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Original Research

A Canadian Primary Care Sentinel Surveillance Network Study Evaluating Antidepressant Prescribing in Canada From 2006 to 2012

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Objective: To evaluate the prescribing patterns of antidepressants (ADs) by primary care providers to youth, adults, and seniors, from 2006 to 2012, using data from electronic medical records (EMRs).

Method: This was a retrospective cross-sectional database study that used primary care data from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN). Data on more than 600 000 Canadian primary care patients were used to determine the prevalence and incidence of AD prescribing to patients 15 years and older who had an encounter in the years of study (from 2006 to 2012). Each study year was evaluated independently.

Results: The study population consisted of 86 927 patients in 2006 (mean age 48.1 years [SD 18.7], 38% male) and grew to 273 529 (mean age 49.6 years [SD 19.3], 40% male) in 2012. The prevalence of AD prescribing increased from 9.20% in 2006 to 12.80% in 2012 ($P < 0.001$). While the incidence rate of AD prescribing dropped from 3.54% in 2006 to 2.72% in 2008 ($P < 0.001$) the rate started to significantly rise again, reaching an incidence of 3.07% by 2012 ($P < 0.001$).

Conclusions: The prevalence of AD prescribing by primary care providers in Canada continued to rise from 2006 to 2012. Conversely, incidence has remained stable or declined during the 6-year study period. While many complex factors likely contribute to the observed prevalence and incidence rates, our findings suggest that the guidelines indicating the efficacy of long-term AD therapy for patients with highly recurrent or severe depression are being followed.

Étude du Réseau canadien de surveillance sentinelle en soins primaires évaluant les prescriptions d'antidépresseurs au Canada de 2006 à 2012

Objectif : Évaluer les modèles de prescription d'antidépresseurs (AD) par les prestataires de soins primaires aux jeunes, aux adultes et aux aînés, de 2006 à 2012, à l'aide des données des dossiers médicaux électroniques (DME).

Méthode : C'était une étude de base de données rétrospective et transversale qui utilisait les données des soins primaires du Réseau canadien de surveillance sentinelle en soins primaires (RCSSSP). Les données sur plus de 600 000 patients des soins primaires canadiens ont été utilisées pour déterminer la prévalence et l'incidence de la prescription d'AD aux patients de 15 ans et plus qui ont eu une rencontre dans les années de l'étude (de 2006 à 2012). Chaque année de l'étude a été évaluée indépendamment.

Résultats : La population de l'étude consistait en 86 927 patients en 2006 (âge moyen 48,1 ans [ET 18,7], et est passée à 273 529 (âge moyen 49,6 ans [ET 19,3], 40 % hommes) en 2012. La prévalence des prescriptions d'AD a augmenté de 9,20 % en 2006 à 12,80 % en 2012 ($P < 0,001$). Bien que le taux d'incidence de prescriptions d'AD ait chuté de 3,54 % en 2006 à 2,72 % en 2008 ($P < 0,001$), le taux s'est remis à grimper significativement, atteignant une incidence de 3,07 % en 2012 ($P < 0,001$).

Conclusions : La prévalence des prescriptions d'AD par les prestataires de soins primaires au Canada a connu une hausse constante de 2006 à 2012. Par contre, l'incidence est demeurée stable ou a diminué durant les 6 années de l'étude. Bien que de nombreux facteurs complexes contribuent probablement aux taux de prévalence et d'incidence observés, nos résultats suggèrent que les lignes directrices indiquant l'efficacité du traitement par AD à long terme pour les patients souffrant de dépression très récurrente ou grave sont observées.

