Journal of Affective Disorders 113 (2009) 296–302

www.elsevier.com/locate/jad

Brief report

Quality of life outcomes among patients with depression after 6 months of starting treatment: Results from FINDER

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Received 12 November 2007; received in revised form 27 May 2008; accepted 27 May 2008
Available online 7 July 2008

Abstract

Background: Health-related quality of life (HRQoL) data in depression are limited. We studied the impact of antidepressant (AD) treatment on HRQoL outcomes in depressed patients and investigated factors associated with these outcomes in routine practice settings.
Methods: The Factors Influencing Depression Endpoints Research (FINDER) study was a 6-month, European, prospective, observational study, designed to estimate HRQoL in 3468 adult patients with a clinically diagnosed episode of depression at baseline and at 3 and 6-months after commencing AD treatment. HRQoL was assessed by the Medical Outcome Short-Form (36) Health Survey (SF-36) and European Quality of Life-5 Dimensions (EQ-5D). Regression analysis identified baseline and treatment variables independently and significantly associated with HRQoL outcomes.
Results: Most HRQoL improvement occurred within 3 months of starting treatment. Better HRQoL outcomes were strongly associated with fewer somatic symptoms at baseline, AD treatment taken and not switching within AD groups. Education and occupational status were also important. Depression variables (number of previous depressions and current episode duration) were consistently associated with worse HRQoL outcomes. Self-rated depression severity was associated with poorer outcomes on the SF-36 mental component only.
Limitations: As this was an observational study, the important finding that between and within AD group switching impacted HRQoL will need to be investigated in more controlled settings.

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doi:10.1016/j.jad.2008.05.021

Conclusions: Receiving an AD treatment was associated with large improvements in HRQoL, but switching within AD groups was consistently associated with poorer outcomes. Somatic symptoms, including painful symptoms, are often present in depressed patients and appear to negatively impact HRQoL outcomes.

Keywords: Antidepressants; Depression; Europe; FINDER; Quality of life; Routine practice setting

1. Introduction

Health-related quality of life (HRQoL) is impaired in patients with depression, especially when compared to the general population and patients with other chronic diseases, such as diabetes, arthritis or cardiovascular disease (Hays et al., 1995; Wells et al., 1989, 1999). There is increasing interest in HRQoL as a measure of response to antidepressant treatment because it encompasses not only symptoms, but also physical, mental and social functioning as well as role performance (Demyttenaere et al., 2002). Thus, assessment of HRQoL may provide a more comprehensive evaluation of treatment response than one based solely on improvement in emotional symptoms of depression.

Factors Influencing Depression Endpoints Research (FINDER) was a 6-month, observational study to assess the HRQoL of outpatients with a depressive episode in routine primary care and specialist settings (Bauer et al., 2008; Garcia-Cebrian et al., 2008). The aims of the present report are to describe the HRQoL outcomes at three and six months after commencing pharmacotherapy for depression and to determine which factors are associated with HRQoL changes over time.

2. Methods

2.1. Study design and subjects

The design and methods of FINDER have been reported in detail elsewhere (Bauer et al., 2008; Garcia-Cebrian et al., 2008). Briefly, primary care physicians or specialists (mostly psychiatrists) enrolled adult patients (≥18 years) presenting during the normal course of care with a clinical diagnosis of depression who were about to commence antidepressant treatment. The study was approved in all countries according to local requirements for ethics and/or regulatory approvals for observational studies, and all patients gave written informed consent. Data were collected at baseline and after 3 and 6 months during routine care visits.

2.2. Data collected

Data recorded at baseline included patient sociodemographics, psychiatric history, duration of the current depressive episode and presence of comorbid chronic medical conditions and functional syndromes.

Antidepressants prescribed were grouped as follows: selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenaline reuptake inhibitors (SNRIs), tricyclic and tetracyclic antidepressants (TCAs), others (including herbal remedies, lithium, monoamine oxidase inhibitors), or combinations of antidepressants from more than one of these groups.

