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Health-related quality of life of primary care patients with depressive disorders

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ABSTRACT

Background: Depressive disorders are known to impair health-related quality of life (HRQoL) both in the short and long term. However, the determinants of long-term HRQoL outcomes in primary care patients with depressive disorders remain unclear.
Methods: In a primary care cohort study of patients with depressive disorders, 82% of 137 patients were prospectively followed up for five years. Psychiatric disorders were diagnosed with SCID-I/P and SCID-II interviews; clinical, psychosocial and socio-economic factors were investigated by rating scales and questionnaires plus medical and psychiatric records. HRQoL was measured with the generic 15D instrument at baseline and five years, and compared with an age-standardized general population sample ($n = 3707$) at five years.
Results: Depression affected the 15D total score and almost all dimensions at both time points. At the end of follow-up, HRQoL of patients in major depressive episode (MDE) was particularly low, and the association between severity of depression (Beck Depression Inventory [BDI]) and HRQoL was very strong ($r = -0.804$). The most significant predictors for change in HRQoL were changes in BDI and Beck Anxiety Inventory (BAI) scores. The mean 15D score of depressive primary care patients at five years was much worse than in the age-standardized general population, reaching normal range only among patients who were in clinical remission and had virtually no symptoms.
Conclusions: Among depressive primary care patients, presence of current depressive symptoms markedly reduces HRQoL, with symptoms of concurrent anxiety also having a marked impact. For HRQoL to normalize, current depressive and anxiety symptoms must be virtually absent.

1. Introduction

Depression is a major public health problem and known to cause distress and disability [1,2]. It has also been found to be associated significantly with decreased health-related quality of life (HRQoL) in both general population [3–6] and primary care studies [2,7–13]. Primary care patients with depressive symptoms have had worse HRQoL than patients with common chronic medical conditions and physical functioning in the midrange [2,8,12]. Convergently, in a study of secondary level psychiatric care patients, HRQoL, assessed by the 15D instrument, was found to be lowest in patients with depression relative to five common physical conditions (operative treatment of cataract, operative treatment of cervical or lumbar radicular pain, hysterectomy due to benign uterine conditions, hip or knee replacement surgery, coronary angiography due to suspected coronary artery disease) before elective treatment [14]. Thus, there is little doubt that HRQoL is impaired among individuals suffering from depression, irrespective of setting, and is typically worse than among subjects suffering from chronic physical diseases. However, the degree to which this is caused by depression or reflects clustering of disorders or adversity among individuals with depression remains less clear.

Although the epidemiological association between low HRQoL and depression is unequivocal, there are key areas of uncertainty that have major implications for health care. Establishing the precise relationship between severity, duration and unique course of depressive syndromes and HRQoL would help untangle the

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effects of depression, somatic illness and other psychosocial adversity linked to the condition. This would be especially important in focusing treatment and support in primary health and social care.

Depressive disorders are also known to be highly comorbid both in the general population [15,16] and primary care patients [17], so in theory, poor HRQoL may well be a result of multiple co-occurring syndromes rather than depression alone. In particular, anxiety disorders are known to affect HRQoL negatively [3,18]. Furthermore, many risk factors for depression, such as poor social support or stressful life conditions, may themselves predispose to poor HRQoL, but remain often partly or fully unmeasured in studies, and the association with depression could thus be partly a matter of co-occurrence rather than causal. However, current literature is largely unable to answer these questions.

Our aim was to investigate HRQoL and its predictors for change within a prospective Finnish cohort study of primary care patients with depressive disorders. We hypothesized that between-subject differences in HRQoL would correlate with severity and change of symptoms of depression and duration of depressive episodes as well as concurrent anxiety. Furthermore, we hypothesized that intraindividual change in HRQoL would be predicted by duration of depression and change in concurrent depressive and anxiety symptoms. We also explored the associations with other clinical and psychosocial factors. Furthermore, to determine whether remission from depression would normalize HRQoL, we compared HRQoL of depressive primary care patients with that of an age-standardized sample of the Finnish general population.

2. Methods

2.1. Patients and procedures of the Vantaa Primary Care Depression Study

The Vantaa Primary Care Depression Study (PC-VDS) was approved by the pertinent Ethics Committee in 2001. Details of methodology of the PC-VDS have been published elsewhere [17,19]. In brief, based on stratified sampling within the city of Vantaa, Finland, altogether 373 of 1119 general practitioners' patients aged 20–69 years screened with the Primary Care Evaluation of Mental Disorders (PRIME-MD) [20] had a positive screen for depression [17]. The presence of at least one core symptom of major depressive disorder (MDD) according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I/P) [21] was confirmed by telephone. All of the 175 potentially eligible patients were interviewed face-to-face using the SCID I/P with psychotic screen. Inclusion criteria were current: MDD, dysthymia, subsyndromal MDD with two to four depression symptoms (minimum one core symptom) and lifetime MDD and minor depression otherwise similar to subsyndromal MDD, but without MDD history. Patients who refused to participate (15%) did not differ significantly in age or gender from those who consented. The diagnostic reliability for current depressive disorder diagnoses was excellent (kappa = 1.0) [17].