It is important that depression be effectively managed, as it is the leading cause of disability worldwide and a major contributor to the global burden of disease.[1] ADs are one of the first lines of treatment for people suffering from depression and a common pharmaceutical prescribed in primary care.[2–4] In the last decade, there have been some complex findings from research on AD prescribing with reports of increased use, but also reports of underuse by patients for whom ADs are clinically indicated.[5–10] In 2011, researchers in the United States found that a large and growing proportion of ADs are prescribed at medical encounters where no clinical psychiatric diagnosis is recorded.[5] The study emphasized the need for deeper inquiry into the prescribing of ADs by general practitioners. There have also been several international and North American studies which found lower rates of AD prescribing for people with MDD.[6–10] Further, the interpretation that these low treatment rates means underuse may be a reflection of a decade of enthusiasm about the efficacy of ADs, but it is unclear if people in need are receiving help or if guidelines are being followed. In the last 5 years, extensive reviews of published and unpublished trials have shown that the superior effects of ADs to placebo have only remained true when administered to patients with severe depression or recurring depression.[11] As a result, new guidelines recommend that ADs should not be used to treat subthreshold depressive symptoms or mild depression, owing to a poor risk–benefit ratio.[12] It is obvious that the current landscape of AD use needs to be exposed to evaluate if the revised guidelines are being put into practice.

Guidelines for AD treatment vary by age group, and it is important to track and evaluate prescribing trends in these subpopulations. Adolescence and young adulthood are critical life stages and depression in these developmental periods are associated with functional impairment and risk of adult depression.[13–16] Further, there has been some evidence that AD use by this vulnerable population is associated with an increased risk of suicidal thinking and behaviour.[15] The treatment of depression in seniors is also becoming increasingly important, owing to the growing size of this demographic and its burden on the Canadian health care system.[17,18]

Clinical Implications

- From 2006 to 2012, there was a significant rise in the prescribing of ADs in primary care in youth, adults, and seniors.
- Incidence of AD prescribing is not rising in adults and seniors, indicating that increasing prevalence may be due to patients remaining on ADs for longer.
- Continued education and training is needed on the use of ADs in primary care.

Limitations

- There may be some selection bias, as the providers that contributed data to the CPCSSN are a convenience sample and were not randomly selected.
- The CPCSSN data were only able to capture AD prescriptions and do not reflect if these prescriptions were filled at pharmacies.
- There is likely some misclassification, owing to EMR data having limited historical records.

Using primary care EMR data to evaluate AD prescribing practices in Canada is an important contribution to this body of literature, as previous reports have relied on survey and administrative data. The CPCSSN is a pan-Canadian organization that collects clinical EMR data on 600 000 patients. In our study, primary care medication data within the CPCSSN were used to describe the current landscape of AD prescribing in Canadian primary care for adolescents, adults, and seniors.

Abbreviations

AD	antidepressant
CPCSSN	Canadian Primary Care Sentinel Surveillance Network
EMR	electronic medical record
MDD	major depressive disorder
YCG	yearly contact groups

Methods

Data Source

The CPCSSN is a network of 11 Practice Base Research Networks, spanning 8 provinces, that collects electronic patient data from participating primary care providers. Data are extracted from various EMRs and de-identified before being cleaned and uploaded to a central data repository. Data elements available for research include patient and provider demographics, health condition data, billing and encounter data, medications, laboratories and examinations, risk factor data, as well as adverse reaction and procedural data. Our study used the patient demographic table and the medications table.

Table 1 Age and sex distribution of the Canadian Primary Care Sentinel Surveillance Network's primary care population (denominator) in Canada from 2006 to 2012

	Year						
Characteristic	2006	2007	2008	2009	2010	2011	2012
n	86 927	142 949	181 054	212 004	240 142	261 673	273 529
Age, years							
15 to 24	12.4	12.9	12.9	13.0	12.6	12.5	12.5
25 to 64	66.5	65.4	65.3	65.1	64.7	64.2	63.5
≥65	21.1	21.7	21.8	21.9	22.7	23.3	24.0
Sex							
Female	61.8	61.3	60.4	60.4	60.2	60.0	60.0
Male	38.2	38.7	39.6	39.6	39.8	40.0	40.0

Table 2 Prevalence and incidence of antidepressant prescribing among youth, adults, and seniors in Canada from 2006 to 2012

