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Research report

What is important in being cured from: Does discordance between physicians and patients matter? (2)

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ABSTRACT

Aims: The influence of discordance in what is important in being cured from depression on clinical outcome at 6 months, assessed with a divergence index.

Methods: 304 outpatients treated for depression by general practitioners or by psychiatrists and completing a 6-month treatment period: a divergence index (divergence between physician and patient view on what is important in being cured from depression) was calculated for each physician–patient pair. The relation between this index and outcome at 6 months was analyzed (including depressive, anxious and somatic symptom severity, positive effect, functional impairment and quality of life (psychological and social relations)).

Results: Response rates (50% improvement) were 65.9% for depressive symptomatology and 46.2% for anxious symptomatology. The subgroup with a poor physician–patient agreement (highest quartile) on expectations had a worse clinical outcome than the subgroup with an excellent physician–patient agreement (lowest quartile): differences in response rate between these groups ranged from 9% to 27%; this difference reached statistical significance for 3 outcome variables (anxiety, positive effect and social relationships).

Conclusions: The study shows that outcomes with standard antidepressant drugs are still suboptimal and that discordance between what patients' and physicians' consider important in the definition of cure from depression significantly influences clinical outcomes at 6 months.

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1. Introduction

A meta-regression analysis showed that response rates are 53.8% for a typical antidepressant and 37.3% for placebo suggesting that about two thirds of antidepressant efficacy is due to a non-specific placebo effect (Papakostas and Fava, 2009). But again, important differences were found between observer-rated and self-rated outcomes. Using non-disease specific scales, it has indeed been reported that the percentage of patients with a 'global improvement' during antidepressant treatment was 10% higher in the physician's assessment than in the patient's assessment (Demyttenaere et al., 2009a, 2009b). Moreover, in a group of patients being in (observer-rated) remission (i.e. a HDRS – Hamilton Depression Rating Scale – ≤ 7), only 55.11% considered themselves in remission (not defined, but

based on personal conceptualization of remission) (Hamilton, 1960; Zimmerman et al., 2012). Interestingly, patients in observer-rated remission who also considered themselves in remission had higher scores on positive mental health and had significantly less functional impairment than patients with only observer-rated remission (Zimmerman et al., 2012).

The reasons for these clinically important discrepancies have been insufficiently investigated and they could theoretically be influenced by clinical variables, trial or design features, patient attitudes and behaviors, and doctor–patient relationship. For example, it has been shown that a higher baseline discrepancy between scores derived from an observer-scale and a self-rating scale leads to a poorer outcome, is generally observed in patients with a comorbid personality disorder and positively correlates with anxiety levels (Rane et al., 2010). Factors related to patient expectations from antidepressant have also been shown to influence outcome. Response rates in patients treated with an antidepressant were found to be 65.4% in drug–drug studies, 57.7% in

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drug–drug–placebo studies and 51.7% in drug–placebo studies while in patients treated with placebo, response rates were 44.6% in drug–drug–placebo trials and 34.3% in drug–placebo trials (Sinyor et al., 2010). This is further illustrated by a study showing higher HDRS scores immediately postrandomization (moving to placebo or staying on fluoxetine): this increase in HDRS scores was found as well in patients staying on fluoxetine as in patients moving to placebo (Rutherford et al., 2014). This suggests that treatment changes influence patients' expectations of improvement, which, in turn, affect their depression symptom severity. These data suggest that the chance of being on active treatment (through physician and patient expectations) is an important predictor of outcome. Another study investigating the influence of baseline attitude to taking (antidepressant) medication showed that patients with a baseline positive/neutral/negative attitude towards antidepressants presented a placebo response rate of 46%, 37% and 30% and an antidepressant response rate of 67%, 60% and 56%, respectively, again suggesting that baseline expectations and attitudes predict outcome (Demyttenaere et al., 2011). The NIMH-funded study on the efficacy of hypericum perforatum did not find any significant difference in response rates between the hypericum arm, the sertraline arm and the placebo arm but a reanalysis taking into account patient's guess of which treatment they got showed important differences in outcome: patients guessing they were on sertraline had a 56% response rate, patients guessing they were on hypericum had a 68% response rate while patients guessing they were on placebo had a 24% response rate (Hypericum Depression Trial Study Group, 2002; Chen et al., 2011). Further, the attitude and behavior of the prescribing psychiatrists are also important: the psychiatrist is not only a provider of treatment but also acts as a mean of treatment. Indeed, the proportion of variability in outcomes was shown to be due less to the antidepressant treatment received (imipramine or placebo) than to the psychiatrist administering the treatment (McKay et al., 2006). Interestingly, the psychiatrist effects were not as dramatic for the observer-rated measure than for the self-report measure (6.7% and 9.1% of the variance, respectively).

