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DEPRESSION TREATMENT BY BEDFORD EAST COMMUNITY MENTAL HEALTH TEAM AN AUDIT TO ASSESS HOW MANY PATIENTS IN A BEDFORDSHIRE COMMUNITY MENTAL HEALTH TEAM MIGHT SAFELY BE TRANSFERRED TO PRIMARY CARE

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SUMMARY

Introduction: *Recently there has been pressure on Secondary Psychiatric services to discharge patients back into Primary care. This project is to show what depression treatments are used by Bedford East Community Mental Health Team (BECMHT) and therefore identify whether some of these patients could be appropriately managed in Primary care.*

Subjects and Method: *We identified, using an anonymised database, patients being treated with different anti-depressant regimens in BECMHT. We compared these treatments with the steps described in NICE Guidelines, and other evidence based treatment modalities which we found on literature search. Based on this data, we attempted to predict which patients it might be safe to discharge to primary care for ongoing treatment.*

Results: *Many different combinations of medications were found. Many patients had other intercurrent mental health diagnoses.*

Discussion: *There are many possible evidence based treatments for depression which can be employed once those listed by NICE are exhausted. We review all of these. Some patients are, accordingly, on combinations of medication as augmentation strategies.It is responsible to only discharge patients into Primary care when their symptoms are controlled.*

Conclusion*: We identified groups of patients who might be transferred back to primary care for maintenance treatment, provided that shared care protocols are in Place, and there is easy access to secondary care services should the need arise.*

Key words: *anti-depressants - shared care with primary care - NICE guidelines - depression*

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INTRODUCTION

Recently there has been pressure on Secondary Psychiatric services to discharge patients back into Primary care. Indeed, it is generally believed that patients who can be treated in Primary care should receive their treatment in Primary care (Agius et al. 2005).

This need to discharge patients back into primary care is in order to relieve the caseloads of Community Mental Health Teams and provide a better service for those patients that indisputably require secondary care intervention. The most difficult cases in this field are those of patients with resistant depression whose symptoms are not alleviated by the standard treatment regimens outlined in the 2004 NICE guidelines (as amended 2007). Here the steps that a secondary health care provider will take in treating patients with depression in order to ensure that all treatment options have been considered before they are discharged back to primary care or else referred onto a tertiary centre specialising in resistant depression if symptoms persist are described. The NICE guidelines, covering both treatment-responsive and treatment-resistant depression will be described. Further options available to doctors caring for these patients as suggested by various trials and meta-analyses as well as an influential US study, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study (Rush et al. 2006) will then be described. Once these alternatives have been considered, they will be applied to the treatments being given to patients with depression in a single Community Mental Health Team, the Bedford East Community Mental Health Team. To our knowledge, no such audit of anti-depressant prescribing in a single Community Mental Health Team has been described in the literature.

The aim of this project is to show what depression treatments are used by Bedford East Community Mental Health Team (BECMHT) and therefore identify whether some of these patients could be appropriately managed in Primary care.

SUBJECTS AND METHOD

BECMHT has a database of all patients seen since 2006. This was anonymised for audit purposes. From this database, 299 patients were identified with either the ICD diagnosis F32 (‘depressive episode’), F33 (‘recurrent depressive disorder’), F41.2 (‘mixed anxiety and depression’) or uncoded but including the phrase “depression”. The information on these patients was analysed, and they were grouped according to evidence based treatments that had previously been identified (Agius et al. 2007). From this, potential patient groups to discharge were identified.

RESULTS

Many different combinations of medications were found, D=Anti-Depressant, P=Anti-Psychotic and M=Anti-Manic as shown in the following graph.

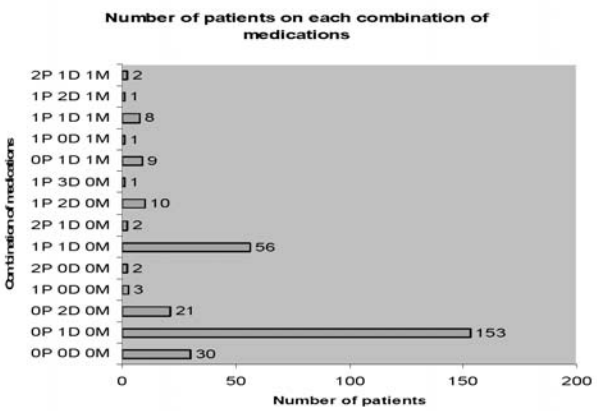

Figure 1. Number of patients on each combination of medications

Of the patients who were on only one antidepressant (0P1D0M-153) there were almost the same number with recurrent depression (F33-68) as those with a depressive episode (F32-65).