	Prevalence, %				Incidence, %			
Year	Youth	Adults	Seniors	Total	Youth	Adults	Seniors	Total
2006	5.14	9.97	9.15	9.20	2.88	3.61	3.69	3.54
2007	4.77	9.87	9.40	9.11	3.08	3.10	2.56	2.97
2008	5.15	10.13	9.87	9.43	2.93	2.77	2.47	2.72
2009	5.34	10.70	10.60	9.99	2.89	2.82	2.46	2.74
2010	6.04	11.83	11.66	11.06	3.00	2.82	2.38	2.73
2011	6.64	12.62	12.72	11.89	3.27	2.97	2.70	2.94
2012	7.64	13.58	13.43	12.80	3.45	3.18	2.62	3.07

Study Design

Our study was a retrospective cross-sectional longitudinal study that evaluated AD-prescribing patterns in a sample of primary care practices across Canada. The study population (denominator) consisted of YCGs between 2006 and 2012. The YCG consists of any patient who had an encounter with a CPCSSN physician (Sentinel) in any of the inclusion years. To illustrate, if a patient visits a physician every other year, they would be included in the year of their visit, but not the following year, and if a patient visits 6 times in 1 year they would only be counted once in that YCG. Only patients with an encounter age of 15 years or older with a valid EMR entry for birth year and sex were included in the study population. Patients were classified into 3 different age groups: youth (15 to 24 years), adults (25 to 64 years), and seniors (65 years and older).

In the last decade, an increasing number of physicians have adopted EMRs, and this has resulted in a steadily increasing number of patients with EMRs. The inclusion years for our study were chosen to maximize the number of patients with robust data, as well as to allow some patient history to be established to determine incident prescription rates. Prior to 2006, there are significantly less patients with EMRs.

Statistical Analysis

Prevalence

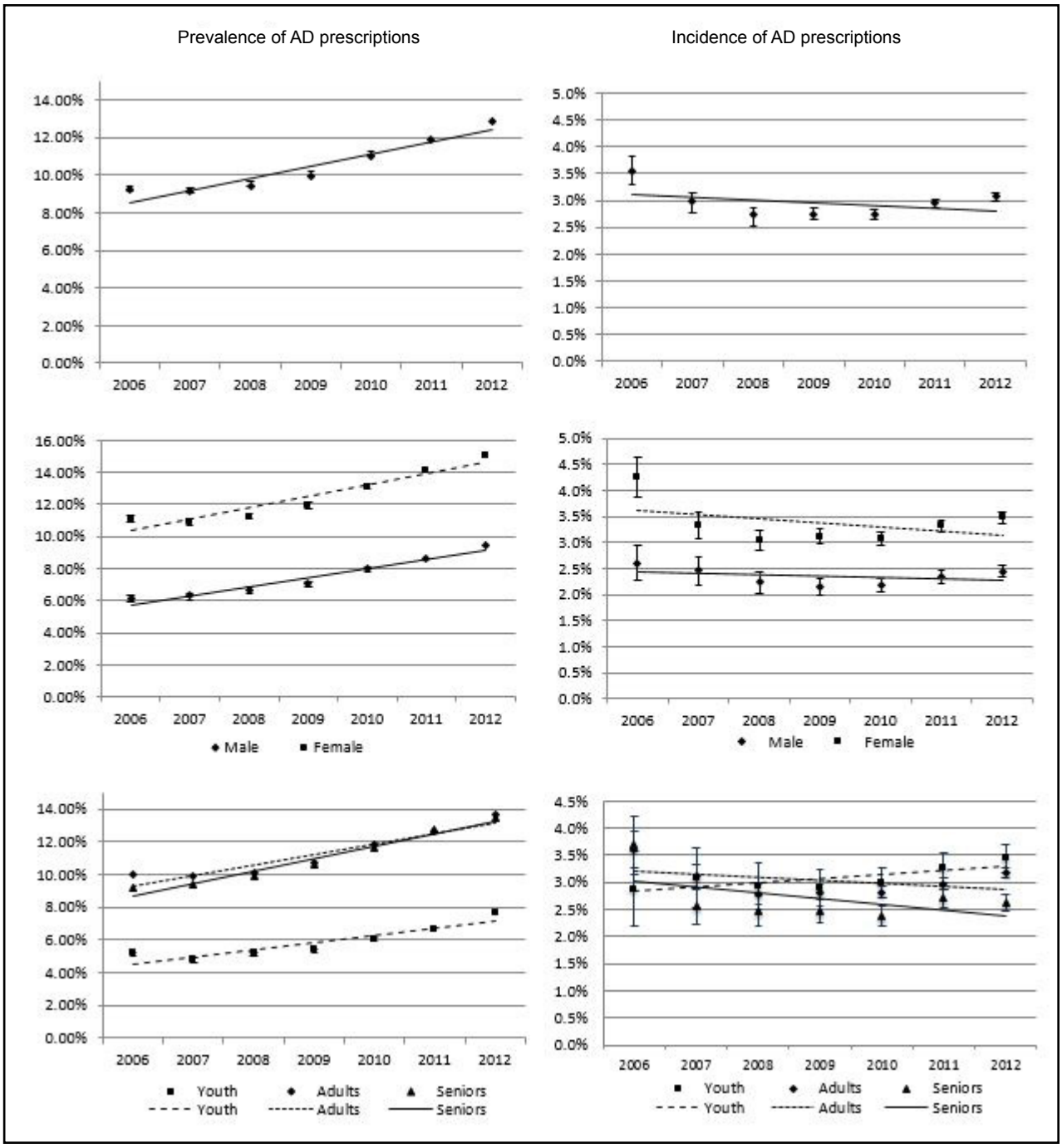
Each study year (from 2006 to 2012) was evaluated independently. The presence or absence of exposure to ADs was established by evaluating if there was at least one prescription for any of the ADs listed in Appendix A. The denominator consisted of the YCG.