HRQoL was scored by patients using the 36-item Short-Form Health Survey (SF-36 version 2.0) (Ware et al., 1998) and the European Quality of Life-5 Dimensions (EQ-5D) (Brooks, 1996). Anxiety and depression symptoms were rated by patients using the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) giving two subscales; HADS-D (depression) and HADS-A (anxiety). Somatic symptoms were assessed by way of the 28-item Somatic Symptom Inventory (SSI-28) (Barsky et al., 1986), consisting of seven pain-related items (SSI-pain) and 21 somatic items (SSI-somatic). Overall pain severity was rated by patients using a Visual Analogue Scale (VAS, 0–100), with ratings >30 considered to be moderate/severe pain.

2.3. Statistical analysis

Descriptive statistics were calculated for each variable for all 3468 patients eligible for analysis at baseline, but only those with at least one follow-up visit were included in the regression analyses.

2.3.1. Analysis of loss to follow-up

We compared the baseline characteristics and change scores from baseline to 3 months for the HRQoL variables for two groups: those with data at 3 months only; and those with either data at both 3 and 6 months or at 6 months only. Logistic regression analysis was performed to identify variables significantly associated with loss to follow-up using the same set of independent

variables as for the main regression analysis, with the following exceptions: (1) baseline score for the dependent variable was not applicable, (2) group of antidepressant (AD) taken between baseline and 3 months was replaced with the group of AD prescribed at baseline, and (3) switching variable (switch of AD treatment taken during the first 3 months and that taken during the second 3 months) was not used (inclusion would have excluded any patient without data at all observations).

2.3.2. Main analysis

Backward regression analysis was performed to identify variables independently associated with HRQoL outcomes. Separate models were fitted for each of the following outcome variables: SF-36 (mental component summary [MCS], physical component summary [PCS]), EQ-5D (visual analogue scale [VAS], health status index [HSI]). A mixed-effects model repeated measures (MMRM) analysis with unstructured covariance structure was used. Independent variables were removed from the full model until only statistically significant ($p \leq 0.05$) variables remained.

3. Results

3.1. HRQoL scores at baseline and follow-up

The socio-demographic and clinical characteristics of the FINDER study population are reported elsewhere (Garcia-Cebrian et al., 2008). The mean unadjusted scores for SF-36 and EQ-5D at baseline, 3 and 6 months (Fig. 1) show HRQoL improvements at 3 months, with a further smaller improvement at 6 months.

3.2. Loss to follow-up analysis

Of the 3468 patients at baseline, 343 (9.9%) had no follow-up data, 271 (7.8%) had data at 3 months only, and 2854 (82.3%) had data at both 3 and 6 months or 6 months only.

Three variables were significantly associated with loss to follow-up: country ($p<0.001$), younger age at first depressive episode ($p=0.001$) and higher SSI-somatic score at baseline ($p=0.019$). Severity of depression (HADS-D) was not significantly associated with the likelihood of remaining in the study. There were no systematic differences in HRQoL change scores during the first 3 months of treatment in patients with and without 6 month follow-up (data not shown).

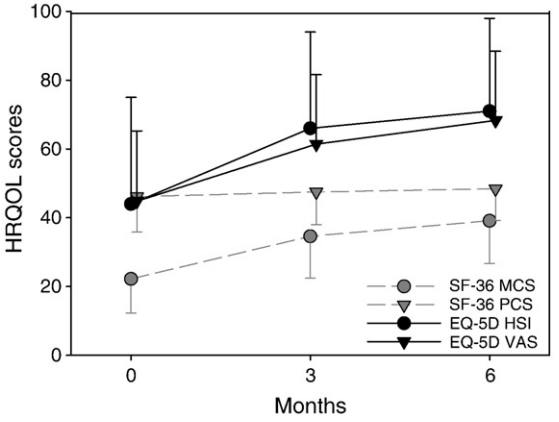

Fig. 1. Mean (and standard deviation) SF-36 and EQ-5D scores at baseline, 3 and 6 months. SF-36 MCS and PCS scores were normalised to a mean of 50 (SD 10) for the general US adult population. Mean EQ-5D Health State Index (HSI) scores were converted from a 0–1 scale to a 0–100 scale. MCS, mental component summary; PCS, physical component summary.