The final study sample comprised 137 patients. Current and lifetime psychiatric disorders were assessed with SCID-I/P and SCID-II interviews [21,22]. In addition to the face-to-face interviews, observer- and self-report scales and all medical and psychiatric records were used to assess retrospective and prospective course of depression, comorbid disorders and psychosocial and socioeconomic factors [17]. Scales comprised Hamilton Rating Scale for Depression (HAMD) [23], Beck Depression Inventory (BDI) [24], Beck Anxiety Inventory (BAI) [25], Beck Hopelessness Scale (HS) [26], Social and Occupational Functioning Assessment Scale for DSM-IV (SOFAS) [27], Scale for Suicidal Ideation (SSI) [28] and Perceived Social Support Scale - Revised (PSSS-R) [29]. Personality was assessed by EPI-Q [30], a short measure based on Eysenck Personality Inventory, form B (EPI) [31].

After baseline, patients were prospectively investigated at 3, 6 and 18 months and 5 years [19]. The 5-year investigation included the same diagnostic interviews, scales and medical and psychiatric records as the baseline investigation. Timing and duration of episodes of depression and substance abuse were integrated into a graphic life-chart. The time after the baseline interview was divided into three categories: state of MDE (five or more of the nine criteria symptoms); partial remission (one to four symptoms); or full remission (no symptoms).

Drop-outs (18%) did not differ from participants in age, gender, baseline depression severity [19] or 15D score. At baseline, 88% (121/137) of all patients and 95% (106/111) of patients followed up for 5 years filled in the 15D questionnaire. Altogether 68% (93/137) of patients who had filled in the 15D questionnaire at both time points were included in the longitudinal regression analyses. Patient characteristics are shown in Table 1. The results are based on our whole sample of patients with depressive disorders.

2.2. Health-related quality of life

Health-related quality of life (HRQoL) was measured at baseline and at 5 years with a generic, self-report and preference-based HRQoL measure: the 15D, which can be used as a profile and a single index utility score measure. The 15D questionnaire is composed of 15 dimensions with five levels of severity: mobility, vision, hearing, breathing, sleeping, eating, speech (communication), excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity. The single index score (15D score), representing the overall HRQoL on a 0–1 scale (1 = full health, 0 = being dead), and the dimension level values, reflecting the goodness of the levels relative to no problems on the dimension (= 1) and to being dead (= 0), are calculated from the questionnaire by using a set of population-based preference or utility weights [32]. The minimum clinically important change or difference in the 15D score is $\pm$ 0.015 [33]. With regard to the important properties (reliability, validity, discriminatory power, responsiveness to change), the 15D performs at least equally to the other preference-based generic instruments [32,34–37]. At baseline, Cronbach's alpha coefficient for the 15D was 0.870.

2.3. National Health 2011 Survey

For purposes of this study, the 15D data of the general population came from the National Health 2011 Survey and represented the Finnish population aged 18 years and over [38]. For this analysis, individuals in the age range of the patients were selected (n = 3707). This sample was weighted to reflect the age distribution of the patients. The mean 15D scores and dimension level values (15D profiles) of our patients and of age-standardized population are shown in Table 2 and Fig. 1.

2.4. Statistical methods

Between-group comparisons were carried out using the Chi^2 test statistic with Yates' continuity correction or Fisher's exact test, the two-sample t-test or ANOVA, and the Mann–Whitney and Kruskal–Wallis tests as appropriate. Bivariate correlational analyses and linear regression models were used to analyse associations of different variables with HRQoL. In multivariate models, variables were included based on our hypotheses. The predetermined independent variables at baseline comprised HAMD (alternatively BDI), history of former MDE, BAI, HS, SSI, SOFAS, PSSS-R, EPI-Q, psychiatric and medical comorbidity, and marital, educational, occupational and economic status. In final

Table 1
Characteristics of patients in the Vantaa Primary Care Depression Study ($n = 93$).

