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Research Paper

Health-related quality of life in hospitalized non-psychiatric medical patients: The impact of depressive symptoms

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1. Introduction

In recent years, the concept of quality of life (QoL) gained importance in mental health clinical research and patient care. This concept aims to understand the patient's perspective of their functioning, in contrast to the classic medical evaluation of symptom levels and mortality rates (Berlim and Fleck, 2003). The World Health Organization (WHO) defines QoL as *the individual's perception of his or her position in life, within the cultural context and value system he or she lives in, and in relation to his or her goals, expectations, parameters, and social relations. It is a broad-ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment* (1995).

Health-related quality of life (HRQoL) differentiates itself from QoL in that it directly targets health matters. Specifically, HRQoL is determined by the patient's perception of their state of mental and physical health (Gigantesco and Giuliani, 2011). Therefore, understanding a patient's HRQoL helps shed light on their health perception while undergoing specific treatment or adapting to their condition in their daily context.

Different generic instruments are used to measure HRQoL; among the most used are the 36-Item Short-Form Health Survey (SF-36) and its short version, the 12-Item Short-Form Health Survey (SF-12). The SF-12 is a multipurpose short-form generic assessment of health status that measures eight concepts, commonly represented in widely-used surveys: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and mental health (psychological distress and psychological wellbeing) (Ware et al., 1994). For its brevity, SF12 is a practical alternative for everyday practice and conserved the psychometric properties of the SF36 (Hurst et al., 1998).

Several studies observed that the HRQoL is impaired in different non-psychiatric medical diseases like chronic obstructive pulmonary disease (Hurst et al., 2020), heart failure (Moradi et al., 2020), arthritis (Zhang et al., 2020), and cancer (Firkins et al., 2020) to mention some. Nowadays, HRQoL is also used as an independent outcome to target different interventions (Coens et al., 2020). However, few studies systematically explore the HRQoL as a transdiagnostic approach, applicable to everyday practice in a real-world setting as it was done in the present study. Depression is a highly prevalent and disabling condition among the general population (Daray et al., 2017; Marcus et al., 2012; Vos et al., 2015). Its prevalence is even higher among non-psychiatric medical illnesses patients (Katon and Ciechanowski, 2002; Katon, 2011; Olver and Hopwood, 2013; Yanzon de la Torre et al., 2016). Almost one out of four patients hospitalized for a non-psychiatric medical condition has a comorbid major depressive episode (MDE) with a much higher prevalence of subsyndromal depressive symptoms (Yanzon de la Torre et al., 2016). Depression in the context of a non-psychiatric medical illness worsens the prognosis (Ludman et al., 2004), increases symptom burden (Gureje et al., 2001; Katon et al., 2007, 2001), complicates self-care and treatment-adherence (Ciechanowski et al., 2000; DiMatteo et al., 2000; Lin et al., 2004), and increases hospitalization time (Saravay et al., 1991), costs of care, and mortality (Ciechanowski et al., 2000; Katon et al., 2003; Sullivan et al., 2002; Unutzer et al., 1997). Despite this, the impact of depression on the HRQoL in a real-world scenario is not entirely understood.

The present study systematically explored the HRQoL in hospitalized non-psychiatric medical patients as a transdiagnostic approach, applicable to everyday practice in a real-world setting of metropolitan public hospitals in a country of South America and assessing the impact of different predictors on this construct, especially depressive symptoms.

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2. Methods

2.1. Study design

This is a secondary analysis of a multicentric, observational and cross-sectional study involving three facilities in Buenos Aires, Argentina: *Bernardo Houssay* Hospital in the Vicente Lopez district, *Eva Perón* Hospital in the San Martín district, and *Bernardino Rivadavia* Hospital in the Autonomous City district. These are general hospitals located in the metropolitan area of Buenos Aires, which has a 12.8 million population and mainly serves low-income patients without health insurance. The study complies with the Declaration of Helsinki. The study protocol was approved by IRBs in all participating Hospitals (approval ID # 20/14), and written informed consent was obtained from all study participants.

2.2. Participants

To have heterogeneity of medical conditions as in the real world, a sampled all consecutive patients hospitalized in these General Hospitals for any non-psychiatric medical illness over six months was obtained. Participants were adult inpatients with at least one primary medical diagnosis, according to the ICD-10 classification. The following categories of physical diseases were included in the sample: infectious (22.0%), neurological (17.0%), metabolic (12.9%), pulmonary (11.1%), cardiovascular (10.4%) neoplastic (9.13%), urological (9.13%), gastrointestinal (7.46%) and hematological (4.56%). Included subjects were native Spanish speakers aged $\geq$ 18 years. Subjects were excluded if they were: [a] unable to participate in clinical assessments or to complete symptom-ratings because of illness, medication, sensory or speech impairment, or lack of language fluency, or [b] scored $<$ 25 on a preliminary Mini-Mental State Examination (MMSE) suggesting dementia or delirium.