3.3. Factors associated with HRQoL changes over 6 months

The independent variables significantly associated with HRQoL outcomes are summarised in Table 1. The estimates given are the change in respective outcome variable (SF-36 or EQ-5D) associated with an increase of 1 unit for continuous variables or between specified levels for categorical variables.

Switching treatment within AD groups was consistently associated with smaller improvements in HRQoL outcomes compared with no switch in AD group, whereas switching AD treatment between groups was either not significantly associated with HRQoL outcome, or, where significant (SF-36 MCS and EQ-5D HSI), the effect on HRQoL was consistently smaller than for switches within groups. For the independent variable "AD taken between baseline and 3 months", both for SF-36 MCS and EQ-5D VAS, the positive effects compared to no treatment were largest for SSRIs followed (in decreasing order) by "other" drugs, SNRIs, TCAs and combinations.

A higher SSI-somatic score at baseline was strongly and consistently associated with a worse HRQoL outcome. Higher overall pain VAS at baseline was significantly associated with worse EQ-5D and there were weaker associations with poorer SF-36. Socio-economic factors, such as education and occupational status, were also consistently associated with HRQoL (except for education with SF-36 PCS) — patients with further education had a better HRQoL outcome than patients with no or mandatory education, and patients

Table 1
Independent variables significantly associated with HRQoL

Independent variable	SF-36 MCS (n=2315)			SF-36 PCS (n=2140)			EQ-5D VAS (n=2224)			EQ-5D HSI (n=2230)		
	Estimate	F value	P value	Estimate	F value	P value	Estimate	F value	P value	Estimate	F value	P value
Age	–	–	–	−0.07	47	<0.001	–	–	–	−0.001	10	0.002
Female (vs. male)	1.08	6	0.016	–	–	–	1.65	5	0.023	–	–	–
Further education (vs. no/mandatory)	1.20	7	0.008	–	–	–	1.90	6	0.011	0.027	7	0.007
Occupational status (reference: paid work)		16	<0.001		9	<0.001		18	<0.001		11	<0.001
Other	−1.12			−1.09			−3.17			−0.028		
Unemployed	−3.74			−1.29			−5.83			−0.064		
Married/domestic partner (vs. other)	–	–	–	–	–	–	1.46	4	0.034	–	–	–
Number of dependants	–	–	–	0.23	5	0.021	–	–	–	–	–	–
BMI	–	–	–	–	–	–	−0.23	11	<0.001	−0.002	7	0.008
Duration of current episode of depression (weeks)	−0.05	15	<0.001	−0.02	8	0.005	−0.09	16	<0.001	−0.001	22	<0.001
Number of previous episodes of depression[a]	−0.72	20	<0.001	−0.32	11	0.001	−1.07	17	<0.001	−0.018	29	<0.001
Any other psychiatric illness[a]	−1.81	16	<0.001	–	–	–	–	–	–	–	–	–
Any chronic medical condition (vs. none)	–	–	–	−1.96	48	<0.001	−2.50	12	<0.001	−0.045	21	<0.001
SF-36 MCS score[b]	0.24	71	<0.001	–	–	–	–	–	–	–	–	–
SF-36 PCS score[b]	–	–	–	0.48	727	<0.001	–	–	–	–	–	–
EQ-5D VAS[b]	–	–	–	–	–	–	0.30	271	<0.001	–	–	–
EQ-5D HSI[b]	–	–	–	–	–	–	–	–	–	0.219	158	<0.001
SSI-somatic	−2.10	31	<0.001	−0.91	13	<0.001	−3.34	33	<0.001	−0.051	41	<0.001
HADS-D	−0.21	11	0.001	–	–	–	–	–	–	–	–	–
HADS-A	–	–	–	0.11	9	0.003	–	–	–	–	–	–
Overall pain VAS	−0.02	5	0.026	−0.02	7	0.007	−0.06	17	<0.001	−0.001	35	<0.001
AD taken between baseline and 3 months (reference: no treatment)		5	<0.001	–	–	–		4	0.001	–	–	–
Combinations	2.78 (ns)						4.61 (ns)					
Other drugs	4.73						7.61					
SNRI	4.44						7.52					
SSRI	5.21						7.68					
TCA	3.22						4.99					
Switch* (reference: no switch)		19	<0.001		9	<0001		10	<0.001		21	<0.001
Between AD group	−1.46			−0.44 (ns)			−0.21 (ns)			−0.041		
Within AD group	−5.55			−2.44			−6.78			−0.117		
Country[c]		3	<0.001		4	<0.001		5	<0.001		4	<0.001