Variable	At baseline		At five years		Change	
	n	%	*n*	%		
Socio-demographic features						
Male gender	19	20.4				
Cohabiting	48	51.6	46	49.5		
Employed	51	54.8	46	49.5		
Unemployed	17	18.3	10	10.8		
Professional education, any	60	64.5				
	Mean	SD	Mean	SD		
Age (years)	43.7	13.5				
	n	%	*n*	%		
Clinical features						
Anxiety disorder (any)	44	47.3	47	50.5		
Generalized anxiety disorder	14	15.1	14	15.1		
Panic disorder	6	6.5	9	9.7		
Social phobia	17	18.3	16	17.2		
Personality disorder	50	53.8	43	46.2		
Cluster B	28	30.1	24	25.8		
Cluster C	32	34.4	32	34.4		
Substance use disorder	12	12.9	9	9.7		
Physical illness interfered with everyday life	40	43.0	50	53.8		
	Mean	SD	Mean	SD	Mean	SD
Hamilton Rating Scale for Depression	16.3	5.6	11.4	7.9	−4.9	7.2
Beck Depression Inventory	19.3	10.3	14.6	11.0	−4.7	9.8
Time spent in MDE during follow-up (months)	–	–	21.0	22.4	–	–
Beck Anxiety Inventory	17.5	12.6	13.5	12.0	−4.0	12.7
Beck Hopelessness Scale	8.3	5.2	7.7	5.5	−0.5	4.7
Scale for Suicidal Ideation	2.9	5.8	1.9	4.7	−1.0	6.6
Perceived Social Support Scale - Revised	44.0	12.5	46.8	13.0	2.5	11.7
Functional and work ability						
Social and Occupational Functioning Assessment Scale	57.4	11.4	64.6	15.9	7.0	4.7
Off work due to depression during follow-up (months)	–	–	15.3	24.0	–	–
Personality						
Neuroticism	6.6	2.0	5.8	2.4		
Extraversion	4.1	2.0	3.5	2.4		
Health-related quality of life, 15D score	0.775	0.124	0.818	0.124	0.044	0.123
Mobility (Move)	0.939	0.124	0.924	0.142	−0.014	0.155
Vision (See)	0.952	0.115	0.916	0.162	−0.036	0.167
Hearing (Hear)	0.951	0.108	0.939	0.145	−0.012	0.132
Breathing (Breath)	0.809	0.247	0.877	0.188	0.068	0.230
Sleeping (Sleep)	0.637	0.257	0.724	0.226	0.087	0.233
Eating (Eat)	0.996	0.037	0.992	0.052	−0.004	0.064
Speech (Speech)	0.949	0.120	0.925	0.154	−0.025	0.169
Excretion (Excret)	0.779	0.195	0.820	0.197	0.041	0.237
Usual activities (Uact)	0.739	0.228	0.787	0.264	0.049	0.271
Mental Function (Mental)	0.685	0.226	0.747	0.247	0.062	0.278
Discomfort and symptoms (Disco)	0.629	0.260	0.684	0.239	0.055	0.248
Depression (Depr)	0.574	0.210	0.733	0.226	0.159	0.255
Distress (Distr)	0.616	0.228	0.716	0.241	0.100	0.239
Vitality (Vital)	0.576	0.223	0.689	0.219	0.113	0.247
Sexual activity (Sex)	0.720	0.262	0.735	0.294	0.015	0.341

models, the non-significant ($P > 0.05$) variables were omitted. All models were adjusted for age and gender, and when appropriate, also for follow-up time, severity of depression and duration of MDEs. To estimate the influence of current depressive state on the variance in the 15D score, we conducted separate sensitivity analyses of patient subgroups in full remission, in partial remission or in MDE at 5 years. Statistical package for the social sciences (SPSS Inc., USA), version 23, was used.

3. Results

3.1. Health-related quality of life among depressive primary care patients

The mean 15 score with its dimensions at baseline and at 5 years and the mean changes in the scores during the follow-up are shown in Table 1. The mean change of the 15D score was 0.044 (median 0.031, SD: 0.123, min −0.29, max 0.47). The 15D score deteriorated in 37% (34/93) and improved in 63% (59/93) of patients.

3.2. Cross-sectional associations between HRQoL and depressive and other symptoms and factors

At the time of the baseline interview, the 15D score was strongly associated with depression, anxiety and many other variables; correlations of all dimensions at baseline are presented in Table 3a. At the end of the five-year follow-up, the current severity of depression was very strongly associated with the 15D score irrespective of whether the correlation was with BDI ($r = -0.804$) or HAMD ($r = -0.764$) (Table 3b). The 15D score of patients in MDE was particularly low (mean 15D score: 0.679)

Table 2
Mean 15D scores, dimension level values and psychiatric symptom scores in full remission (FR), in partial remission (PR), and in major depressive episode (MDE) at five years in the Vantaa Primary Care Depression Study ($n = 106$).

	FR $n = 50$	PR $n = 35$	MDE $n = 21$	
	Mean	Mean	Mean	P
15D score	0.887	0.821	0.679	< 0.001
Mobility (Move)	0.943	0.928	0.854	0.053
Vision (See)	0.954	0.914	0.871	0.109
Hearing (Hear)	0.929	0.976	0.902	0.116
Breathing (Breath)	0.941	0.834	0.775	0.001
Sleeping (Sleep)	0.833	0.701	0.551	< 0.001
Eating (Eat)	0.986	1.000	1.000	0.326
Speech (Speech)	0.947	0.951	0.860	0.046
Excretion (Excret)	0.831	0.834	0.752	0.221
Usual activities (Uact)	0.892	0.786	0.533	< 0.001
Mental function (Mental)	0.852	0.743	0.581	< 0.001
Discomfort and symptoms (Disco)	0.761	0.702	0.498	< 0.001
Depression (Depr)	0.877	0.749	0.437	< 0.001
Distress (Distr)	0.836	0.744	0.482	< 0.001
Vitality (Vital)	0.823	0.670	0.445	< 0.001
Sexual activity (Sex)	0.814	0.792	0.576	0.003
Psychiatric symptoms				
Beck Depression Inventory	6.6	15.0	30.6	< 0.001
Hamilton Rating Scale for Depression	5.1	12.3	23.1	< 0.001
Beck Anxiety Inventory	6.7	13.7	27.3	< 0.001

ANOVA.

(Table 2). The mean 15D profiles differed significantly according to the current state of depression (full remission, partial remission or MDE) (Table 2). Only one of the 15 dimensions (eating) was not associated with depression (Tables 3a–c).

