**NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR\*D)**

*Rush et al, Acute and longer term outcomes in depressed outpatients requiring one or several treatment steps: A STAR\*D report. Am J Psych. 2006;163:1905-1917*

**Clinical Question:** How do I treat a patient with MDD who has not gotten better on the first treatment?

**Clinical Take Homes:**

* Only 1/3 will achieve remission with initial SSRI choice (consider switch or augmentation)
* Need to ensure treatment is at sufficient dose, for adequate length (8 weeks), and to remission
* Augmentation with Lithium, Buproprion, Buspirone, or Thyroid hormone all worked ‘somewhat’
* Most patients will relapse within 1 year and faster if not treated to remission or needed more steps

**Study Population:** 4,041 subjects (18-75 with unipolar MDD w/o psychosis) from 41 centers across the USA (18 primary care and 23 psychiatric) scoring at least 14 on HDRS (moderate depression) & self-referred for treatment

**Study Endpoints:** Depression scale remission on QIDS-SR <5 & HDRS <7, clinician/patient self report of response

**Study Design:** All patients entered stage 1, could stay in each stage for 14 weeks, if remission then maintained and followed x 1 year, otherwise moved to next stage where subject identified acceptable txts

Citalopram

Bupropion-SR

Sertraline

Venlafaxine-XR

CBT

Bupropion-SR

Buspirone

CBT

Mirtazapine

Nortriptyline

Lithium

T3

Tranylcypromine

Venlafaxine-XR + Mirtazapine

Switch

Switch

Switch

Augment

Augment

**Results:**

No statistically significant difference across steps due to low numbers of subjects/effect size

Relapse rate by 12 months after stage 4 were 50% for remitters and 83% for non-remitters

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| --- | --- | --- |
| **Step** | **Remission %** | **Specific agent comments (last visit mean daily dose)** |
| **I** | Stage 27-33 | Citalopram 40 mg/day |
| **II** | Stage 20-25; Cumulative 57 | Bup-SR 282 mg/day, Setraline 135 mg/day, Ven-XR 193 mg/day, Bup-SR augmenting 267mg/day more effective (p<.02) and tolerated (p<.009) than Buspirone 41 mg/day |
| **III** | Stage 12-20; Cumulative 63 | Trend towards remission with TCA, Augmentation with T3 45 mg/day had a trend over Lithium 859 mg/day with blood level of 0.6mEq/L which had more side effects |
| **IV** | Stage 13; Cumulative 67 | No statistically significant difference between MAOI and combination but due to washout period most patients got MAOI for less than 6 weeks |

**Criticism:**

* Open label design without placebo control, blurring of endpoints through choosing which scale
* Insufficient enrollment/power to reach statistical significance across all steps

**References:**

1. Website: https://www.nimh.nih.gov/funding/clinical-research/practical/stard/index.shtml
2. General Review Summary: Warden et al, The STAR\*D project results: a comprehensive review of findings, Current Psychiatry Reports. 2007;9:449-459.
3. Criticism: Pigott, The STAR\*D trial: it is time to reexamine the clinical beliefs that guide the treatment of major depression. Can.J.Psychiatry. 2015;60:9-13.