Incidence

A patient was eligible to be an incident case if they had an encounter in the year of study (from 2006 to 2012), had any record(s) within the CPCSSN dating back at least 2 years, and had no previous record of an AD prescription. In each year of study, the denominator consisted of a YCG that had a record within the CPCSSN dating back at least 2 years, less any patient with any AD record in a previous year.

Prevalence and incidence estimates and the corresponding confidence limits were computed using an exact binomial test in SAS 9.3 (SAS Institute Inc, Cary, NC). Yearly estimates were pooled and an average obtained after weighting by sample size to account for the increasing number of observations in each subsequent study year. Estimates were compared between sexes, age groups, and years using the chi-square test and the Cochran–Mantel–Haenszel test for stratified data.

Figure 1 Prevalence and incidence of antidepressant (AD) prescriptions in Canadian primary care



The CPCSSN has received ethics approval from the research ethics boards of all host universities for all participating networks and from the Health Canada Research Ethics Board.

Results

The study population (15 years and older) consisted of 86 927 patients in 2006 (mean age 48.1 years [SD 18.7], 38% male) and grew to 273 529 (mean age 49.6 years [SD 19.3], 40% male) in 2012 (Table 1). Compared with the Canadian population, the study population was more likely to be older and female which is reflective of most primary care patient populations.

The prevalence of AD prescribing increased from 9.20% in 2006 to 12.80% in 2012 ($P < 0.001$) (Table 2, Figure 1). In each year of study the estimates differed by age and sex; females having an average prevalence across the study years, weighted by yearly sample size, of 12.33% (95% CI 11.22% to 13.45%), compared with 7.23% (95% CI 6.34% to 8.13%) in males. Across the 6 years of study, the weighted average prevalence of AD prescribing for seniors was 10.60% (95% CI 9.32% to 11.88%), which was not

Table 3 Prevalence and incidence of antidepressant prescribing among men and women in Canada from 2006 to 2012

	Prevalence, %			Incidence, %		
Year	Men	Women	Total	Men	Women	Total
2006	6.12	11.10	9.20	2.61	4.25	3.54
2007	6.26	10.91	9.11	2.46	3.32	2.97
2008	6.65	11.25	9.43	2.24	3.03	2.72
2009	7.02	11.93	9.99	2.14	3.12	2.74
2010	7.95	13.12	11.06	2.18	3.08	2.73
2011	8.64	14.06	11.89	2.34	3.33	2.94
2012	9.43	15.05	12.80	2.45	3.48	3.07

significantly different than the 11.10% (95% CI 10.10% to 12.1 0%) observed in the adult population ($P = 0.49$). In comparison with adults, the weighted average prevalence found in the youth population was significantly lower (5.72%, 95% CI 4.99% to 6.44%, $P < 0.001$).