3.3. Baseline predictors for health-related quality of life at five-year follow-up among depressive primary care patients

Many variables predicted HRQoL after five years. In univariate linear regression, adjusted for age and gender, the following baseline variables were significant predictors for better HRQoL at 5 years: younger age ($P = 0.004$), higher professional education ($P < 0.001$), economic situation (not receiving welfare benefit, $P < 0.001$), non-smoking ($P = 0.010$), lower BDI ($P < 0.001$), HAMD ($P < 0.001$), BAI ($P < 0.001$), HS ($P = 0.007$) and SSI ($P = 0.020$), higher SOFAS ($P = 0.011$), less panic disorder ($P < 0.001$), somatoform disorder ($P = 0.017$), personality disorder cluster B ($P = 0.003$), borderline personality disorder ($P = 0.001$), substance use disorder ($P = 0.001$) and alcohol abuse or dependence ($P = 0.030$), and less neuroticism ($P = 0.001$).

However, not all of these variables were independent predictors of HRQoL. In the final multivariate analyses for HRQoL at 5 years (adjusted for age and gender), younger age (−0.003 [95% CI: −0.005–−0.002]; $P < 0.001$), higher professional education (0.076 [95% CI: 0.035–0.118]; $P < 0.001$), lower BDI (−0.003 [95% CI: −0.005–−0.001]; $P = 0.001$), less substance use (−0.063 [95% CI: −0.121–−0.001]; $P = 0.034$) and less panic disorder (−0.082 [95% CI: −0.163–−0.002]; $P = 0.044$) remained significant predictors of better HRQoL ($R^2 = 0.428$, adjusted $R^2 = 0.393$).

When time spent in MDEs during follow-up was included (adjusted for age, gender and follow-up time), significant predictors of better HRQoL were younger age (−0.003 [95% CI: −0.004–−0.001]; $P < 0.001$), less time spent in MDEs during follow-up (−0.003 [95% CI: −0.004–−0.002]; $P < 0.001$) and higher professional education (0.089 [95% CI: 0.053–0.125]; $P < 0.001$) ($R^2 = 0.514$, adjusted $R^2 = 0.495$). However, time spent in MDEs ($P = 0.272$) did not predict HRQoL, when adjusted for current BDI ($P < 0.001$) or current HAMD ($P < 0.001$).

3.4. Predictors for change in health-related quality of life during the five-year follow-up among depressive primary care patients

Significant bivariate correlations between changes in the 15D variables and changes in other variables during the five-year follow-up are presented in Table 3c.

In univariate linear regression, significant predictors of an improvement in HRQoL were a decrease in the HAMD, BDI, BAI, HS and SSI scores. Time spent in MDEs during follow-up was not associated with an improvement in HRQoL. In multivariate linear regression analyses, only a decrease in the BDI and BAI scores remained significant predictors of an improvement in HRQoL (Table 4).

3.5. Health-related quality of life of depressive primary care patients vs the general population

At the end of the 5-year follow-up, the mean 15D scores and profiles of patients in MDD and partial or full remission, compared with an age-standardized sample of the general population, are presented in Fig. 1. HRQoL of depressive primary care patients differed from that of the general population even among patients reaching full clinical remission, and all but one dimension of the 15D (eating) differed significantly from the general population.

We conducted a further analysis of the role of mild residual symptoms among clinically remitted patients. In a multivariate regression analysis within this population, the variation in BDI (−0.004 [95% CI: −0.007–−0.001]; $P = 0.014$) and BAI (−0.003 [95%

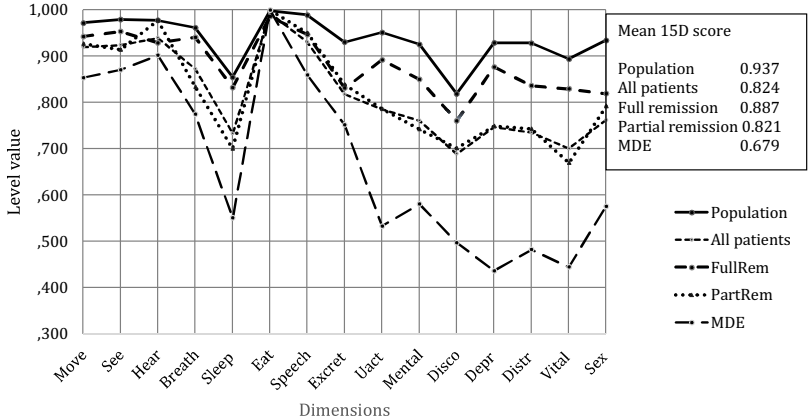

Fig. 1. Mean 15D profiles and 15D scores of all Vantaa Primary Care Depression Study patients (All patients, $n = 106$) and separately for patients in full remission (FullRem, $n = 50$), in partial remission (PartRem, $n = 35$) and in MDE (MDE, $n = 21$) at five years, and those of an age-standardized sample of the general population (Population).

Table 3a
Significant bivariate Pearson correlations of the 15D variables and other variables at baseline in the Vantaa Primary Care Depression Study ($n = 121$).