2.3. Procedure

Participants were interviewed on days 2–6 after admission and assessed by a psychiatrist or psychiatric resident. Each participant went through the administration of the Hospital Anxiety and Depression Scale (HADS) and the SF-12 on a random sequence to limit re-test artifacts. Then the investigator collected demographic and clinical data. The disease was obtained from the medical chart and classified according to the ICD-10. Since we could not find a definition that allows us to operationalize the course of the disease for all the clinical conditions included in this study, we have decided to operationalize the disease course into acute or chronic, depending on whether or not the patient had been diagnosed the month before the current hospitalization. The presence of hypertension and diabetes was acquired from the medical chart; in case of having one or the other, the patient was classified as having medical comorbidity. These comorbidities were used since both are systematically explored and recorded in the medical charts of all hospitalized patients in the three recruitment centers regardless of their medical illness.

2.4. Assessment tools

The HADS is a self-rated depression questionnaire designed to measure depressive and anxiety symptoms, especially in patients with physical illness. This instrument excludes somatic symptoms that may overlap with psychological/cognitive symptoms. The HADS contains two subscales measuring symptoms of depression (HADS-D) and anxiety (HADS-A) during the previous week. Each subscale includes seven statements, and each response consists of a four-point rating scale (0 to 3); a higher score indicates a worse condition (Herrero et al., 2003; Zigmond and Snaith, 1983). This questionnaire has been validated (Gercovich et al., 2009) and calibrated (Daray et al., 2019) in Argentina. In the present, study depressive symptoms were assessed with the HADS-D subscale.

HRQoL was evaluated with the SF-12. It is psychometrically comprehensive, reliable, and precise in its estimates as the SF-36 (Augustovski et al., 2008; Sanderson and Andrews, 2002). The measure was made of two components, a physical component score (PCS) and a mental component score (MCS). Thus, higher scores of the SF-12 indicate greater mental or physical HRQoL.

2.5. Statistical analyses

Categorical measures were reported as frequencies or percentages; continuous measures were reported as mean $\pm$ standard deviation (SD). The ANOVA was used to evaluate the association between HRQoL scales and categorical variables, while Spearman's correlation was used to explore the association between HRQoL scales and continuous variables. In all cases, an initial significance level of 0.05 was considered, which was corrected according to the Bonferroni criterion concerning the number of hypothesis tests performed in each analysis.

Ordinary least square (OLS) regression analysis was conducted to examine whether HRQoL scales were associated with depressive symptoms (HADS-D score), adjusting for variables identified in the preliminary bivariate comparisons, those clinically relevant, and sex and age. Independent variables were manually included from the most significant to the least significant. Beta (β) coefficients and p-values from linear regression modeling were reported, with significance evaluated using a *t*-test. Statistical significance was set at two-tailed $p < 0.05$. OLS assumptions were tested, and a robust analysis was performed to adjust our model to account for heteroskedasticity. To check for outliers, we use the added-variable plots. A few numbers of patients that showed very low or high HRQoL for the severity of depressive symptoms reported; however, no observations were removed. Shapiro-Wilk test for normality and graphical tests were conducted to test the hypothesis that the residuals follow a normal distribution.

All analyses were carried out using the Microsoft Windows® versions v.25 of both IBM SPSS Statistics®.

3. Results

A total of 754 participants were screened consecutively, and 343 were classified as potentially eligible (Fig. 1). From these, 33 refused to consent, and forty-nine additional participants were excluded due to incomplete outcome data, leaving a total of 257 participants for analysis. Table 1 shows the demographic and clinical data of the study population. The sample included 152 (59.1%) men and 105 (40.9%) women, and the average age was 54.15 $\pm$ 16.57 years. The mean value of the HADS-D subscale was 5.46 $\pm$ 4.09 and for the HADS-A was 6.85 $\pm$ 4.42. The other demographic and clinical variables are described in Table 1.

As shown in Table 2, the presence of medical comorbidities ($p <$ 0.001) was associated with lower scores of the PCS derived from the SF-12. Moreover, there was a negative correlation between the PCS of the SF-12 and the age of the participant (Spearman's $\rho = -0.22$, $p <$ 0.0001), and the severity of depressive symptoms (Spearman's $\rho = -0.28$, $p < 0.0001$, Table 3). On the other hand, having a history of psychiatric treatment ($p < 0.001$), the severity of depressive symptoms (Spearman's $\rho = -0.67, p < 0.0001$) and anxiety symptoms (Spearman's $\rho = -0.61, p < 0.0001$), were associated with lower scores of the MCS of the SF-12 scale (Tables 2 and 3).