P values <0.05 are reported as statistically significant. Estimates represent the change in the dependent variable associated with a difference of 1 unit (or 1 category for categorical variables) in the independent variable. Greater F values and smaller P values give an indication of the relative strength of association of the independent variables with the HRQoL outcome. All independent variables are at baseline unless otherwise specified.
Other independent variables included in the regression analysis but not significant in any of the HRQoL outcome models were: age at first episode, smoking.
[a]In 24 months preceding baseline [b]Only included in the relevant HRQoL model. [c]Country is a known source of variation which was adjusted for in the current analysis but estimates are not presented.
*Switch between what was taken between baseline and 3 months and what was taken between 3 months and 6 months.
SF-36 scores 0–100; higher scores reflect better HRQoL.
EQ-5D VAS scores 0–100 and HSI scores 0–1; higher scores reflect better HRQoL.
AD, antidepressant; BMI, body mass index; EQ-5D, EuroQol 5-dimensions; HSI, health state index; MCS, mental component summary; ns, not statistically significant; PCS, physical component summary; SF-36, 36-item Short-Form Health Survey SNRI, serotonin noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic and tetracyclic antidepressants; VAS, visual analogue scale.

who were unemployed had a worse HRQoL outcome than those working for pay.

Depression variables, such as the number of previous episodes of depression and the duration of the current depressive episode, were consistently associated with worse HRQoL outcomes. In addition, severity of depression (HADS-D score) at baseline was significantly associated with a worse SF-36 MCS score.

4. Discussion

The results of this large observational study showed that outpatients with an untreated episode of depression experienced improvements in HRQoL after starting antidepressant medication. The majority of this improvement occurred in the first 3 months of follow-up. The SF-36 summary scores show that the HRQoL impairment at baseline and the improvements during treatment were much greater for mental health dimensions than for physical health. Although the study population did not reach HRQoL levels comparable to general population norms, the improvements in HRQoL during treatment were consistent with clinical studies (Kroenke et al., 2001; Miller et al., 1998; Detke et al., 2002; Dunner et al., 2001; Walker et al., 1995; Peveler et al., 2005).

EQ-5D has not been widely used to assess HRQoL in depressed patients. A recent longitudinal study (Sobocki et al., 2007) found reduced HRQoL in Swedish primary care patients with depression; baseline EQ-5D HSI (0.47) and VAS (40) scores were similar to those in the FINDER study (0.44 and 44.8, respectively). Likewise, 6 months' treatment resulted in comparable HRQoL improvements.

A new finding of this study was that switching antidepressant within AD groups was consistently associated with a worse HRQoL outcome than not switching treatment, and that a between-group AD switch was associated with a worse SF-36 MCS and EQ-5D HSI compared with no switch. This finding may be a reflection of the harder-to-treat nature of patients requiring a switch of antidepressant rather than the effectiveness of switching itself. It is common clinical practice to switch antidepressant medication for patients who have an insufficient response and/or cannot tolerate their initial antidepressant. However, there is little information available to guide physicians on which antidepressant medication to switch to or the consequences of such switching. After unsuccessful treatment with an SSRI, remission rates were similar after switching to another antidepressant, regardless of the class of antidepressant used (Rush et al., 2006). Moreover, a recent systematic review concluded that there is no evidence that a between-group switch has advantages over a within-group switch for response and remission rates (Ruhe et al., 2006). Our findings suggest that if a treatment switch is necessary, a switch between antidepressant groups may be less disadvantageous for HRQoL outcomes than a within-group switch. However, this needs to be confirmed in more controlled settings.