	15D score	Move	See	Hear	Breath	Sleep	Eat	Speech	Excret	Uact	Mental	Disco	Depr	Distr	Vital	Sex
Beck Depression Inventory	−0.644**	0.226*	0.214*		0.385**	0.345**				0.454**	0.523**	0.519**	0.692**	0.617**	0.632**	0.497**
Hamilton Rating Scale for Depression	−0.576**		0.280**		0.298**	0.479**				0.401**	0.442**	0.510**	0.564**	0.475**	0.581**	0.509**
Beck Anxiety Inventory	−0.751**	0.294**	0.234**	0.200*	0.585**	0.494**		0.285**	0.342**	0.462**	0.619**	0.622**	0.570**	0.661**	0.605**	0.477**
Beck Hopelessness Scale	−0.487**	0.216*			0.376**	0.252**	0.184*		0.180*	0.217*	0.423**	0.328**	0.523**	0.384**	0.476**	0.370**
Scale for Suicidal Ideation	−0.294**									0.241**	0.319**	–	0.461**	0.291**	0.427**	0.219**
Social and Occupational Functioning Assessment Scale	0.447**	−0.297**	−0.255**		−0.269**	−0.192*		−0.183*	−0.217*	−0.284**	−0.377**	−0.408*	−0.394**	−0.263**	−0.299**	−0.430**
Perceived Social Support Scale-R	−0.340**		−0.208*		0.327**						−0.336**	−0.211**	−0.323**	−0.222*	−0.294**	−0.221*
Anxiety disorder, any	−0.248**										0.209*	0.185*	0.233*	0.285**	0.210*	
Substance use disorder	−0.375**		0.271**		0.369**				0.225*	0.343*	0.330**	0.234**	0.295**	0.255**	0.322**	0.210*

* $P < 0.050$.
** $P < 0.010$

Table 3b
Significant Pearson bivariate correlations between the 15D variables and other variables in the Vantaa Primary Care Depression Study at five years ($n = 106$).

	15D score	Move	See	Hear	Breath	Sleep	Eat	Speech	Excret	Uact	Mental	Disco	Depr	Distr	Vital	Sex
15D	1	0.486**	0.531**	0.327**	0.623**	0.632**		0.445**	0.478**	0.721**	0.687**	0.700**	0.746**	0.714**	0.789**	0.610**
Beck Depression Inventory	−0.804**	−0.263**	−0.397**		−0.442**	−0.547**		−0.275**	−0.351**	−0.548**	−0.533**	−0.524**	−0.851**	−0.707**	−0.773**	−0.492**
Hamilton Rating Scale for Depression	−0.764**	−0.276**	−0.330**		−0.403**	−0.571**		−0.267**	−0.270**	−0.537**	−0.524**	−0.524**	−0.763**	−0.604**	−0.759**	−0.456**
Beck Anxiety Inventory	−0.718**	−0.276**	−0.407**		−0.345**	−0.470**		−0.216*	−0.481**	−0.430**	−0.522**	−0.559**	−0.656**	−0.705**	−0.636**	−0.344**
Beck Hopelessness Scale	−0.537**				−0.303**	−0.385**		–	−0.267**	−0.356**	−0.356**	−0.334**	−0.709**	−0.609**	−0.553**	−0.343**
Scale for Suicidal Ideation	−0.417**		−0.199*	−0.237*	−0.196*	−0.311**		−0.213**	−0.262**	–	−0.246*	−0.219*	−0.495**	−0.410**	−0.414**	−0.304**
Social and Occupational Functioning Assessment Scale	0.638**	0.294**	0.274**		0.361**	0.347**			0.271**	0.563**	0.484**	0.408**	0.531**	0.414**	0.592**	0.453**
Perceived Social Support Scale-R	0.408**				0.222*	0.345**			0.343**	−0.260**	0.278**	0.204*	0.445**	0.496**	0.298**	0.275**
Anxiety disorder, any	−0.315**		−0.279**		−0.209*	−0.217*		−0.330**		−0.210*	−0.264**		−0.360**	−0.365**	−0.266**	
Generalized anxiety disorder	−0.213*									−0.193*		−0.201*	−0.248*	−0.237*	−0.318**	
Panic disorder				−0.334**									−0.194*	−0.299**		
Social phobia	−0.199*							−0.291**	−0.259**					−0.243*		
Substance use disorder	−0.300**				−0.207*			−0.219*		−0.245*	−0.281**		−0.351**	−0.355**	−0.228*	
Alcohol Use Disorders Identification Test	−0.218*									−0.255**				−0.325**		
Time spent in Major Depressive Episodes BL-5y	−0.585**	−0.276**		−0.200*	−0.278**	−0.379**		−0.199*		−0.556**	−0.369**	−0.314**	−0.595**	−0.535**	−0.472**	−0.445**
Time spent unable to work due to depression BL-5y	−0.197*							−0.220*			−0.263**		−0.223*	−0.217*		
Duration of sick leaves due to depression BL-5y	−0.364**		−0.279*			−0.339**				−0.398**	−0.290*		−0.300*		−0.271*	−0.410**
Disability pension due to depression	−0.328**	−0.201*		−0.318**				−0.251**	−0.270**	−0.276**	−0.263**		−0.242*			−0.376**

BL-5y: during the five-year follow-up.
* $P < 0.050$.
** $P < 0.010$.