While the incidence rate of AD prescribing dropped from 3.54% in 2006 to 2.72% in 2008 ($P < 0.001$) the rate started to significantly rise again, reaching an incidence of 3.07% by 2012 ($P < 0.001$) (Table 2, Figure 1). Between 2006 and 2012, there was a significant drop in the incidence of AD prescribing for females ($P < 0.001$) but there was no significant decrease for males ($P = 0.38$) (Table 3, Figure 1). Incidence differed by age, with youth having a small, but insignificant, increase in the incidence of AD prescribing ($P = 0.16$), whereas adults and seniors showed a significant reduction in the incidence of AD prescribing over time ($P = 0.02$ and $P < 0.001$, respectively) (Table 2, Figure 1).

Discussion

Our large population study found that from 2006 to 2012 the overall prevalence of AD prescribing in primary care patients aged 15 years and older has increased. A study published in 2007 by Raymond et al,[19] that used pharmacy records to evaluate the prevalence and incidence of AD use in British Columbia found that the prevalence of ADs doubled from 3.4% to 7.2% between 1996 and 2004. Our study confirms that the prevalence of ADs has continued to rise, 7.86% in 2006 to 11.07% in 2012, but appears to be increasing at a slower rate. As was hypothesized in the study by Raymond et al,[19] the rising prevalence could be owing to increased evidence and improved clinician awareness of the efficacy of long-term AD treatment for severe and recurring depression.[19] That there has been very little progress in the last decade in terms of novel drugs or more effective targets in AD therapy may explain the deceleration in the rate with which ADs are being prescribed.[20]

The proportion of youth being prescribed an AD is lower than that seen in adults, which may be a spillover effect of the 2004 Health Canada warning against the use of newer ADs for children.[21] Across all years of study, a similar proportion of seniors are being prescribed ADs, compared with that of the adult population (Figure 3). This may be an indication that seniors are undertreated, because MDD has shown to be more prevalent in community-dwelling elderly populations with comorbid chronic medical conditions, who comprise most seniors seen in primary care.[17,22]

We found the incidence rate of AD prescribing decreased from 2006 to 2012 in the CPCSSN population. Note, this finding indicates that the increasing prevalence of AD prescriptions is likely not a result of prescriptions to new users of ADs. Patients with MDD, where AD therapy has proven effective, may be staying on the medication longer, and this may account for the increased prevalence. The rate at which physicians are prescribing to new users is decreasing, and this could be evidence that guidelines, which indicate that AD therapy is only effective for people with moderate-to-severe depression, are being followed and other options to treat mild depression are being explored. Another factor to consider is that ADs are now being used to treat various psychiatric indications, such as anxiety, as well as nonpsychiatric indications, particularly sleep and pain-related conditions.[23,24] The expansion of therapeutic indications for AD therapy likely contributes to the increasing prevalence of AD prescriptions observed in our study. As well, previous studies have shown that over 30% of AD prescriptions are off-label.[25,26] This means that some of the increase in prevalence of AD prescribing could be for indications that have not received regulatory approval. However, previous studies have shown that the most common AD prescribed in primary care, the selective serotonin reuptake inhibitor, is almost exclusively given for indications of depression and (or) anxiety.[23,24] Consequently, the prevalence and incidence of AD prescribing described in our paper can mostly be attributed to the treatment of depression and depression-related disorders.

When comparing incidence of AD prescribing in males, compared with females, it is clear that the incidence rate is dropping more quickly in females, and in fact the incidence of AD prescribing in males is relatively stable at 2.5%. It is well known that females see a primary care physician on a more regular basis than males and are more likely to seek help for mental health problems than males.[27] This difference in help seeking behaviour between the sexes may

contribute to the different trend observed in the incidence of AD prescribing.