Over a third of patients (109/36.5%) had at least 1 intercurrent psychiatric diagnosis.

The number of patients that are on no medication (0P0D0M), on medications in exact concordance with NICE guidelines (NICE 2004), those with an evidence base (Agius et al. 2007) and 'other' (do not fit into any of above) are shown in the following graph; In summary, the NICE steps are; First Step: Citalopram or Fluoxetine to maximum dose; Second Step; Other SSRI, SNRI, NaSSA, Tricyclic or Moclobemide; Third Step; Maximise SNRI, Lithium augmentation or NASSA and SSRI.

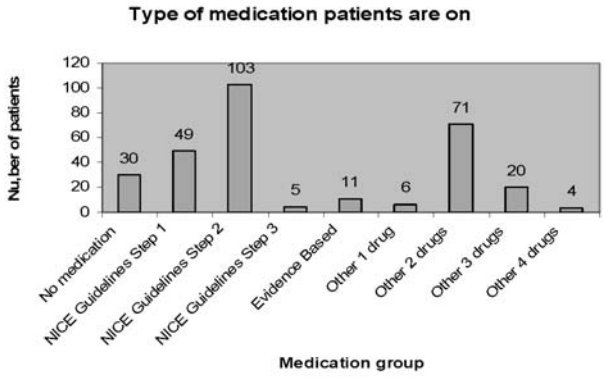

Figure 2. Type of medication patients are on

DISCUSSION

The NICE Guidelines for depression will first be described, then other evidence based treatments, including those used in the STAR-D trial will be described. Finally, we will apply the guidelines to the patients in BECMHT.

NICE Guidelines

In NICE, the recommended initial management of patients with moderate to severe depression is to prescribe a selective serotonin reuptake inhibitor (SSRI) such as Citalopram or Fluoxetine at an adequate dose according to the BNF and maintain them on treatment for 6 weeks before reassessing the choice of treatment (unless there is absolutely no improvement at all, in which a change of treatment can be considered after a month) (NICE 2007). Commencement of twice-weekly Cognitive Behavioural Therapy (CBT) sessions for one month can also be considered straight away in patients who have severe depression at presentation. If treatment is ineffective at the time of reassessment, as measured by one of the standardised methods such as the Hamilton Depression Score, the patient should be switched to a different SSRI or to an antidepressant from a different class, such as Mirtazepine (a pre-synaptic alpha 2 adrenoreceptor antagonist) and again reassessed after 6 weeks. Moclobemide (a reversible mono-amine oxidase inhibitor), Reboxetine (a selective inhibitor of noradrenaline reuptake) and Lofepramine (a tricylclic antidepressant) are possible alternatives during this second step. Other tricyclics (except Dosulepin) and Venlafaxine (a serotonin and noradrenaline reuptake inhibitor or SNRI) could be considered in more severe depression (NICE 2007). Factors such as drug-specific side-effects, cautions, contraindications, interactions, appropriate dosing, compliance, risk-status, patient profile (e.g. age, sex, comorbidities) and patient's preference must of course be considered at every stage of treatment planning but will not be covered here in detail for the sake of simplicity.