Multivariate linear regression was used to assess the predictive variables of the PCS and MCS domains of the SF-12 (Table 4). Those variables found statistically significant in our previous analysis, together with clinically relevant variables and age and sex, were included in the regression model. The severity of depressive symptoms ($\beta = -0.65$; $p <$ 0.001) and the age of the participant ($\beta = -0.14$; $p < 0.001$) were significant predictors of the PCS component of SF-12. The model explains

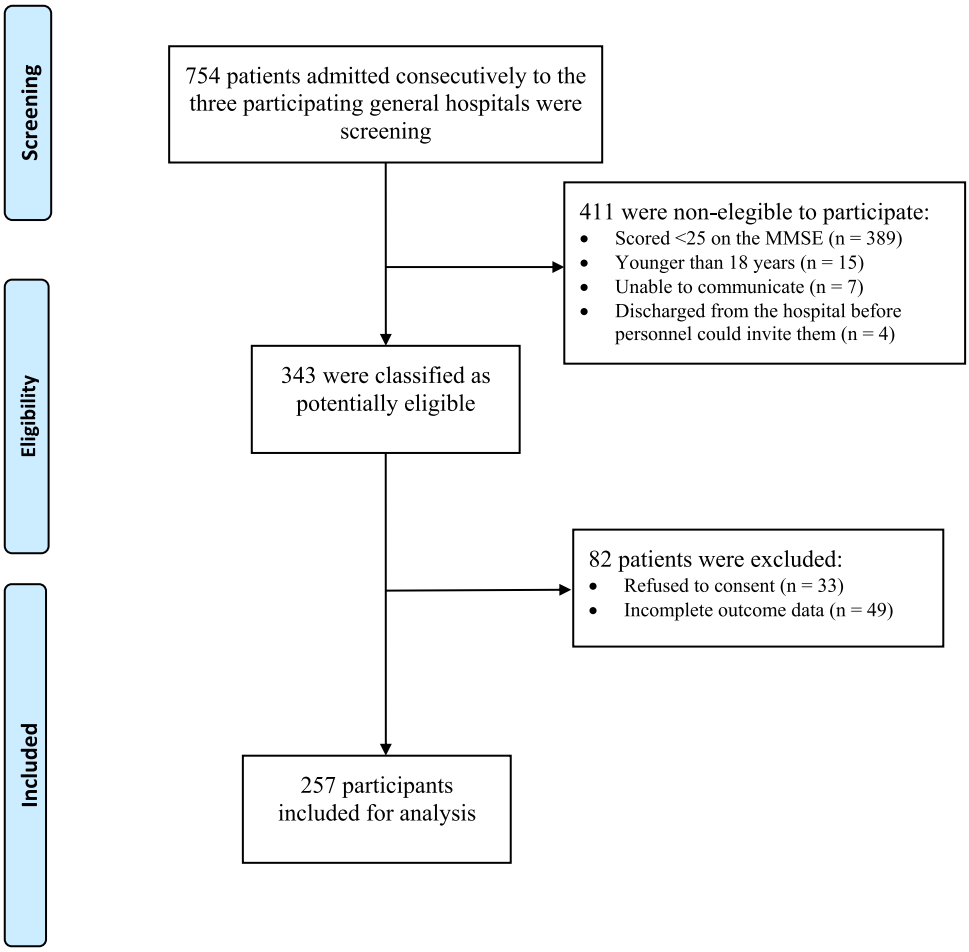

Fig. 1. Flow chart.

16% of the overall variance (Table 4). The severity of depressive symptoms ($\beta = -1.80$; $p < 0.001$) was the only variable that remains significantly associated with the MCS component of SF-12 and explains 38% of the variance.

4. Discussion

The present study shows that the HRQoL in hospitalized non-psychiatric medical patients is lower than that reported in the general population. Furthermore, it was observed that depressive symptoms impair not only the mental domain of HRQoL but also the physical domain. Finally, being older is also associated with lower levels of the physical composite of the HRQoL.

