

Commonly Prescribed Antidepressants: What Clinicians Need To Know

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Introduction

According to two Cochrane collaboration reviews (Moncrieff, Wessely, & Hardy, 2004; Turner, Mathews, Linardatos, Tell, & Rosenthal, 2008), the efficacy of modern antidepressants has yet to be conclusively demonstrated to be greater than that of active placebo. In one review, Turner et al. (2008) assessed all studies of antidepressants which had ever been submitted to the Federal Drug Administration (FDA) in the United States (US). They reported that findings of studies finally published in peer review journals indicated antidepressants had a 94% success rate in treating depression. However, when unpublished results were also examined by the authors of this review, the success rate of antidepressants fell below 50%, and, when combined, published and unpublished studies showed a 51% level of efficacy in antidepressants. This result was minimally better than that of the results for placebos. Fournier et al. (2010) also investigated this phenomenon and concluded that the extent of benefit of antidepressants compared with a placebo appears to increase with the severity of depressive symptoms. They reported that antidepressants showed a significant treatment effect for those with severe depression. They added that the extent of benefit for patients with mild or moderate depressive symptoms may be minimal or non-existent.

Despite these equivocal results, antidepressants are one of the most commonly prescribed drugs in primary care in Ireland. According to the National Centre for Pharmacoeconomics in Ireland (NCPI), antidepressants accounted for approximately 4% of prescription items on the General Medical Service Scheme (GMS) in 2004. This brief report will outline some essential facts about antidepressants that clinicians need to know, including the main classes of antidepressants, the five most commonly prescribed antidepressants in Ireland, problems with adherence to prescriptions and treatment course guidelines.

Classes of Antidepressants

There are four classes of antidepressants available, these are:

- Tricyclic antidepressants (TCAs)
- Monoamine oxidase inhibitors (MAOIs)
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and noradrenaline reuptake inhibitors (SNRIs)

TCAs

TCAs are the oldest class of antidepressant drugs. They act by blocking the reuptake of noradrenaline and serotonin. Particular varieties of TCAs (e.g., amitriptyline, dothiepin) can be extremely dangerous in overdoses, as they may cause a fatal arrhythmia (McWilliams & O'Callaghan, 2006). Side effects include increased heart rate, drowsiness, dry mouth, constipation, urinary retention, blurred vision, dizziness, confusion, and sexual dysfunction. These side effects usually present before therapeutic benefits and may result in nonadherence to a prescription (Teicher, Glod, & Cole, 1993; McWilliams & O'Callaghan, 2006).

Newer antidepressants are thought to have fewer and less intense side effects. Nonetheless, the TCAs are still used for treatment-resistant depression that has failed to respond to therapy with other antidepressants (Gervasoni, Aubry, Gex-Fabry, Bertschy, & Bondolfi, 2009). Clients on TCAs should avoid the risk of cholinergic rebound syndrome by titrating slowly off the medication with the advice of their prescribing physician (McWilliams & O'Callaghan, 2006).

MAOIs

These work by blocking the enzyme monoamine oxidase. This breaks down the neurotransmitters dopamine, serotonin, and noradrenaline. Due to potentially fatal interactions with foods rich in tyramine, which include certain cheeses, pickles, wines and over-the-counter and prescribed decongestants, physicians are careful in advising and selecting the patients who are suitable to take these medications (McWilliams & O'Callaghan, 2006). Thankfully, a transdermal patch form of the drug is also available. Transdermally administered MAOIs do not enter the gastrointestinal system, and this reduces the dangers of the previously mentioned dietary interactions (Massaro, 2002).

In the last decade a new generation of MAOIs has been introduced. These are known as reversible inhibitors of monoamine oxidase A (RIMAs). They importantly do not require a special diet (Yamada & Yasuhara, 2004).

SSRIs

SSRIs are among the newest class of antidepressant. They work by selectively preventing the reuptake of serotonin in the synapse. Fortunately, they have fewer side effects than older classes of antidepressants, leading to greater treatment adherence. Commonly reported side effects include nausea and diarrhoea (27% of patients). Dry mouth, sexual dysfunction and blurred vision are also common. Insomnia is common in patients taking SSRIs, with the exception of citalopram, while paroxetine is associated with fewer anorectic symptoms. For clients with cardiac histories, SSRIs are the drugs of choice due to their reduced cardiotoxic side effects (McWilliams & O'Callaghan, 2006).