The similar rate of deceleration in the incidence of AD prescribing in adults and seniors is not unexpected, given that the prevalence from 2006 to 2012 was also very similar. Again, this could reflect that people whose depression is effectively being managed by drug therapy are staying on ADs and that only those with moderate-to-severe depression are being prescribed ADs for the first time. Conversely, the slight rise in incidence of youth AD prescribing from 2006 to 2012 may be an indication that the spillover effect of the 2004 Health Canada regulatory warnings for children, which may have caused a drop in prescribing rates in youth, is waning and rates are rising back to levels seen before the warning was issued.[21] This may be a reflection of good care, as young adulthood has shown to be a vulnerable time in the human lifespan for depression and anxiety.[28]

Overall, our findings of a decrease in the incidence of AD prescribing are consistent with the results found in the 2007 Canadian study by Raymond et al.[19] Further, international primary care studies support our findings and hypotheses that the increase in the prevalence of AD prescribing is due to a greater number of patients being on longer-term medication rather than an indication that there is an increase in the incidence of AD use.[29–33]

Our study used data extracted from primary care records on more than 600 000 Canadians. There may be some selection bias, as the providers that contribute data to the CPCSSN represent a convenience sample and were not randomly selected. Thus the data may only be generalizable to practices similar to those of the CPCSSN primary care providers. Our data were only able to capture if a patient was prescribed an AD and does not reflect prescriptions filled at pharmacies by patients.

Most patients within the CPCSSN database have less than 10 years of historical records. Lacking the full prescription history for a patient is a limitation of using EMR data for research, and we had to make the assumption that a patient was unexposed based on the limited historical records within the CPCSSN database. Consequently, the incidence of AD prescriptions may have some measurement bias. However, only including patients that had at least 2 years of recorded medical history in our incidence calculations reduced this potential misclassification. In addition, using this approach ensured that our results were comparable with the British Columbia study by Raymond et al,[19] who used a similar method.

In recent years, the indications for AD therapy have expanded, and some classes of ADs, specifically selective serotonin reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors, are now prescribed for anxiety disorders, adjustment disorder, back pain, and neuropathy. However, these indications only account for a small proportion of AD prescriptions and likely do not have a major impact on the evaluation of AD prescription data to reveal trends in depression treatment.[23,24]

Lastly, any conclusions about the length of time a patient remains on an AD must be made with caution, as our study does not have a steady-state population, nor did we use a model to mathematically relate incidence and prevalence.

Conclusion

Despite these limitations, our study is an important contribution to the understanding of AD prescribing in primary care in Canada in the last 6 years. Our results are consistent with previous reports from the United States,[31] southern Italy,[32] and Taiwan[33] on the prevalence and incidence of AD prescribing in primary care. We have shown that the prevalence of AD prescribing by primary care providers in Canada continued to rise from 2006 to 2012. Conversely, incidence has remained stable or declined during the 6-year study period. While many complex factors likely contribute to the observed prevalence and incidence rates, our findings suggest that the guidelines indicating the efficacy of long-term AD therapy for patients with highly recurrent or severe depression are being followed.

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Appendix A Antidepressant drugs

Medication classification	Generic name of medication	
Selective serotonin reuptake inhibitors	• Citalopram • Dapoxetine • Escitalopram • Fluoxetine	• Fluvoxamine • Paroxetine • Sertraline
Tricyclics and tetracyclics	• Amitriptyline • Amoxapine • Butriptyline • Clomipramine • Desipramine • Dothiepin	• Doxepin • Imipramine • Maprotiline • Nortripytyline • Protriptyline • Trimipramine
Serotonin–norephinephrine reuptake inhibitors	• Desvenlafaxine • Duloxetine	• Venlafaxine
Serotonin antagonist and reuptake inhibitors:	• Trazodone	
Atypical antipsychotics	• Bupropion	• Mirtazapine
Monoamine oxidase inhibitors	• Moclobemide • Phenelzine	• Selegiline • Tranylcypromine