Discontinuation of antidepressants in people with dementia and neuropsychiatric symptoms: double blind, randomised, parallel group, placebo controlled trial
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Josh's pet peeves about the literature
1. Harms and benefits of a medication often can not come from the same study.
2. Average scores are reported instead of categorized groups. NNT not able to be continued.
   So there is no definition of response outcome (is it working, how do we tell)
3. Discontinuation is not studied so we are held hostage.
   Medications I would love to see studied include: Seizure meds, amiodarone, bisphosphonates, cholesterol medications, Plavix, Aricept

Summary of evidence (prevalence, treatment)
Cornell scale
Review of the study

I. Review of SSRI’s for depression in dementia
   A. Prevalence: Major: 5-40%, Minor: 5-15%
   B. Effectiveness:
      1. 7 studies evaluated. 2 with positive results. Only 1 had more than 50 subjects and underpowered according to an accompanying editorial. Defined benefit as 50% improvement in a rating scale such as Hamilton Depression Rating Scale and the Cornell Scale for Depression in Dementia (CSDD) and others. Remission was a HDRS of <7 or CSDD<6. Craig Nelson. A systematic Review and Meta-Analysis of Placebo Controlled Antidepressant Studies in People with Depression and Dementia.

   B. Previous Cessation Study- “The dose that gets you well keeps you well.”
      People randomized to Paxil vs none with psychotherapy vs none

II. Review of SSRI’s for behaviors in dementia
   Aggression (Hostile actions directed towards self/others/objects): Verbal, physical, vocal, sexual
   Hitting, kicking, pushing, scratching, tearing, biting, spitting, threats, accusations, name calling, obscenities
   Agitation (Inappropriate verbal/vocal/motor activity not explained by apparent needs, confusion, medical condition, social/environmental disturbances):
Pacing, disrobing, wandering, handling things inappropriately, restlessness, complaining, requests for attention, negativism, repeated questions, screaming

Other: Psychosis, delusions, hallucinations, depression, apathy, anxiety, euphoria, irritability

Normal delusions in dementia: people are stealing, people are trying to hurt me, strangers are in my house, my house is not my home, misidentification of people, marital infidelity.

Behaviors in Dementia
Delusions, Hallucinations, Agitation/aggression, Depression, Apathy, Elation, Anxiety, Disinhibition, Irritability, Aberrant motor behavior.

Point prevalence for any symptom was 56% at baseline and 76–87% subsequently.
Ninety-seven percent experienced at least one symptom. Symptom severity was consistently highest for apathy.


Effectiveness of treatment
9 trials reviewed. 5 of SSRI. Change in 0.89 on the Cohen Mansfield Agitation Inventory (140 point scale?). Two of the 5 studies showed benefit Seitz DP et al. Antidepressants for agitation and psychosis in dementia. Cochrane Database Syst Rev. 2011:

Summary of evidence
Modest equivocal benefit for a common problem with efficacy defined by research scales

Hypothesis of the study
Stopping the medication would have a small effect

III Methods review
Population chosen: NH residents from 16 centers in Norway with
Dementia: (AD, vascular, mixed)
NH residents > 4 weeks
Had a neuropsych symptom
Prescribed SSRI for >3 months
Excluded:
Clinical hx of depression/schizophrenia
Severe somatic disease/terminal illness
Inability to take prescribed medications
205 patients assessed. 77 excluded.
63 assigned randomly to discontinue, 65 to continue
59 and 58 were included in analysis
35 and 46 finished the study

Intervention:
SSRI tapered over 1 week and replaced by placebo
SSRI changed to a "placebo" pill with active ingredient (same drug/dose)
Lexapro 56%

- Outcome chosen
  Cornell Scale of Depression in Dementia (see sheet)
  38 point scale. 0-7 is not depressed, 8-12 is mild depression, ≥13 is severe depression. Response is defined as 50% change.

Neuropsych inventory:
  10 items (1-4 points for frequency, 1-3 points for severity then multiplied) = 120 point scale. Affective, psychosis, agitation
  ≥4 is a clinically relevant symptom
  ≥9 is a severe symptom

Outcomes:
  CSDD: Average score, Average score in those initially 0-8 and ≥9, change in 30%, those who changed from 0-12 to ≥13

- Statistics

IV Results

<table>
<thead>
<tr>
<th></th>
<th>Discontinuation</th>
<th>Continuation</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average score</td>
<td>CSDD:</td>
<td></td>
<td>Worsening of 2.89</td>
</tr>
<tr>
<td></td>
<td>Pre: 5.03</td>
<td>Pre: 5.89</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post: 6.03 CSD</td>
<td>Post: 4.42</td>
<td></td>
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<tr>
<td></td>
<td>NPI</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Pre: 17.78</td>
<td>Pre: 17.63</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post: 22.5</td>
<td>Post: 14.74</td>
<td></td>
</tr>
<tr>
<td>0-8</td>
<td></td>
<td></td>
<td>Worsening of 3.36</td>
</tr>
<tr>
<td>≥8</td>
<td></td>
<td></td>
<td>Improvement of 2.2</td>
</tr>
<tr>
<td>&gt;30% worsen in CSDD</td>
<td>32 (54%)</td>
<td>17 (29%)</td>
<td>NNH 4</td>
</tr>
<tr>
<td>Change from</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;13 to ≥14</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥13 to ≤14</td>
<td>0</td>
<td>2</td>
<td>NNH 9</td>
</tr>
</tbody>
</table>

V Authors conclusions
Worsening of depression but 86% of people never switched categories. Maybe these meds are effective. Meds can be discontinued but monitored.