In 2004 the Committee of Safety of Medicines in the United Kingdom (UK) reviewed the evidence which related antidepressants to a significant dependence liability and development of a dependence syndrome according to internationally accepted criteria. They found no such association. Nonetheless, withdrawal symptoms have been reported in some cases (McWilliams & O'Callaghan, 2006). These have included nausea, headache, dizziness and sweating and paraesthesia (i.e., tingling and numbness in extremities). Of note is that most SSRIs (except fluoxetine) are not licensed for use in people under the age of 18 (National Institute for Health and Clinical Excellence [NICE], 2009). Despite concerns, there has been no conclusive evidence of an increased risk of

suicidal thoughts in adults as a result of taking an SSRI (Khan, Khan, Kolts, & Brown, 2003; Stone & Jones, 2006). However, the Royal College of Psychiatrists (2010) in the UK warns that individuals mature at different rates, and note that because young adults are more likely to complete suicide than older adults they should be closely monitored when taking an SSRI.

Recent studies have found that younger women with depression are more responsive to selective serotonergic reuptake inhibitor antidepressants than postmenopausal women. It is thought that this may relate to changes in menstrual status (Grigoriadis, Kennedy, & Bagby, 2003).

SNRIs

SNRIs are the newest form of antidepressant. They act to increase the availability of both noradrenaline and serotonin and they typically have similar side effects to the SSRIs.

Thase (2008), in a review of the evidence in relation to efficacy of SNRIs as compared to older and cheaper SSRIs, recommended that SSRIs should be the first port of call for prescribing physicians. The data suggested that although the SNRIs show a modest treatment effect over SSRIs, the real-world effect to reach this difference in treatment response is that one needs to treat 10 to 15 additional patients on an SNRI as opposed to an SSRI in order to document one additional case of remission or antidepressant response. As a cautionary note, SNRIs have also been associated with a greater toxicity in overdose. Due to the above factors, Thase (2008) has recommended that SNRIs should be considered as an alternative treatment to those patients who do not respond to an initial treatment of an SSRI. In the next section of this article, the five most commonly prescribed antidepressants in Ireland are reviewed.

The Five Most Commonly Prescribed GMS Antidepressants in Ireland.

The five most commonly prescribed antidepressants in the GMS in Ireland, according to the NCPI (2004), are presented in Table 1 below. (The NCPI is currently collating a more up to date analysis of prescribing patterns which are yet to be published).

Table 1. Five Most Commonly Prescribed Antidepressants through the GMS in Ireland in 2004

Drug	Brand	Class
Fluoxetine	Prozac	SSRI
Citalopram	Cipramil	SSRI
Escitalopram	Lexapro	SSRI
Paroxetine	Seroxat	SSRI
Venlafaxine	Effexor	SNRI

Fluoxetine/Prozac

According to the Irish Medicines Board (IMB; 1995, 2006), Prozac is approved for the treatment of major depressive episodes and obsessive compulsive disorder (OCD). For children over 8 years of age if their depression is unresponsive to psychological therapy after 4 to 6 sessions, Prozac can be prescribed for those in the moderate to severe major depressive range. The IMB report that antidepressants should only be offered to children when in combination with a concurrent psychological therapy. For depressed adults and the elderly, the recommended dose of Prozac is 20mg daily up to a maximum of 60mg. For children and adolescents

aged 8 years and above, the starting dose is 10mg/day, to be increased to a maximum of 20mg/day.

With respect to side effects for individuals taking Prozac, increased anxiety symptoms can occur in up to 15% of patients and it may also be associated with low sodium and glucose levels in the blood (McWilliams & O'Callaghan, 2006).

Citalopram/Cipramil

According to the IMB (1995, 2006), Cipramil is approved for the treatment of major depressive episodes and panic disorder, with or without agoraphobia. Here, the usual dose for depressed adults is 20mg once daily, with a maximum recommended dose of 60mg/day. For an elderly patient, the recommended daily dose is 10mg once daily up to a maximum of 30mg/day.

Citalopram and Escitalopram are distinct from some other agents in their class in that they exhibit linear pharmacokinetics and minimal drug interaction potential. These features make Citalopram attractive for the treatment of depression, especially among the elderly and patients with comorbid illness (Keller, 2000). Citalopram should be used with caution in patients with a history of mania/hypomania (Stahl, 2009).

Escitalopram/Lexapro

Escitalopram is the most selective of the SSRIs (Owens, Knight, & Nemeroff, 2001). According to the IMB (1995, 2006), Lexapro is approved for the treatment of major depressive episodes, panic disorder with or without agoraphobia, social anxiety disorder (SAD), generalised anxiety disorder and OCD. The usual adult dosage is 10mg once daily up to a maximum of 20 mg/day. In elderly depressed patients, initial treatment should be half the usually recommended dose and a lower maximum dose should also be considered.