Table 3c
Significant bivariate Pearson correlations between changes in the 15D variables and changes in other variables during the five-year follow-up in the Vantaa Primary Care Depression Study ($n = 93$).

	15D score	Move	See	Hear	Breath	Sleep	Eat	Speech	Excret	Uact	Mental	Disco	Depr	Distr	Vital	Sex
Beck Depression Inventory	−.624**		−.389**		−.343**	−.317**				−.354**	−.457**	−.299**	−.609**	−.561**	−.513**	−.514**
Hamilton Rating Scale for Depression	−.415**		−.320**			−.337**				−.286**	−.319**		−.386**	−.252**	−.432**	−.327**
Beck Anxiety Inventory	−.610**	−.279**	−.424**		−.304**	−.399**				−.308**	−.493**	−.458**	−.401**	−.436**	−.538**	−.300**
Beck Hopelessness Scale	−.452**		−.227*			−.343**				−.247*	−.311**		−.447**	−.434**	−.462**	−.295**
Scale for Suicidal Ideation	−.289**										−.224*		−.467**	−.271**	−.315**	−.293**
Social and Occupational Functioning Assessment Scale	.375**		.308**							.317**	.406**		.254*	.268**	.269**	.326**
Perceived Social Support Scale R	.289**							.237*			.235*	.252*	.239*	.286*	.282**	.291**

* $P < 0.050$.
** $P < 0.010$.

Table 4
Multivariate linear regression for the change in health-related quality of life (change in 15D score) during follow-up in the Vantaa Primary Care Depression Study ($n = 93$).

	B	95% CI	P
Age	−0.001	−0.002–0.000	0.160
Gender	−0.020	−0.067–0.026	0.382
Beck Depression Inventory, change	−0.005	−0.007–−0.003	< 0.001
Beck Anxiety Inventory, change	−0.004	−0.006–−0.002	< 0.001

$R^2 = 0.513$, adjusted $R^2 = 0.491$.

CI: −0.005–0.000]; $P = 0.022$) significantly predicted HRQoL. Among remitted patients (50/106) whose BDI and BAI scores were < 6 (26%, 13/50), HRQoL reached the level of general population scores (0.929); if both BDI and BAI scores were < 5 (16%, 8/50), HRQoL was very good (0.991).

4. Discussion

The HRQoL, measured by the 15D score, and almost all of the dimension values were strongly related to the current severity of depression in depressive primary care patients. The mean HRQoL was particularly low among patients in MDE at the end of follow-up, but even in clinically remitted patients it did not reach the mean population score, unless the patients were virtually free of residual symptoms of depression and anxiety. The adverse influences of comorbid disorders, particularly anxiety but also substance use, were significant. In addition, socio-demographic factors, such as education, affect the HRQoL of patients with depression.

This study has several major strengths. These include a screened medium-sized cohort of depressive patients derived from a stratified sampling of 1119 primary health attenders, structured interviews with SCID-I/*P* and SCID-II by psychiatrists and a longitudinal study design with a five-year follow-up and a small drop-out rate. The life chart methodology enabled evaluation of the longitudinal course of illness and time-related psychosocial factors. Depressive disorders in this primary care cohort were typically MDD of mild to moderate severity, usually recurrent or chronic in nature [17,19]. Comprehensive clinical interviews allowed us to analyse the influence of clinical symptoms and other characteristics on HRQoL; use of life charts enabled measurement of the time spent in different states of depression during the preceding five years. In addition, we carefully evaluated the presence of psychiatric comorbidity [17]. A major strength of the study was also that the HRQoL of patients could be compared with that of a representative and age-standardized sample of the Finnish general population from the Health 2011 Study.

The findings should, however, be interpreted in light of some methodological limitations. First, the sampling of the cohort was based on stratified screening of depression to ensure representativeness [17]. However, inclusion of consecutive patients with depressive disorders unavoidably enriches chronicity, as longer duration of depression increases the probability of becoming recruited. Nevertheless, the sample accurately reflects characteristics of actual patients and the actual workload of physicians. Second, despite the moderate sample size, the number of patients in some subgroups remained small, thus increasing risk of type II errors. Third, the study was naturalistic and the treatment received was not controlled. Fourth, generalizability of our findings remains uncertain. Our study sample comprised urban and suburban primary care patients, while the general population sample was collected from the whole country. Finally, we investigated HRQoL by using the 15D. Given consistency of findings between different measures of HRQoL (Hawthorne et al., 2001; Mihalopoulos et al., 2014), we expect our findings to be representative rather than specific to the instrument used, but this remains to be verified.