The assessment of HRQoL has become an essential element in the comprehensive care of patients. As a result, several generic HRQoL instruments have been developed to apply across a wide range of populations and interventions (Coons et al., 2000). The SF-36 health survey is one of the most commonly used questionaries, and the SF-12 is the abridged practical version. Herein the two primary SF-12 scales (i.e., PCS and MCS) were examined instead of the eight scales because summary scores facilitated hypothesis testing and reduced the risk associated with multiple statistical comparisons between scales or significant findings arising by chance. Also, the interpretation of scores obtained by the two major scales of the SF-12 is possible via comparison with population norms (Hurst et al., 1998). In the present study, it was observed that hospitalized non-psychiatric medical patients reported a mean value of 32.76 and 47.83 for the PCS and MCS, respectively. These values are lower in comparison with those observed, with the same questionnaire, in a previous study in the general population of Argentina (49.3 and 51.8 for the PCS and MCS, respectively) (Daray et al., 2017). Although this is an expected finding since prior studies in patients with different medical conditions reported lower levels of HRQoL, our study has an original approach since HRQoL was systematically evaluated in all consecutive patients admitted to a hospital, regardless of the diagnosis (a "transnosographic approach") and provides new information from public hospitals of a metropolitan area in a country of South America, usually an underrepresented sample in the literature. Additionally, these data has great value since it was collected in hospitalized patients before the onset of the SARS-CoV-2 (COVID-19) pandemic and can be useful for future studies on HRQoL of patients hospitalized for COVID-19 .

The study aims to analyze which factors are associated with the low HRQoL in this group of patients. The association between physical illness and depressive symptoms has been explored for the high frequency of this comorbidity (Yanzon de la Torre et al., 2016) and because of some potential common pathophysiological mechanisms underlying this comorbidity (Rosenblat et al., 2020). This bidirectional relationship is explained by several pathophysiological mechanisms, including the inflammation caused by some non-psychiatric medical diseases that can cause an increase in pro-inflammatory cytokines such as IL-6, which cross the blood-brain barrier and modulate serotonergic or adrenergic neurotransmission (Liu et al., 2019). Also, some lifestyle risks, including physical inactivity, smoking, and poor diet, can explain this high comorbidity (Thom et al., 2019). Others have proposed that psychosocial factors associated with depression that are common to many chronic medical illnesses include physical limitations, disability, role transitions, and loss of independence/autonomy (Thom et al., 2019). Finally, factors such as the stigma associated with some diseases such as HIV can lead to

Table 1
General characteristics of the participants included in the sample (N=257).

Variables	N	%
Sex		
Female	105	40.9
Male	152	59.1
Married or living with someone		
No	46	18.0
Yes	210	82.0
Has children		
No	54	21.1
Yes	202	78.9
Smoker		
No	189	73.5
Yes	68	26.5
Acute medical disease		
No	159	64.9
Yes	86	35.1
History of psychiatric treatment		
No	213	
Yes	44	17.1
Medical Comorbidities		
No	104	40.6
Yes	152	59.4
Living assistance required		
No	200	77.8
Yes	57	22.2
	Mean ± SD	Range
Age (years)	54.15 ± 16.57	18 – 95
Education (years)	8.95 ± 3.69	0 – 20
HADS-D	5.46 ± 4.09	0 – 18
HADS-A	**6.85 ± 4.42**	**0 – 19**
SF-12 PCS	32.76 ± 10.04	11.4-61.2
SF-12 MCS	47.83 ± 12.55	18.8-71.2

HADS-D: subscale measuring depression, SF-12 PCS, Physical Composite Scale; SF-12 MCS, Mental Composite Scale.

isolation (Green et al., 2012).

To measure depressive symptoms, the HADS-D was used, a questionnaire designed to measure depression in patients with physical illness. Despite the growing body of literature about HRQoL over the last 20 years, few studies have focused on understanding the impact of depression in the HRQoL of hospitalized patients, and the only published studies dealt with a specific illness (e.g., cancer or cardiovascular diseases) or a particular age group (e.g., elderly patients) (Helvik et al., 2010, 2013; Mystakidou et al., 2008; Patron et al., 2016). Herein the impact of depression on HRQoL was studied in a sample including different age groups hospitalized for multiple health problems in a real-world practice scenario. We observed that the severity of depressive symptoms is negatively associated with both the physical and mental domains of HRQoL. Furthermore, this association remains significant after adjusting for different variables.

Moreover, the multivariate linear regression model showed that beside depressive symptoms, being older is independently associated with the physical subscale of the SF-12. The model explained 16% of the variance of PCS. The association between age and the physical subscale of the SF-12 is similar to that observed by Helvik et al. (2010) and can be explained by the disease-specific physical symptoms; the use of health and social services; the reduced cognitive function, and reduced capacity to perform both personal or instrumental activities of daily living. When considering the mental subscale of the SF-12 as the outcome variable, the model showed that depressive symptoms were the only predictor, and it accounts for 38% of the variance.