Kennedy, Andersen and Lam (2006) conducted a meta-analysis comparing the efficacy of Escitalopram with Citalopram, Fluoxetine, Paroxetine, and Venlafaxine. They found that Escitalopram was significantly superior to the other SSRIs in terms of treatment effect and was comparable to Venlafaxine. Similarly, the withdrawal rate due to adverse events was 6.7% for Escitalopram compared with 9.1% for its comparators.

Paroxetine/Seroxat

According to the IMB (1995, 2006), Seroxat is approved for the treatment of major depressive episodes, OCD, panic disorder with or without agoraphobia, SAD, generalised anxiety disorder and post-traumatic stress disorder (PTSD). The recommended dose is 20mg daily, up to a maximum of 50mg daily, which is achieved in 10mg steps. In elderly patients the maximum dose is recommended at 40mg per day.

Seroxat has been found to be associated with clinically significant weight gain (Papakostas, 2008) and is often associated with patients reporting nausea and a feeling of general weakness or lethargy (known as asthenia). This sedative effect is reported in up to 21% of patients (McWilliams & O'Callaghan, 2006). Lethargy and weight gain can contribute to a patient deciding to discontinue their medication. However, clinicians need to warn their clients that the sudden discontinuation of Paroxetine has been associated with a high risk of a withdrawal syndrome, and reduction in their medications needs to be done in association with their prescribing psychiatrist or general practitioner (GP) (Haddad, 2001).

Venlafaxine/Effexor

According to the IMB (1995, 2006), Effexor is indicated for the treatment of depression that may be also accompanied by anxiety. The usual recommended dose for adults and elderly

patients is 37.5mg twice daily up to a maximum recommended dose of 75mg twice daily. For severely depressed or hospitalised patients up to 375mg/day can be prescribed. Nausea, hypertension and sexual dysfunction have been reported but the side effect profile is generally the least severe of all the antidepressants (McWilliams & O'Callaghan, 2006). Similar to Paroxetine, Venlafaxine, due to its short half-life, carries a high risk of discontinuation syndrome symptoms (Haddad, 2001). Indeed, as far back as 1998, Parker and Blennerhassett – two Irish consultant psychiatrists – noted that missing even a single dose of this medication can induce discontinuation effects in some patients.

The NICE Guidelines

The NICE (2009) guidelines do not recommend that antidepressants, due to their poor risk-benefit ratio, are to be used for the treatment of mild depression. They should be considered for people who present with a past history of moderate to severe depression, subthreshold depressive symptoms that have been present for a long period (typically at least 2 years), or depression that persists after other interventions such as talking therapy have failed.

Once a decision has been made to use an antidepressant, a starting dose is prescribed and change is monitored over a 4 to 6 week period. A dose may be increased if it is seen as necessary. If ineffective, a second antidepressant, often of a different class, may be tried. Most antidepressants have a delayed onset of action of 2 to 6 weeks (Carr & McNulty, 2006). Knowing this, clinicians can actively support their clients in their treatment adherence. An effective antidepressant should be continued for at least 4 to 6 months after resolution of symptoms and withdrawn gradually over 2 to 4 weeks in order to avoid a withdrawal syndrome or reemergence of symptoms (Carr & McNulty, 2006). As stated above, it usually takes a number of weeks for patients to notice any obvious therapeutic benefit. However, the effects of antidepressants on emotional processing can be observed within hours of the first dose in healthy volunteers and depressed patients (Harmer, Shelley, Cowen, & Goodwin, 2004; Harmer, Goodwin, & Cowen, 2009).

According to NICE (2009), all patients should also be informed that, although the drugs are not associated with tolerance and craving, withdrawal symptoms may occur on stopping or missing doses, or, occasionally, on reducing the dose of the drug. Clear communication to patients has often been lacking, as found in a recent UK study conducted by Haw and Stubbs (2011). The authors found a significant disparity in the content, quality and usefulness of information leaflets inserted into packets of antidepressants. Not all leaflets warned about discontinuation syndromes, side effects were listed inconsistently (e.g., some listed them according to severity while other listed them by frequency) and almost half of the leaflets did not warn against using St John's Wort during treatment, even though this was found to be a common occurrence in patients. Of note, however, is that it is estimated up to 40% of patients taking SSRIs do not attain relief from their depression, where relief is defined as a 50% reduction in depressive symptomatology following 6 to 8 weeks of therapy (Thase, Entsuah, & Rudolph, 2001).

