

# Painful physical symptoms and treatment outcome in major depressive disorder: a STAR\*D (Sequenced Treatment Alternatives to Relieve Depression) report

## Background

The most common symptom in medicine is pain. More than half of complaints to physicians are reports of pain – commonly headache or back pain, on a chronic or acute basis. Up to 40% of the general population complains of chronic pain, with nearly 15% complaining of pain on a daily basis. Commonly, the basis for pain is not clearly identified.

The relationship between pain and depression is complex. Depression may be both a cause and a consequence of painful physical symptoms (PPS), with similar brain areas regulating both mood and the affective components of pain. From 15% to 100% of patients complain of PPS at some point during an episode of major depressive disorder (MDD). Painful physical symptoms (PPS) are both common and reduce the likelihood of remission in major depressive disorder (MDD), based upon results of clinical trials in selected populations. Whether poorer outcomes would be seen among 'real-world' patients from both primary care and psychiatric settings remains unclear, as do contributions of other factors such as age, race, gender, chronicity or severity of depression, or the presence of chronic physical illness, to the possible association between PPS and poorer treatment outcome.

The 'Sequenced Treatment Alternatives to Relieve Depression' (STAR\*D) trial provides an excellent opportunity to help clarify the relationship between PPS and treatment outcome in out-patients with MDD who presented naturalistically for treatment.

## Method

Out-patients (n=2876) with DSM-IV criteria for non-psychotic MDD and had a score of  $\geq 14$  (moderate severity) on the 17-item Hamilton Rating Scale for Depression (HAMD<sub>17</sub>) were treated in the first step of the Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) trial with citalopram up to 60 mg/day for up to 14 weeks. Presence of painful symptoms, as well as severity of depression, physical illness, and demographic and treatment factors were examined. Time to and overall rates of remission were analysed in relation to the presence of PPS. The presence of pain was determined using the Inventory of Depressive Symptomatology (IDS-C30) item no. 26, 'somatic complaints', from the baseline visit.

## Results

Of the participants, 80% complained of PPS. More than one-third had mild complaints, but more than 25% reported pain present most of the time and approximately 20% complained of pain that interfered with function. Subjects with PPS had significantly greater severity of depressive symptoms at initiation of treatment than did those without PPS. These patients, both in primary and specialty psychiatric settings, had significantly lower response and remission rates and took longer to remit (Fig. 1&2). Increasing severity of PPS was associated with greater physical illness burden, lower socio-economic status, absence of private insurance and being female, African-American or Hispanic. After adjustment for these factors, patients with PPS no longer had significantly poorer treatment outcomes. There were no significant differences in current suicide risk according to level of pain complaints. Subjects who endorsed PPS were more likely, however, to have anxious, atypical or melancholic features of depression. Those reporting higher degrees of pain also were more likely to meet criteria for a greater overall number of co-morbid Axis I conditions.

## Conclusions

Presence and severity of PPS is an indicator of MDD that may have poorer treatment outcome with an initial selective serotonin reuptake inhibitor. These poorer outcomes may reflect the cumulative effect of psychosocial and neurobiological factors. Elucidation of the linkages between the presence and intensity of PPS and poorer outcome could help direct selection of the most effective treatments for patients with these symptoms in MDD.

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