We previously showed that what physicians and patients consider to be important in being cured from depression is different, and the present paper investigates whether these differences influence outcome in depressed patients treated with antidepressants.

2. Methods

Ethics statement, patient recruitment and data collection were described in the previous paper (Demyttenaere et al., submitted).

2.1. Treatment and clinical outcome

The protocol stipulated that the treatment was entirely left to the discretion of the physician: one antidepressant was prescribed to 92.5% of the patients and two antidepressants were prescribed to 7.1% of the patients (no antidepressant was prescribed to 0.2% of the patients and 43 different antidepressants were prescribed to 0.2% of the patients). In 45.2% of the patients, at least one modification in the antidepressant treatment was observed during the 6-month study period.

The clinical status of the patient was assessed with the following mentioned self-rating scales: the Patient Health Questionnaire-Depression (PHQ-depression; depressive symptoms), Hospital Anxiety and Depression Scale-anxiety (HADS-anxiety; anxious symptoms), Patient Health Questionnaire-Somatic Symptoms Severity (PHQ-somatic; somatic symptoms), the Positive And Negative Affect Schedule-Positive effect subscale (PANAS-positive effect), the

Sheehan Disability Scale (SDS; functional impairment), and the Abbreviated World Health Organization QoL (WHOQOL-BREF; quality of life-psychological and social relationships), at baseline and after 6 months of treatment (Kroenke et al., 2001, 2002; Zigmond and Snaith, 1983; Watson et al., 1988; Sheehan et al., 1996; WHO-QOL group, 1998).

2.2. Statistical analysis

Discordance index based on the top 10 DEsCRIBE™ items of the patient.

The discordance between what patients and physicians consider important in defining cure from depression was based on their respective baseline scores on the DEsCRIBE™ questionnaire, where a ranking (importance for being cured from disorder) was given to depressive, anxious and somatic symptoms, positive effect, disability and quality of life items (Demyttenaere et al., submitted). A discordance index (DI) was constructed to evaluate the baseline agreement between physician and patient on the definition of being cured from depression. The discordance index was calculated for each possible pair (physician–patient) by using the differences between the item scores given by the physician and his/her patient. The items considered in the construction of the discordance index were the 10 DEsCRIBE™ items classified in first position of importance by the patients in the definition of being cured from depression. To correct for the fact that patients always gave higher scores than physicians, individual patient's scores were standardized by subtracting the corresponding mean of each item. The same correction was applied to the individual physician's scores. The absolute difference between the standardized score of the patient and the standardized score of the physician was calculated for each of the 10 selected items. The discordance index was then defined as the average of the 10 absolute differences. DI scores range between 0 and 5, where high values indicate strong divergence and low values strong agreement between physician and patient about the definition of being cured from depression

$$DI = \frac{\sum_{i=1}^{10} |(score\ item\ i - mean\ item\ i)_{phys} - (score\ item\ i - mean\ item\ i)_{pat}|}{10}$$

The mean DI was 1.1 ± 0.57 and the median 0.99. Based on their DI value, patients were classified into 4 groups (according to the quartiles): excellent agreement with physician ($DI < 0.71$), rather good agreement ($0.71 \leq DI < 0.99$), rather poor agreement ($0.99 \leq DI < 1.47$), and poor agreement ($DI \geq 1.47$).

Results were summarized as mean and standard deviation (SD) for quantitative variables and scores; counts and proportions (%) were used for categorical variables. The correlation coefficient was computed to measure the association between two quantitative variables. Mean values were compared by one-way analysis of variance (ANOVA). Proportions were compared by the chi-squared test for contingency tables. The comparison of the clinical score at 6 months according to DI-categories was made by ordinal logistic regression. A Cochran–Armitage test for trend was used to compare the 6-month response rates between the DI groups. Results were considered significant at the 5% critical level ($P < 0.05$). Calculations were always done on the maximum number of data available. All statistical calculations were performed by using SAS (version 9.3 for Windows) and S-PLUS (version 8.1) packages.

3. Results

Of the 426 patients analyzed in the study, 304 (71.3%) completed the 6-month follow-up. Clinical status (responses and

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