Our results found that depressive symptoms were strongly associated with health status outcomes as the HRQoL, extending to a transdiagnostic sample previous observations in cardiac patients reported in The Heart and Soul Study (Ruo et al., 2003). Considering that 50% of patients who suffer comorbid depressive symptoms when hospitalized are not detected by clinicians (Rentsch et al., 2007), an essential factor that negatively impacts the HRQoL is overlooked. As previously recommended in cardiovascular diseases (Lichtman et al., 2008), routine screening for depression should be considered mandatory to improve the outcome and prognosis of patients hospitalized for any medical condition.

4.1. *Strengths and limitations*

One of the study's strengths is that it is a multicentric study including heterogeneity of medical conditions in the real world scenario, making the sample more representative.

Some limitations of the present study should be underscored. The three General Hospitals involved serve low-income patients, and some variables that were not quantified (e.g., income) might contribute to

Table 2
Comparison of SF-12 scores between categorical variables.

	SF-12 PCS			SF-12 MCS		
	Mean	SD	*p*-value	Mean	SD	*p*-value
Sex						
Female	33.23	-0.82	0.37	49.41	-0.97	0.015
Male	32.08	-0.92		45.51	-1.29	
Married or living with someone						
No	33.47	-1.30	0.60	49.92	-1.64	0.22
Yes	32.61	-0.71		47.42	-0.89	
Smoker						
No	32.27	-0.73	0.19	48.90	-0.87	0.022
Yes	34.16	-1.22		44.79	-1.68	
Acute medical disease						
No	34.12	-0.82	0.011	47.67	-1.00	0.78
Yes	30.63	-1.00		48.15	-1.38	
History of psychiatric treatment						
No	33.06	-0.69	0.31	49.21	-0.82	<0.001
Yes	31.35	-1.46		41.07	-2.03	
Medical Comorbidities						
No	34.95	-1.00	0.006	48.21	-1.17	0.78
Yes	31.30	-0.79		47.58	-1.06	
Living assistance required						
No	33.48	-0.72	0.032	48.62	-0.84	0.06
Yes	30.26	-1.19		45.09	-1.91	

HADS-D: subscale measuring depression, SF-12 PCS, Physical Composite Scale; SF-12 MCS, Mental Composite Scale. Bonferroni corrected significance level: 0.005

Table 3
Correlation between SF-12 scores and continuous variables.

	SF-12 PCS		SF-12 MCS	
	Spearman's ρ	*p*-value	Spearman's ρ	*p*-value
Age (years)	-0.22	<0.0001	0.01	0.90
Education (years)	0.10	0.10	0.03	0.60
HADS-D	-0.28	<0.0001	-0.61	<0.0001
HADS-A	**-0.16**	**0.011**	**-0.67**	**<0.0001**

HADS-D: subscale measuring depression, SF-12 PCS, Physical Composite Scale; SF-12 MCS, Mental Composite Scale. Bonferroni corrected significance level: 0.005

Table 4
Multiple linear regression model for factors associated with the SF-12 Physical Composite Scale (PCS) and Mental Composite Scale (PCS).

	β coefficient	t- statistic	*p*-values
SF-12 PCS (dependent variable)			
Depressive symptoms (HADS-D)	**-0.65**	**-4.48**	**<0.001**
Age (years)	**-0.14**	**-3.84**	**<0.001**
Acute illness	0.47	2.06	0.04
Medical comorbidities	-1.32	-1.06	0.29
Sex	-0.14	-0.12	0.91
R-squared	16%		
F-statistic	9.19		
p-value	<0.001		
SF-12 MCS (dependent variable)			
Depressive symptoms (HADS-D)	**-1.80**	**-11.47**	**<0.001**
Smoker	-2.73	-1.87	0.06
Sex	-1.72	-1.32	0.19
Age (years)	0.02	0.51	0.61
R-squared	38%		
F-statistic	37.63		
p-value	<0.001		

HADS-D: subscale measuring depression, SF-12 PCS, Physical Composite Scale; SF-12 MCS, Mental Composite Scale.

lower HRQoL; therefore, extrapolation of the conclusions should be made with caution. Furthermore, since we exclude those participants with an MSSE score < 25, patients with dementia or a confusional syndrome may not be represented in our sample, limiting the generalizability of the conclusions.

Disclosures

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Declaration of Competing Interest

No author a potential for conflicts of interest.

CRediT authorship contribution statement

Federico M. Daray: Conceptualization, Visualization, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Fernando Hunter:** Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Mercedes Mac Mullen:** Conceptualization, Visualization, Formal analysis, Data curation, Writing – original draft, Writing – review & editing.

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