A Measurement-based Care Algorithm for the Use of Antidepressants in Primary Care

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Disclosures

- None

"I know nothing about the subject, but I'm happy to give you my expert opinion."

Objectives

1. Review epidemiology and treatment of depression in the primary care setting
2. Review the evidence base to learn what may potentially improve outcomes when using antidepressants to treat depression in the primary care setting
3. Be introduced to an algorithm being developed to assist with the use of antidepressants for depression

Rationale for algorithm

- Depression is very common in primary care settings
  - A recent Canadian study found a prevalence of 14%
- Studies indicated that depression is often under recognized and undertreated
- Our own experience in the primary care settings we work in indicates:
  - significant gaps in knowledge about the use of antidepressants
  - Inconsistencies in how they are used and how the response to treatment is monitored

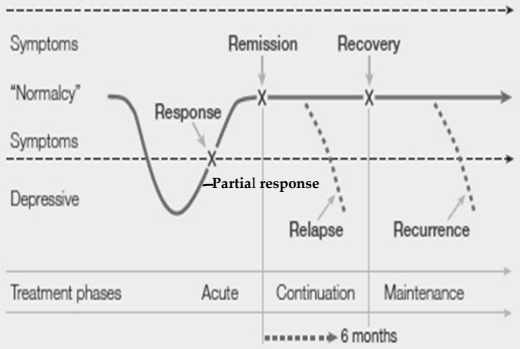
Our Goal: Develop an evidence-based algorithm for using antidepressants in primary care

What does the evidence tell us?

First some terminology

Terminology

- **Response:** Defined as a clinically meaningful reduction in symptoms (i.e. a reduction in at least 50% in baseline symptom levels)
- **Partial response:** Greater than 20% but less than 50% response to treatment
- **Remission:**
  - Virtual absence of symptoms
  - Aim of depression treatment
  - Associated with better functioning and prognosis than is response
  - PHQ-9 score of less than



What are the outcomes in depression treatment under study conditions?

- **Remission** with antidepressant medication:
  - 25-40%
- **Response** (defined as greater than 50% improvement on a standardized rating scale):
  - 30-50%

Placebo vs. true response

- High placebo response rates found in antidepressant studies
- **30-40% rates of remission found with placebo** making it difficult to determine true treatment effects except in those patients with more severe depression

But what about patients treated under usual (non-study) conditions?

Study vs. Usual Care conditions

- Patients under usual care conditions do considerably worse than those in study conditions
- Meyer et al found that remission after 3 months treatment by a group of psychiatrists was 30% (compared to 30-40% response rate to placebo under study conditions)

What does the evidence tell us about why this is?

A Systematic Approach to Pharmacotherapy for Geriatric Major Depression

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KEYWORDS
• Major depressive disorder • Geriatrics • Old age • Antidepressant agents
• Drug therapy • Guidelines • Algorithm • Stepped care

KEY POINTS

- The effectiveness of antidepressants depends in large part on the way they are used. Under usual care conditions, the outcomes of antidepressant pharmacotherapy for geriatric depression have been shown to be mediocre at best.
- Trying to individualize treatment by matching each patient with a specific antidepressant based on the patient's symptoms and an antidepressant putative side-effect profile is ineffective. Instead, the outcomes of antidepressant pharmacotherapy for geriatric depression can be improved markedly when antidepressants are prescribed following an algorithmic ("stepped-care").
- Published guidelines and algorithms for the antidepressant pharmacotherapy for geriatric depression are informed by published evidence but they do not necessarily conform to this evidence. This article presents an updated algorithm for the antidepressant pharmacotherapy for geriatric depression that is based on the authors' interpretation of the available evidence.

Process of Care

1. Frequency, duration and quality of visits
2. Quality and quantity of pharmacotherapy offered

Patient contact

- One meta-analysis showed that in placebo-controlled RCTs of antidepressants for adult MDD lasting 6 weeks, **2 additional follow-up visits at weeks 3 and 5 improved outcomes** of both placebo and active antidepressants
- **Accounted 41% of the improvement with placebo and 27% for active treatment**

Process of Care

1. Frequency, duration and quality of visits
2. **Quality and quantity of pharmacotherapy offered**

Pharmacotherapy of depression in primary care

- Evidence from practice settings demonstrate that antidepressant treatment is often:
  - Inadequate in dose
  - Inadequate in duration
  - Associated with high dropout rates
- All of these factors are thought to contribute to lower remission rates

Pharmacotherapy in studies

- Dose titration and change in treatment is often based on a treatment algorithm
- May employ **measurement-based care** which includes the routine measurement of symptoms and side effects at specified time points
- Includes guidance as to when and how to modify medication doses based on these measures