The NICE guidelines for people presenting with depression in primary care (2009) recommended SSRIs as a first treatment option. They are as effective as TCAs and are less likely to be discontinued because of side effects and are also safer in overdose than TCAs. SSRIs were also recommended to treat a variety of other disorders such as anxiety and eating disorders. This means that they can be useful in treating a patient with a comorbid presentation. This latter finding is all the more

important due to recent findings that anxious depression was associated with poorer treatment response than non-anxious depression in patients with major depressive episode (Domschke, Deckert, Arolt, & Baune, 2010).

Adherence to Prescribed Treatment for Depression

Serna, Cruz, Real, Gascó and Galván (2010) investigated adherence to antidepressants in over 7000 patients. They found that 56% of patients abandoned medication during the first 4 months, and that males were more likely to stop taking their medication than females. Furthermore, food compliance was recorded in 22% of patients and was twice as frequent in patients with high levels of polypharmacy compared to those with low levels. Finally, patients receiving Venlafaxine, Citalopram, and Fluoxetine presented among the highest percentages with good compliance.

Summary and Conclusion

Antidepressants are commonly prescribed treatments for depression in Ireland. Their effectiveness is not yet clearly demonstrated for patients with mild to moderate depression. For patients with more severe depressive presentations, however, there appears to be evidence of positive treatment effects. Treatment adherence is complicated by differential side effect profiles and problems with treatment adherence. It is important for clinicians to be aware of the different classes of antidepressants, their side effect profiles, dosage and the degree of withdrawal symptoms associated with each specific prescription.

References

- Carr, A., & McNulty, M. (Eds.). (2006). *The handbook of adult clinical psychology*. London: Routledge.
- Committee on Safety of Medicines (2004). *Report of the CSM Expert Working Group on the safety of selective serotonin reuptake inhibitor antidepressants*. Retrieved 28 July, 2010, from <http://www.mhra.gov.uk/home/groups/pl-p/documents/drugsafetymessage/con019472.pdf>.
- Domschke, K., Deckert, J., Arolt, V., & Baune, B.T. (2010). Anxious versus non-anxious depression: Difference in treatment outcome. *Journal of Psychopharmacology*, 24(4), 621–622.
- Fournier, J.C., Robert, M.A., DeRubeis, J., Hollon, S.D., Dimidjian, S., Amsterdam, J.D., Shelton, R.C., & Fawcett, J. (2010). Antidepressant drug effects and depression severity. *The Journal of the American Medical Association*, 303(1), 47–53.
- Gervasoni, N., Aubry, J.M., Gex-Fabry, M., Bertschy, G., & Bondolfi, G. (2009). Is there a place for tricyclic antidepressants and subsequent augmentation strategies in obtaining remission for patients with treatment resistant depression? *Pharmacological Research*, 59(3), 202–206.
- Grigoriadis, S., Kennedy, S., & Bagby, M. (2003). A comparison of antidepressant response in younger and older women. *Journal of Clinical Psychopharmacology*, 23(4), 405–407.
- Haddad, P. (2001). Antidepressant discontinuation syndromes. *Drug Safety Journal*, 24(3), 183–197.
- Harmer, C.J., Goodwin, G.M., & Cowen, P.J. (2009). Why do antidepressants take so long to work? A cognitive neuropsychological model of antidepressant drug action. *British Journal of Psychiatry*, 195(2), 102–108.
- Harmer, C.J., Shelley, N.C., Cowen, P.J., & Goodwin, G.M. (2004). Increased positive versus negative affective perception and memory in healthy volunteers following selective serotonin and norepinephrine reuptake inhibition. *American Journal of Psychiatry*, 161(7), 1256–1263.
- Haw, C., & Stubbs, J. (2011). Patient information leaflets for antidepressants: Are patients getting the information they need? *Journal of Affective Disorders*, 128, 165–170.
- Irish Medicines Board (1995 & 2006). *Irish Medicines Board Acts 1995 and 1996*. Retrieved 21 August, 2010, from <http://www.irishstatutebook.ie/acts.html>.
- Khan, A., Khan, S., Kolts, R., & Brown, W.A. (2003). Suicide rates in clinical trials of SSRIs, other antidepressants, and placebo: Analysis of FDA reports. *American Journal of Psychiatry*, 160, 790–792.
- Khawaja, I.S., Westermeyer, J.J., Gajwani, P., & Feinstein, R.E. (2009). Depression and coronary artery disease, the association, mechanisms, and therapeutic implications. *Psychiatry (Edgmont)*, 6(1), 38–51.
- Keller, M.B. (2000). Citalopram therapy for depression: A review of 10 years of European experience and data from US clinical trials. *Journal of Clinical Psychology*, 61(12), 896–908.
- Kennedy, S.H., Andersen, H.F., & Lam, R.W. (2006). Efficacy of escitalopram in the treatment of major depressive disorder compared with conventional selective serotonin reuptake inhibitors and venlafaxine XR: A meta-analysis. *Journal of Psychiatry and Neuroscience*, 31(2), 122–131.
- Levenson, M., & Holland, C. (2006). *Statistical evaluation of suicidality in adults treated with antidepressants. Overview for December 13 meeting of Psychopharmacologic Drugs Advisory Committee (PDAC)*. Retrieved 27 August, 2010, from <http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4272b1-01-FDA.pdf>.
- National Centre for Pharmacoconomics in Ireland (2004). *Drug utilisation trends on the GMS scheme*. Retrieved 13 August, 2010, from <http://www.ncpe.ie/document.php?cid=30&sid=78&docid=106>.
- McWilliams, S., & O'Callaghan, E. (2006). Biomedical approaches and use of drugs to treat adult mental health problem. In A. Carr & M. McNulty (Eds.) *The handbook of adult clinical psychology* (pp. 220–252). London: Routledge.
- Massaro, E.J. (2002). *Handbook of neurotoxicology*. Totowa: Human Press Inc.
- Moncrieff, J., Wessely, S., & Hardy, R. (2004). Active placebos versus antidepressants for depression. *Cochrane Database Systematic Reviews*, (1):CD003012.
- National Institute of Health and Clinical Excellence (2009). *Depression: The treatment and management of depression in adults CG90*. London: Author.
- Owens, M.J., Knight, D.L., & Nemeroff, C.B. (2001). Second-generation SSRIs: Human monoamine transporter binding profile of escitalopram and R-fluoxetine. *Biological Psychiatry*, 50, 345–350.
- Papakostas, G.I. (2008). Tolerability of modern antidepressants. *Journal of Clinical Psychiatry*, 69, 8–13.
- Parker, G., & Blennerhassett, J. (1998). Withdrawal reactions associated with venlafaxine. *Australian and New Zealand Journal of Psychiatry*, 32(2), 291–294.
- Royal College of Psychiatrists (2010). Antidepressants. Retrieved 12 August, 2010, from <http://www.rcpsych.ac.uk/mentalhealthinformation/mentalhealthproblems/depression/antidepressants.aspx>.
- Serna, M.C., Cruz, I., Real, J., Gascó, E., & Galván, L. (2010). Duration and adherence of antidepressant treatment (2003 to 2007) based on prescription database.