The NICE Guidelines define treatment-resistant depression as that which fails to respond to two or more antidepressants given sequentially at an adequate dose for an adequate time (NICE 2007). Therefore, if both the steps already mentioned above have failed to lead to an improvement, the patient automatically falls into this category. About 17.5% of patients presenting with severe depression will eventually fulfil these criteria, which brings up the question of whether the threshold for applying this label is too low (Mcallister-Williams 2006). Secondary care teams would most likely become involved at this point and would have the opportunity to assess the patient again in great detail, including factors such as the patient's symptom profile, suicide risk, psychiatric and medical history, psychosocial stressors, relationships and personality factors. NICE suggests that the first step in resistant depression should be to augment pharmacotherapy with psychological treatment, ideally CBT (as opposed to Inter-Personal Therapy or IPT) for 16-20 sessions over 6-9 months (NICE 2007) (Keller et al. 2000). Switching medication to Venlafaxine at the maximal dose without intolerable

side-effects, can be considered if this drug has not already been tried (NICE 2007) (Poirier et al. 1999). If this still does not provide adequate results, augmentation with Lithium should be considered, taking into account all the possible hazards of this treatment and need for a baseline ECG (NICE 2007) (Bauer et al. 1999). This can be a particularly successful option if there is there is the suggestion of some hypomanic features amongst the patient's depressive episodes, pointing tentatively towards a possible diagnosis of bipolar. Augmentation of an SSRI with Mianserin or Mirtazepine is an option in treatment resistant depression but would require careful monitoring for side effects, serotonin syndrome and possible agranulocytosis in elderly patients on Mianserin (NICE 2007) (Licht et al. 2002) (Debonnel et al. 2002). The next option at this point would be Phenelzine (a monoamine oxidase inhibitor) and issues surrounding side-effects, dietary restrictions and potential toxicity in overdose would have to be considered here (NICE 2007). The NICE guidelines advise against routine use of Dosulepin (TCA) as well as routine augmentation of antidepressants with Carbamazepine, Lamotrigrine, Buspirone, Pindolol, Valproate, Thyroid supplement or Benzodiazepines (NICE 2007). If at any point, a patient with treatment resistant depression is discharged back into primary care following a good response to a new treatment regimen, they should continue taking antidepressants for 2 years and if, for example, they were taking Lithium which triggered this improvement, that should also be continued for at least 6 months (NICE 2007). However, if all the above treatment strategies have failed to produce an adequate response, NICE would suggest that the next step would be for the secondary healthcare team to refer on to a clinician with a specialist interest in treatment resistant depression or at least seek a second opinion before considering Electro-Convulsive Therapy (ECT) as a final option, with a view to producing a rapid improvement in severe symptoms (NICE 2007). It is worth noting that a meta-analysis of 113 studies (760 patients) showed ECT to be significantly more effective that pharmacotherapy in the short term but it remains one of the most controversial treatments in medicine (UK ECT Review Group 2003).

So in summary, on the part of the secondary care team, the options that NICE suggests are open to us after receiving a patient with correctly managed treatment-resistant depression are augmentation with CBT, maximum tolerated Venlafaxine treatment (if not already tried), augmentation with Lithium, Mirtazepine/Mianserin or Phenylzine, followed by tertiary referral and ECT.

SCHEMATIC SUMMARY OF NICE GUIDELINES

Moderate to Severe Depression
↓
SSRI (Citalopram or Fluoxetine)
(+ twice weekly CBT for 1 month if Severe)
↓
Reassess treatment options at 6 weeks
(Or possibly 4 weeks if complete lack of response)
↓
Switch to different SSRI or Mirtazepine.
(Or possibly Moclobemide (Rev MAOI), Reboxetine (SINR), Lofepramine (TCA))
(Consider other tricyclics (except Dosulepin) or Venlafaxine (SNRI) if Severe)
↓
Reassess at 6 weeks
Treatment resistant depression? (Issue re: Threshold)
↓
Initiate course of 16-20 CBT sessions over 6-9 months
↓
Non-responsive?
↓
Options:
Switch to max tolerated dose Venlafaxine (SNRI) if not already tried.
Trial of Lithium (Mood Stabiliser) Augmentation.
Mianserin or Mirtazepine (α2 blocker) Augmentation.
Switch to Phenylzine (MAOI) – difficult.
↓
Referral to clinician with a specialist interest
ECT

Figure 3. Schematic Summary of NICE Guidelines

Is that all we can do?

However, the NICE guidelines do not cover all the possible options that are available and indeed, with the prevalence of treatment resistant depression and the significant drawbacks of some of the treatments suggested (such as the weight gain associated with Lithium treatment) which may discourage patients from adhering to their medications, the guidelines seem somewhat inadequate. In this next section findings from various trials are introduced which suggest other possible courses of action when the above procedures have failed to give a good outcome.