Using PHQ-9 Diagnosis and Score for Initial Treatment Selection

PHQ-9 Score	Provisional Diagnosis	Treatment Recommendations
5-9	Minimal Symptoms	Support Educate to call if worse; return in 1 month
10-14	Minor depression++	Support, watchful waiting
10-14	Dysthymia	Antidepressant or psychotherapy
10-14	Major depression, *mild*	Antidepressant or psychotherapy
15-19	Major depression, moderately severe	Antidepressant or Psychotherapy
≥20	Major Depression, severe	Antidepressant and psychotherapy (especially if not improved on monotherapy)

Available at www.phqscreeners.com

Using the PHQ-9 to Assess patient Response to Treatment

* **Initial Response after Four - Six weeks of an Adequate Dose of an Antidepressant**

PHQ-9 Score	Treatment Response	Treatment Plan
Drop of ≥ 5 points from baseline	Adequate	No treatment change needed Follow-up in four weeks.
Drop of 2-4 points from baseline	Probably Inadequate	Often warrants an increase in antidepressant dose.
Drop of 1 point or no change	Inadequate	Increase dose: Augmentation; Switch; Informal or formal psychiatric consultation; Add psychological counseling.

Initial Dosing

DEPRESSION AND ANXIETY 29:506–514 (2012)

Research Article

THE ASSOCIATION BETWEEN ANTIDEPRESSANT DOSAGE TITRATION AND MEDICATION ADHERENCE AMONG PATIENTS WITH DEPRESSION

Chung-Hsien Wu, Ph.D., M.H.P.A., R.Pharm.,* Joel F. Farley, Ph.D.,† and Bradley N. Gaynes, M.D., M.P.H.‡,§

Background: *To evaluate the association between upward dose titration of antidepressants and medication adherence during the first 6 months of a newly initiated antidepressant treatment for patients with major depressive disorder (MDD).* **Methods:** *We conducted a retrospective observational cohort study using Thomson Reuters MarketScan Commercial Claims and Encounters Claims data. We identified 40,873 patients aged 18–64 with MDD newly initiating a selective serotonin reuptake inhibitor, serotonin–norepinephrine reuptake inhibitor, or bupropion between July 1, 2005 and June 30, 2007. Patients with titration (defined as antidepressant initiation at dose equal or lower than American Psychiatric Association treatment guidelines with a dosage increase in the first 60 days of treatment) were compared to patients with no titration. Adherence was measured as the proportion of days covered (PDC) on antidepressant treatments. Patients with PDC ≥ 80% were considered adherent. Persistence was measured as the duration of time from initiation to a 30-day gap in antidepressant treatments. Multivariate logistic regression and Cox-proportional hazard models examined the influence of titration on adherence and persistence, respectively.* **Results:** *Adherence was greater in the titration group than in the nontitration group (67.5% versus 45.2%, P < .01). After adjustments for selected covariates, patients in the titration group were more likely to adhere to antidepressant treatments (odds ratio = 2.60, 95% confidence interval (CI) = 2.47–2.74) and less likely to have a 30-day gap in treatment (hazard ratio = 0.48, 95% CI = 0.45–0.51).* **Conclusions:** *Upward dose titration on antidepressant treatment was associated with improved medication adherence and persistence. For clinicians initiating antidepressant treatments, titrating antidepressant doses may improve patient outcomes. Depression and Anxiety 29:506–514, 2012.*

Results

- Found that adherence is significantly higher when the antidepressant dose is titrated

➢ **Suggest that adherence may be improved by initiating treatment at low doses and titrating upwards**

Timing of response

Response time

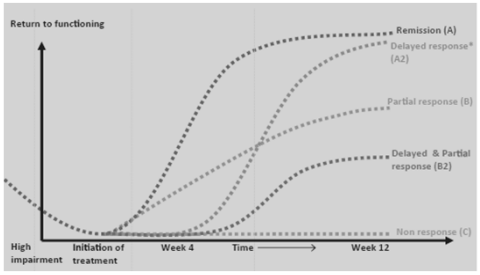
- Several meta-analyses have concluded that **antidepressant effect can occur within 1-2 weeks**
- Early response can be an indicator of eventual remission

➢ **CANMAT guidelines suggests that those with little improvement after 2 weeks may need a change in treatment**

Response time

- In real world samples response and remission may take longer however

➢ **Evidence from STAR*D trial suggests that patients showing more than 20% improvement after 4-6 weeks should continue on that antidepressant for another 2-4 weeks**



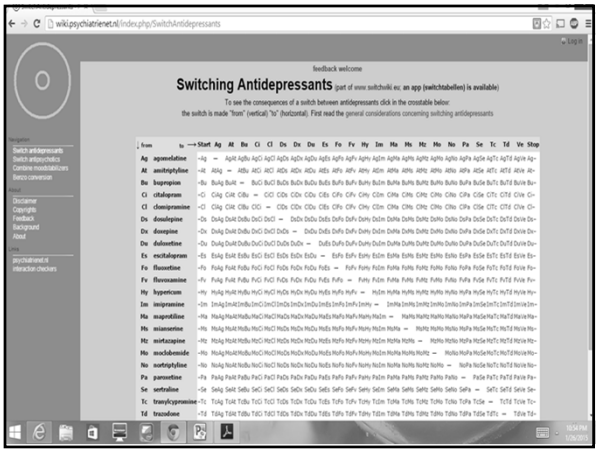
Approach to non-response or partial response