Among our depressive primary care patients, HRQoL correlated strongly with current severity of depressive symptoms. Two-thirds of patients experienced an improvement in HRQoL during follow-up. However, one-third of patients showed a deterioration in HRQoL. This reflects the rather chronic and recurrent tendency of depression among primary care patients. The HRQoL of our patients in MDE at the end of follow-up was even worse than the HRQoL of depressive patients in secondary care [14]. The change in HRQoL during follow-up correlated strongly with changes in the severity of depression and anxiety. These findings are consistent with our hypothesis and also in accordance with earlier literature [7,8,11,13]. Only few studies have taken into account the duration of time spent in MDEs. We found HRQoL to be moderately related to the time spent in depressive episodes during the preceding five years. Thus, the most consistent relationship was between HRQoL and current symptoms. The mean 15D score in remitted patients approached, but did not quite reach the mean population score, unless clinical remission was complete [3]. Within the remitted subgroup, severity of the remaining mild residual symptoms of depression was more strongly associated with HRQoL than the duration of depression. Besides depression, severity of anxiety symptoms was a significant explanatory factor. These findings are highly relevant for clinical definitions of remission from depression [39,40], as it appears that patients must be virtually free of residual symptoms for their HRQoL to normalize.

We set out to investigate whether the presence of psychiatric comorbidity significantly influences HRQoL among patients with depression and found that it does. Especially concurrent anxiety was associated with poor HRQoL; the former result is consistent with epidemiological findings pertaining to the adverse influence of anxiety disorders on HRQoL [3,18]. This is of both theoretical and practical significance, as individuals suffering from depressive disorder both in the general population [15,16] and in primary care

commonly suffer from concurrent psychiatric disorders and somatic illnesses [17]. This clustering of illnesses and syndromes needs to be elucidated in future studies. Furthermore, it appears that remission of not only depression but also anxiety symptoms is a precondition for HRQol to normalize in primary care patients with depressive disorders. Finally, besides psychiatric symptoms, other factors may affect HRQoL. Of the socio-demographic factors explored, completed professional education was a significant predictor of better HRQoL.

The 15D instrument showed a good responsiveness to change in depression. BDI was a better predictor of HRQoL than HAMD, in line with our earlier findings [19]. The subjective measurement scales 15D and BDI both seem to perform well as prognostic instruments. BDI is easiest to use in everyday busy primary care practice, whereas 15D is useful also in patient groups beyond of psychiatric illnesses. Apart from one dimension (i.e. eating), all dimensions of the 15D were negatively affected by depression. Thus, the effects of depression are wide-ranging. As a generic instrument, the 15D with its dimensions is valuable in studying the health problems, psychiatric and physical, caused by various diseases. This emphasizes the importance of the profile property of the 15D.

In conclusion, among depressive primary care patients, the relationships between depression and concurrent anxiety and HRQoL, measured by the 15D, were strong, even in primary care. For HRQoL to normalize in clinical remission from depression, virtually all symptoms of depression or anxiety must be absent.