An important finding of this study was that increasing severity of depression at baseline (HADS-D) was significantly associated with a worse HRQoL outcome for SF-36 MCS only. Baseline results of FINDER (Garcia-Cebrian et al., 2008) and other studies (Pyne et al., 1997; Sapin et al., 2004; Saarijarvi et al., 2002; Trivedi et al., 2006) have found that, in cross-sectional analysis, quality of life is lower in patients with more severe depression. Several depression-related factors (longer duration of the current depressive episode and a higher number of previous depressive episodes) were also consistently associated with a poorer HRQoL outcome.

Although somatic symptoms are often present in depressed patients and may influence depression outcomes (Tylee and Gandhi, 2005), few studies have addressed the impact of somatic symptoms on HRQoL. We found that greater 'bother' due to somatic symptoms at baseline resulted in poorer HRQoL outcomes during antidepressant treatment. 'Bother' in this context could be understood as a patient's assessment of the frequency and severity of the somatic symptoms being evaluated.

In FINDER, a higher overall pain VAS score at baseline was associated with a poorer HRQoL outcome. Similarly, Munoz et al. (2005) found that greater severity of painful somatic symptoms was associated with a reduced quality of life among Latin American outpatients with depression. Moreover, in primary care patients, severity of pain was a strong predictor of a poor treatment response and poor HRQoL outcome at 3 months after beginning antidepressant therapy (Bair et al., 2004). Taken together, this indicates that somatic/painful symptoms influence patient quality of life, and that depressed patients with high levels of somatic/painful symptoms may be more difficult to treat than other patients.

The FINDER study has several limitations. Firstly, important findings such as the association between HRQoL outcomes and between- and within-AD group switching need to be investigated further in more controlled settings. Secondly, HRQoL instruments partly measure concepts that are also contained in depression instruments. However, SF-36 and EQ-5D focus more on the impact on activities of daily living, social interactions and related aspects. Symptom severity and impact on everyday life are probably closely correlated, which may explain much of the parallel improvement in HRQoL and depression symptoms. Lastly, our observation period was limited to 6 months during which time patients did not approach general population values for the SF-36 MCS. We are, therefore, not able to assess whether the time course to achieving mental HRQoL scores comparable to the general population is longer than 6 months or whether, even after treatment, participants remain impaired in this respect.

5. Conclusions

This study showed that several patient- and treatment-related factors are associated with HRQoL outcomes of depressive episodes in everyday clinical practice. Receiving an AD treatment was associated with large improvements in HRQoL, but switching within AD groups was consistently associated with poorer outcomes. Somatic symptoms, including painful symptoms, are often present in depressed patients and appear to negatively impact HRQoL outcomes.

Role of Funding Source

FINDER was funded by Eli Lilly and Company Limited, Windlesham, Surrey, UK & Boehringer Ingelheim GmbH, Ingelheim, Germany. The sponsors were involved in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Conflict of Interest

Catherine Reed, David Perahia, Ana Garcia-Cebrian and Deborah Quail are Lilly employees and Brigitta Monz is a Boehringer Ingelheim employee. Paul Ghandi was employed by Eli Lilly & Company Ltd, Basingstoke, UK at the time the research was performed. Michael Bauer, Nicolas Danchev, Koen Dymettenaere, Luigi Grassi, Angel Luis Montejo and Andre Tylee have received economic compensation for participation in the FINDER Advisory Board.

Acknowledgements

We would like to thank all investigators and patients who participated in the FINDER study, as well as all colleagues from Eli Lilly and Boehringer Ingelheim, especially Mary Lou Furstnau, for implementing FINDER in the various countries. The authors also thank Deirdre Elmhirst for her editorial assistance in preparing the manuscript.

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