VI Reviewers Critique
VII Summary for practice implications
### Table 1: Summary of Characteristics of Depression Symptom Measures

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cornell Scale for Depression in Dementia&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Patient Health Questionnaire-9- Observation Version&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of administration</td>
<td>Clinician interview of caregiver and patient (discrepancies resolved with second caregiver interview); chart review for weight loss item.</td>
<td>Staff assessment of behaviors, signs, or symptoms of mood distress.</td>
</tr>
<tr>
<td>Time to complete</td>
<td>Caregiver interview = 20 minutes; resident interview = 10 minutes</td>
<td>Caregiver interview = 10 minutes</td>
</tr>
<tr>
<td>Time frame</td>
<td>Past week</td>
<td>Past 2 weeks</td>
</tr>
<tr>
<td>Number of items</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Content</td>
<td>1. Anxiety, 2. Sadness, 3. Lack of reactivity to pleasant events, 4. Irritability, 5. Agitation, 6. Retardation, 7. Multiple physical complaints, 8. Loss of interest&lt;sup&gt;c&lt;/sup&gt;, 9. Appetite loss, 10. Weight loss&lt;sup&gt;d&lt;/sup&gt;, 11. Lack of energy&lt;sup&gt;e&lt;/sup&gt;, 12. Diurnal variation of mood, 13. Difficulty falling asleep, 14. Multiple awakenings during sleep, 15. Early morning awakening, 16. Suicide (i.e., feels life is not worth living, has suicidal wishes, or makes suicide attempts), 17. Poor self-esteem, 18. Pessimism, 19. Mood-congruent delusions</td>
<td>1. Little interest or pleasure in doing things, 2. Feeling or appearing down, depressed, or hopeless, 3. Trouble falling or staying asleep; sleeping too much, 4. Feeling tired or having little energy, 5. Poor appetite or overeating, 6. Indicating feeling bad about self, is a failure, or has let self or family down, 7. Trouble concentrating on things, such as reading the newspaper or watching television, 8. Moving or speaking so slowly that other people have noticed, or the opposite—being so fidgety or restless that resident has been moving around a lot more than usual, 9. States that life isn’t worth living, wishes for death, or attempts to harm self, 10. Being short-tempered, easily annoyed</td>
</tr>
<tr>
<td>Scaling method</td>
<td>Items are rated as:</td>
<td>Frequency of positive symptoms:</td>
</tr>
<tr>
<td></td>
<td>a = unable to evaluate</td>
<td>0 = never or 1 day</td>
</tr>
<tr>
<td></td>
<td>0 = absent</td>
<td>1 = 2 to 6 days</td>
</tr>
<tr>
<td></td>
<td>1 = mild or intermittent</td>
<td>2 = 7 to 11 days</td>
</tr>
<tr>
<td></td>
<td>2 = severe</td>
<td>3 = 12 to 14 days</td>
</tr>
<tr>
<td>Score range</td>
<td>0 to 38</td>
<td>0 to 30</td>
</tr>
<tr>
<td>Score interpretation</td>
<td>0 to 7 = no depression</td>
<td>0 to 4 = minimal depression</td>
</tr>
<tr>
<td></td>
<td>8 to 12 = mild depression</td>
<td>5 to 9 = mild depression</td>
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<tr>
<td></td>
<td>&gt;12 = major depression</td>
<td>10 to 14 = moderate depression</td>
</tr>
<tr>
<td></td>
<td>(Watson et al., 2003)</td>
<td>15 to 19 = moderately severe depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 to 30 = severe depression</td>
</tr>
</tbody>
</table>

<sup>a</sup> Alexopoulos, Abrams, Young, and Shamoian (1988).
<sup>b</sup> A component of the Minimum Data Set, version 3.0.
<sup>c</sup> Symptoms must have been present during the past week and have developed acutely (i.e., within the past month).
<sup>d</sup> Response based on individual’s weight over past month with a score of 2 if weight loss >5 pounds in 1 month.

Alexopoulos, Abrams, Young, and Shamoian (1988). Internal consistency reliability in the current study was acceptable (Cronbach's alpha coefficient = 0.75). The CSDD is the most common measure of depression in dementia populations and has performed well when compared against psychiatrist-diagnosed depression ($r = 0.83$) and the HDRS ($r = 0.96$) (Alexopoulos et al., 1988; Burrows, Morris, Simon, Hirdes, & Phillips, 2000; Hamilton, 1960). At a cut-off point of 7, the CSDD has shown...