | | |
| | 295.7 | Schizo-affective disorder | | |
| | 295.8 | Other specified types of schizophrenia | | |
| | 295.9 | Unspecified schizophrenia | | |
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| | 625.0 | Dyspareunia | | |
| | 625.1 | Vaginismus | | |
| | 625.2 | Mittelschmerz | | |
| 625 | 625.3 | Dysmenorrhea | | |
| (Pain and other | 625.4 | Premenstrual tension syndromes | 716 | 2.35 |
| symptoms associated | 625.5 | Pelvic congestion syndrome | | |
| with female genital | 625.6 | Stress incontinence female | | |
| organs) | 625.7 | Vulvodynia | | |
| | 625.8 | Other specified symptoms associated with female genital organs | | |
| | 625.9 | Unspecified symptom associated with female genital organs | | |
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| Other medical | | | 13,406 | 44.08 |
| conditions | | | | |
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