The most simple approach would appear to be adjusting the doses of medications the patient is already on. Whereas there is little evidence of any benefit in increasing the dose of SSRIs, studies have shown that increasing the dose of the TCA Imipramine from 150mg to 300mg daily does produce a significant benefit (Licht et.al. 2002) (Simpson et al. 1976). Another option is augmentation with drugs other than those already mentioned by NICE (Lithium, Mirtazepine, Mianserin and Phenylzine). For example, one randomised controlled trial carried out in 2000 concluded that augmentation of the SSRI Fluoxetine with Tryptophan produced a significant decrease in the HDRS-29 depression score in the first week of treatment, although this benefit was not evident in later weeks (Levitan et al. 2000). Other combinations of antidepressant drugs can also be tried such as TCAs with MAOIs, or Venlafaxine with Mirtazepine (Mcallister-Williams 2006). Drugs other than antidepressants can also be added. A meta-analysis carried out by Aronson et al (Aronson et al. 1996) concluded that augmentation with Triiodothyronine (T3) may benefit patients unresponsive to TCAs but that more research was needed as trial sizes were small. It has also been suggested that antipsychotics can also be used to augment antidepressant therapy. Shelton et al undertook a randomised controlled trial with the atypical antipsychotic Olanzapine in combination with Fluoxetine and reported a significant improvement in the relief of depression (Shelton et al. 2001). There is evidence that use of the anxiolytic Buspirone may also benefit patients on SSRIs and that Benzodiazepines may be useful as adjuncts to antidepressant treatment, although their potential for dependence and increased accident proneness must be taken into account (Appleberg et al. 2001, Furukawa et al. 2001). A meta-analysis by Taylor (Taylor et al. 2004) concluded that from the limited data available, is seems that Folate may have a potential role as a supplement to other antidepressant treatments. Omega 3 augmentation also seems to have a positive effect as was shown in the double-blind, placebo-controlled trial in 2003 conducted by Su (Su et al. 2003). Metyrapone, a competatitve inhibitor of 11β-hydroxylation in the adrenal cortex resulting in decreased cortisol synthesis, was also shown to be effective in augmenting the effect of antidepressants in severe depression (Jahn et al. 2004). Anticonvulsants such as Valproate and Carbemazepine have been used although there are no RCTs assessing their efficacy as yet. Stimulants are used extensively in the US although their use is not as yet commonplace in the UK (Mcallister-Williams 2006). It is clear that far more research is needed into this area. Other possible strategies include Transcranial Magnetic Stimulation (TMS) and Vagus Nerve Stimulation (VNS). TMS is a non-invasive method of neuronal excitation in the brain whereby a rapidly changing magnetic field induces weak electrical currents (electromagnetic induction). The most recent Cochrane review concluded that there was no strong evidence for benefit from this treatment but that the small sample sizes did not exclude that such a benefit could exist (Martin et al. 2001). VNS uses an implanted stimulator to send electrical impulses to the left vagus nerve (tenth cranial nerve). Little is known about how vagal stimulation modulates mood but preliminary evidence from open trials seems favourable. However, the only available double-blind study has given inconclusive results and more research is needed into the area (Daban et al. 2008). Thus, in summary, other possibilities may include ; Increased dosage, T3, Tryptophan, Olanzepine, Buspirone, Benzodiazepines, Folate, Omega 3, Metyrapone, possibly Anticonvulsants, possibly Stimulants, and procedures such as TMS and VNS.

The STAR*D Trial

In November 2006, an influential American study entitled the Sequenced Treatment Alternatives to Relieve Depression Study, or STAR*D, published its findings in the American Journal of Psychiatry. There were 4000 adult participants aged 18-75 from primary and secondary care backgrounds (Rush et al. 2004). The study compared the efficacy of a range of antidepressant therapies over four sequential levels of treatment, with the aim of achieving remission (according to the Quick Inventory of Depressive Symptomatology–Self-Report ($QIDS\text{-}SR_{16}$) score). The four steps were:

Step 1 Citalopram.