European Psychiatry, 25(4), 206–213

Stahl, S. (2009). *Stahl's essential psychopharmacology: The prescriber's guide*. New York: Cambridge University Press.

Stone, M.B., & Jones, M.L. (2006). *Clinical review: Relationship between antidepressant drugs and suicidality in adults. Overview for December 13 Meeting of Psychopharmacologic Drugs Advisory Committee (PDAC)*. Retrieved 27 July, 2010, from <http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4272b1-01-FDA.pdf>.

Teicher, M., Glod, C., & Cole, J. (1993). Antidepressant drugs and the emergence of suicidal tendencies. *Drug Safety Journal*, 8(3), 186–212.

Thase, M.E., Entsuah, R., & Rudolph, R.L. (2001). Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *British Journal of Psychiatry*, 178, 234–241.

Thase, M. E. (2008). Are SNRIs more effective than SSRIs? Problems with assessing antidepressant efficacy. *Psychopharmacology Bulletin*, 41, 58–85.

Turner, E.H., Matthews, A.M., Linardatos, E., Tell, R.A., & Rosenthal, R. (2008). Selective publication of antidepressant trials and its influence on apparent efficacy. *New England Journal of Medicine*, 358(3), 252–260.

Yamada, M., & Yasuhara, H. (2004). Clinical pharmacology of MAO inhibitors: Safety and future. *NeuroToxicology*, 25(1-2), 215–221.

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Name of Speaker	Date & Time	Title of Seminar (Provisional)	Venue
Dr John Greaney (IADT)	6 October 2011, 1pm	Encouraging use of emergency contact details on mobile phones.	A021
Dr Mark Campbell (UL)	20 October 2011, 1pm	A Case Study in Sport Psychology: Working with an elite golfer	A021
Dr Arlene Egan (Building2Think)	17 November 2011, 1pm	Teaching Thinking Skills at University	A021
Mr Jonathon Sinden (Paddy Power)	26 January 2012, 1pm	Paddypower.com	A021
Dr Elizabeth Nixon (TCD)	9 February 2012, 1pm	Parenting and family contexts in Ireland.	A021
Dr Maura Conway (DCU)	8 March 2012, 1pm	Terrorism and the Internet	A021