Disclosure of interest

H. Sintonen is the developer of the 15D instrument and obtains royalties from its electronic versions.

K. Riihimäki, M. Vuorilehto, P. Jylhä, S. Saarni, E. Isometsä declare that they have no competing interest.

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References

[1] Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. Lancet 2012;380(9859):2197–223.
[2] Wells KB, Sherbourne CD. Functioning and utility for current health of patients with depression or chronic medical conditions in managed, primary care practices. Arch Gen Psychiatry 1999;56(10):897–904.
[3] Saarni SI, Harkanen T, Sintonen H, Suvisaari J, Koskinen S, Aromaa A, et al. The impact of 29 chronic conditions on health-related quality of life: a general population survey in finland using 15D and EQ-5D. Qual Life Res 2006;15(8):1403–14.
[4] Sullivan PW, Lawrence WF, Ghushchyan V. A national catalog of preference-based scores for chronic conditions in the united states. Med Care 2005;43(7):736–49.
[5] Burstrom K, Johannesson M, Diderichsen F. Health-related quality of life by disease and socio-economic group in the general population in sweden. Health Policy 2001;55(1):51–69.
[6] Burstrom K, Johannesson M, Diderichsen F. Swedish population health-related quality of life results using the EQ-5D. Qual Life Res 2001;10(7):621–35.
[7] Andriopoulos P, Lotti-Lykousa M, Pappa E, Papadopoulos AA, Niakas D. Depression, quality of life and primary care: a cross-sectional study. J Epidemiol Glob Health 2013;3(4):245–52.
[8] Brenes GA. Anxiety, depression, and quality of life in primary care patients. Prim Care Companion J Clin Psychiatry 2007;9(6):437–43.
[9] Cerne A, Rifel J, Rotar-Pavlic D, Svab I, Selic P, Kersnik J. Quality of life in patients with depression, panic syndrome, other anxiety syndrome, alcoholism and chronic somatic diseases: A longitudinal study in Slovenian primary care patients. Wien Klin Wochenschr 2013;125(1–2):1–7.
[10] Garcia-Campayo J, Ayuso-Mateos JL, Caballero L, Romera I, Aragones E, Rodriguez-Artalejo F, et al. Relationship of somatic symptoms with depression severity, quality of life, and health resources utilization in patients with major depressive disorder seeking primary health care in Spain. Prim Care Companion J Clin Psychiatry 2008;10(5):355–62.
[11] Sobocki P, Ekman M, Agren H, Krakau I, Runeson B, Martensson B, et al. Health-related quality of life measured with EQ-5D in patients treated for depression in primary care. Value Health 2007;10(2):153–60.
[12] Vetter ML, Wadden TA, Lavenberg J, Moore RH, Volger S, Perez JL, et al. Relation of health-related quality of life to metabolic syndrome, obesity, depression and comorbid illnesses. Int J Obes (Lond) 2011;35(8):1087–94.
[13] Lima AF, Fleck MP. Quality of life, diagnosis, and treatment of patients with major depression: a prospective cohort study in primary care. Rev Bras Psiquiatr 2011;33(3):245–51.
[14] Suominen K, Karlsson H, Rissanen A, Valtonen HM, Rasanen P, Sintonen H, et al. Perceived burden of illness in patients entering for treatment in a university hospital–is the threshold to secondary care higher for patients with depression than for those with somatic disorders? Eur Psychiatry 2011;26(7):441–5.
[15] Gadermann AM, Alonso J, Vilagut G, Zaslavsky AM, Kessler RC. Comorbidity and disease burden in the national comorbidity survey replication (NCS-R). Depress Anxiety 2012;29(9):797–806.
[16] Pirkola SP, Isometsa E, Suvisaari J, Aro H, Joukamaa M, Poikolainen K, et al. DSM-IV mood-, anxiety- and alcohol use disorders and their comorbidity in the finnish general population–results from the health 2000 study. Soc Psychiatry Psychiatr Epidemiol 2005;40(1):1–10.
[17] Vuorilehto M, Melartin T, Isometsa E. Depressive disorders in primary care: recurrent, chronic, and co-morbid. Psychol Med 2005;35(5):673–82.
[18] Saarni SI, Suvisaari J, Sintonen H, Pirkola S, Koskinen S, Aromaa A, et al. Impact of psychiatric disorders on health-related quality of life: general population survey. Br J Psychiatry 2007;190:326–32.
[19] Riihimaki KA, Vuorilehto MS, Melartin TK, Isometsa ET. Five-year outcome of major depressive disorder in primary health care. Psychol Med 2011;1–11.
[20] Spitzer RL, Williams JB, Kroenke K, Linzer M, deGruy 3rd FV, Hahn SR, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. JAMA 1994;272(22):1749–56.
[21] First MB, Spitzer RL, Gibbon M, Williams JBW, editors. Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition with psychotic screen. New York: New York State Psychiatric Institute; 2002.
[22] First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS, editors. Structured clinical interview for DSM-IV axis II personality disorders (SCID-II). Washington D.C.: American Psychiatric Press, Inc.; 1997.
[23] Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62.
[24] Beck AT, Ward C, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–71.
[25] Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988;56(6):893–7.
[26] Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: The hopelessness scale. J Consult Clin Psychol 1974;42(6):861–5.
[27] Goldman HH, Skodol AE, Lave TR. Revising axis V for DSM-IV: A review of measures of social functioning. Am J Psychiatry 1992;149(9):1148–56.
[28] Beck AT, Kovacs M, Weissman A. Assesment of suicidal intention: the scale for suicide ideation. J Consult Clin Psychol 1979;47:343–52.
[29] Blumenthal JA, Burg MM, Barefoot J, Williams RB, Haney T, Zimet G. Social support, type A behavior, and coronary artery disease. Psychosom Med 1987;49(4):331–40.
[30] Floderus B. Psychosocial factors in relation to coronary heart disease and associated risk factors. Nordisk Hygienisk Tidskrift 1974;l6:1–148.
[31] Eysenck H, Eysenck S. Manual of the Eysenck personality inventory. London: University of London Press Ltd; 1964.
[32] Sintonen H. The 15D instrument of health-related quality of life: properties and applications. Ann Med 2001;33(5):328–36.
[33] Alanne S, Roine RP, Räsänen P, Vainiola T, Sintonen H. Estimating the minimum important change in the 15D scores. Qual Life Res 2015;24(3):599–606.
[34] Hawthorne G, Richardson J, Day NA. A comparison of the assessment of quality of life (AQoL) with four other generic utility instruments. Ann Med 2001;33(5):358–70.
[35] Moock J, Kohlmann T. Comparing preference-based quality-of-life measures: results from rehabilitation patients with musculoskeletal, cardiovascular, or psychosomatic disorders. Qual Life Res 2008;17(3):485–95.
[36] Stavem K. Reliability, validity and responsiveness of two multiattribute utility measures in patients with chronic obstructive pulmonary disease. Qual Life Res 1999;8(1–2):45–54.
[37] Mihalopoulos C, Chen G, Iezzi A, Khan MA, Richardson J. Assessing outcomes for cost-utility analysis in depression: comparison of five multi-attribute utility instruments with two depression-specific outcome measures. Br J Psychiatry 2014;205(5):390–7.
[38] Koskinen S, Lundqvist A, Ristiluoma N. Health, functional capacity and welfare in Finland in 2011. Helsinki: National Institute for Health and Welfare (THL); 2012 [report 68/2012, http://urn.fi/URN:ISBN:978-952-245-769-1. 2012].
[39] Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder, remission, recovery, relapse, and recurrence. Arch Gen Psychiatry 1991;48(9):851–5.
[40] Keller MB. Past, present, and future directions for defining optimal treatment outcome in depression: remission and beyond. JAMA 2003;289(23):3152–60.