Approach to partial and non-response

- If unable to tolerate the medication, or no further improvement after increasing the dose, options include:
  - **Switching** to another antidepressant or
  - **Adding on** (augmenting with another non-antidepressant medication or combining with another antidepressant)

Switch vs. adding on

- Evidence exists for efficacy of switch and for adding on another medication
- Little information on how these strategies compare against each other or how they should be sequenced
- CANMAT guidelines recommend switching for non-response and adding on for partial response



CANMAT Guidelines

Recommendations for non-response and incomplete response to an initial antidepressant.

• First-line	• Switch to an agent with evidence for superiority	• Duloxetine [Level 2] • Escitalopram [Level 1] • Milnacipran [Level 2] • Mirtazapine [Level 2] • Sertraline [Level 1] • Venlafaxine [Level 1]
	• Add-on another agent	• Aripiprazole [Level 1] • Lithium [Level 1] • Olanzapine [Level 1] • Risperidone [Level 2]
• Second-line	• Add-on another agent	• Bupropion [Level 2] • Mirtazapine/mianserin [Level 2] • Quetiapine [Level 2] • Triiodothyronine [Level 2] • Other antidepressant [Level 3]
	• Switch to an agent with evidence for superiority, but with side effect limitations	• Amitriptyline [Level 2] • Clomipramine [Level 2] • MAO Inhibitors [Level 2]
• Third-line	• Add-on another agent	• Buspirone [Level 2] • Modafinil [Level 2] • Stimulants [Level 3] • Ziprasidone [Level 3]

What about psychotherapy as an augmentation strategy?

Cognitive behavioural therapy as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression: results of the CoBalT randomised controlled trial

Nicola Wiles, Laura Thomas, Anna Abel, Nicola Ridgway, Nicholas Turner, John Campbell, Anne Garland, Sandra Hollinghurst, Bill Jerrom, David Kessler, Willem Kuyken, Jill Morrison, Katrina Turner, Chris Williams, Tim Peters, Glyn Lewis

Summary

Background Only a third of patients with depression respond fully to antidepressant medication but little evidence exists regarding the best next-step treatment for those whose symptoms are treatment resistant. The CoBaIT trial aimed to examine the effectiveness of cognitive behavioural therapy (CBT) as an adjunct to usual care (including pharmacotherapy) for primary care patients with treatment resistant depression compared with usual care alone.

Methods This two parallel-group multicentre randomised controlled trial recruited 469 patients aged 18–75 years with treatment resistant depression (on antidepressants for ≥6 weeks, Beck depression inventory [BDI] score ≥14 and international classification of diseases [ICD]-10 criteria for depression) from 73 UK general practices. Participants were randomised, with a computer generated code (stratified by centre and minimised according to baseline BDI score, whether the general practice had a counsellor, previous treatment with antidepressants, and duration of present episode of depression) to one of two groups: usual care or CBT in addition to usual care, and were followed up for 12 months. Because of the nature of the intervention it was not possible to mask participants, general practitioners, CBT therapists, or researchers to the treatment allocation. Analyses were by intention to treat. The primary outcome was response, defined as at least 50% reduction in depressive symptoms (BDI score) at 6 months compared with baseline. This trial is registered, ISRCTN38231611.

Findings Between Nov 4, 2008, and Sept 30, 2010, we assigned 235 patients to usual care, and 234 to CBT plus usual care. 422 participants (90%) were followed up at 6 months and 396 (84%) at 12 months, finishing on Oct 31, 2011. 95 participants (46%) in the intervention group met criteria for response at 6 months compared with 46 (22%) in the usual care group (odds ratio 3·26, 95% CI 2·10–5·06, p<0·001).

Interpretation Before this study, no evidence from large-scale randomised controlled trials was available for the effectiveness of augmentation of antidepressant medication with CBT as a next-step for patients whose depression has not responded to pharmacotherapy. Our study has provided robust evidence that CBT as an adjunct to usual care that includes antidepressants is an effective treatment, reducing depressive symptoms in this population.

In summary

- Outcomes in treating depression using antidepressants can potentially be improved by:
  1. using **measurement-based care**
  2. starting the antidepressant at half the target dose to minimize side effects
  3. Having contact with the patient every 1-2 weeks after initiating antidepressant treatment
  4. Considering a dose adjustment after 2 weeks at therapeutic dose if not showing any improvement
  5. Augmentation(including with psychotherapy) or switching can be used in event of lack of remission

Depression Management Algorithm

References

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Thank you!