Step 2 7 possible treatments. 4 switch treatments (Citalopram stopped, new treatment initiated: sustained-release Bupropion, Cognitive Therapy, Sertraline, or extended-release Venlafaxine) and 3 augmentation options (Citalopram plus Bupropion, Buspirone, or Cognitive Therapy).

Step 3 2 medication switch strategies (Mirtazapine or Nortriptyline) or 2 medication augmentation strategies (Lithium or T_3).

Step 4 Either Tranylcypromine or extended-release Venlafaxine plus Mirtazapine.

Steps 2 to 4 were kept open label, and patients could accept or refuse treatments as long as sufficient options remained to allow randomisation between at least two

different regimens (Howland et al. 2008). Patients not achieving remission or unable to tolerate a treatment step would be encouraged to move onto the next step. Remission rates came back as 36.8%, 30.6%, 13.7%, and 13.0% for Step 1, 2, 3, and 4 respectively (Rush et al. 2006). Patients who required an increased number of treatment steps showed lower acute remission rates and greater relapse rates. The results highlighted the prevalence of treatment-resistant depression and suggested potential benefit in more vigorous treatments in the early steps, which could be seen as a window of therapeutic opportunity (Warden et al. 2007, Huynh et al. 2008). The authors again reiterated the need for more research into the most effective multi-step treatment sequences. However, the overall cumulative rate of remission with all treatment steps was reported as a substantial 67%, suggesting that it would be a reasonable model to follow here in the UK as well as in the US (Rush et al. 2006).

We should now apply these guidelines to the patients in BECMHT. The database used for this project included some discharged patients and some patients who have not been seen for a number of years. Although this means we do not have an accurate snapshot of current treatments of depression, the data gives a good overview of the pattern of medication prescribing by the BECMHT.

A significant number of patients have an intercurrent psychiatric diagnosis. This often complicates treatment and therefore means many of these patients will require Secondary care.

Other patients requiring more specialist Psychiatric care (Secondary) include anyone on Venlafaxine, since NICE recommends careful monitoring (NICE 2004) and patients in the 'other' group, that is, those on medications not covered by the NICE guidelines. Since this requires expertise for less well known drugs and atypical combinations. Caution must at all events be exercised when discharging to primary care patients who are on combinations of anti-depressants, which General Practitioners have little expertise in managing.

It is responsible to only discharge patients into Primary care when their symptoms are controlled. Patients who fall into the following groups could potentially be considered for management in Primary care, provided that control of their symptoms (including suicidality) has been demonstrated;

- patients on no medication or on 1D, especially if F32 diagnosis
- patients on the first step of the NICE guidelines or even second step if not Moclobemide
- patients on SSRI and Lithium, provided adequate monitoring in primary care can be arranged, especially since Primary care receives Lithium specific QOF points(MH QOF 2009) (Note, QOF is a system whereby General Practitioners receive extra payments for carrying out particular tasks).

CONCLUSION

Primary healthcare workers should be reassured that before a patient with treatment-resistant depression is discharged back to them from secondary care, many treatment options will have been explored. It is however true that there remains a paucity of evidence for many of the approaches that can be considered and clinicians will have to continue relying upon their own judgement and that of their peers in deciding the best path to follow once they have reached the end of the NICE guidelines. More well executed research is needed into this field, with objectively measured scores of depression which can be used to compare different treatment strategies. It is worth noting that clinicians may choose to deviate from the NICE guidelines (provided that they justify and document their reasons well), informed by other trials and studies. Many factors can influence treatment choices for particular patients such as the drawbacks and side effects of each intervention, the patient's own preference, their social and personal circumstances, other co-morbidities and so on. But however difficult it may be to manage these patients, it is vital to continue striving for adequate symptom control as treatment resistant depression is an extremely debilitating condition for the sufferer as well as a huge public health issue which needs to be tackled with more high-quality research in order to optimise treatment.

This project has identified the groups of patients that need Secondary level care and also significant numbers of those that have potential to be discharged into Primary care. In order to achieve this however, the notes of each individual patient would need to be investigated to make sure that the treatment that they would be discharged on is adequate. Additionally, there should be good communication with Primary care and a service appropriate to their needs has to be available before discharge.

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