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SOMATIC COMORBIDITIES ARE INDEPENDENTLY ASSOCIATED WITH THE POOR HEALTH-RELATED QUALITY OF LIFE IN PSYCHIATRIC PATIENTS

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SUMMARY

Background: *Despite the increased risk, the quality of somatic healthcare is lower for patients with mental illnesses. Currently dominant approach separates physical and mental, primary and secondary healthcare. Objective of our study was to explore whether somatic comorbidities are associated with a poor HRQoL independently of some sociodemographic and clinical factors. Majority of studies have explored particular somatic and psychiatric illnesses. Therefore we decided to access the problem from the general perspective of the universe of somatic and mental illnesses in the large psychiatric institution.*

Subjects and methods: *This nested cross-sectional study was done during May 2016 at Psychiatric hospital Sveti Ivan, Zagreb, Croatia on the sample of 506 patients diagnosed with psychiatric illnesses (ICD-10: F00-F99). Key outcome was the lowest 25% results on the SF-36 General health sub-scale, indicating the worst HRQoL. Predictors were all detected somatic illnesses. By multivariate logistic regression we controlled different sociodemographic, vital and clinical factors.*

Results: *After adjustment for different sociodemographic and clinical factors, three somatic comorbidities remained independently associated with the worst HRQoL: endocrine, nutritional and metabolic diseases (E00-E90), diseases of respiratory system (J00-J99) and diseases of musculoskeletal system and connective tissue (M00-M99)*

Conclusions: *Somatic comorbidities in psychiatric patients are associated with the poor HRQoL independently of different sociodemographic, vital and clinical factors and they should be treated seriously and integrally with mental aspects of HRQoL. Early comorbidities detection and adequate pharmacological and psychotherapeutic treatment, as well as the prevention of risk factors, may improve the quality of life and reduce morbidity and mortality of psychiatric patients.*

Key words: *mental disorders - somatic comorbidity - psychiatric comorbidity - quality of life*

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INTRODUCTION

Somatic illnesses are more common in patients with mental disorders than in general population, and consequently, their mortality rates are more than two times higher (Walker et al. 2015). The median reduction in life expectancy due to natural causes of death is approximately 10 years in patients with mental disorders compared to the general population (Walker et al. 2015).

Patients diagnosed with mental disorders have more prevalent chronic diseases risk factors like smoking, alcohol and other substances abuse, inactivity and unsatisfactory diet (Björkenstam et al. 2012, Lasiü et al. 2014, Laursen et al. 2014, Olfson et al. 2015, Walker et al. 2015). Also, growing body of literature indicates that some psychotic disorders and some somatic illnesses share common genetic risk and etiological biological mechanisms (Dieset et al. 2016). Additionally, several antipsychotics, antidepressants, and mood stabilizers are associated with dyslipidemia, glucose dysregulation, hyponatremia, hypertension, pneumonia, liver function test abnormalities, constipation, osteoporotic fractures and decreased bone mineral density, nephropathy, and obesity (Correll et al. 2015, Dieset et al. 2016,, Pérez-Piñar et al. 2016). It seems that various somatic comorbidities and chronic somatic disease risks are unequally prevalent and elevated to the different extent in patients with the particular mental disorders (Foguet-Boreu et al. 2016). Prevalence of comorbidity and multimorbidity has a significant impact on positive responses to treatment (Jakovljeviü & Ostojiü 2013). Physical comorbidities and lower quality of life in psychiatric population are partially caused and significantly aggravated by unhealthy life-style and risk factors like lower physical activity, obesity, smoking, alcohol consumption or low fruit and vegetable intake. (De Hert et al. 2011, Kang 2015, Pérez-Piñar et al. 2016, Callaghan et al. 2014, Suvisaari et al. 2016).

Despite the increased risk, the quality of somatic healthcare is lower for patients with mental illnesses (Björkenstam et al. 2012). Their access to primary and secondary prevention programs, lifestyle counseling and

early diagnosis is beyond the availability in general population (Smith et al. 2013, Walker et al. 2015). Currently dominant approach separates physical and mental, primary and secondary healthcare (Fleischhacker et al. 2008, Smith et al. 2013). This could be one of the causes of worse somatic healthcare in psychiatric patients. If it is so, it means that the problem that exists independently of us - large prevalences of somatic illnesses among psychiatric patients - we make even worse by inadequate healthcare strategies.

A large number of studies indicated a negative association of somatic and psychiatric comorbidities and health related quality of life (HRQoL) (Abraham et al. 2014, Baumeister et al. 2005). General quality of life is more affected by mental and somatic disorder in comorbidity than by somatic and somatic or - to a lesser extent - mental and mental comorbidity pair (Baumeister et al. 2005).The objective of our study was to explore whether somatic comorbidities are associated with a poor HRQoL independently of some sociodemographic and clinical factors in psychiatric patients. Majority of studies have explored particular somatic and psychiatric illnesses. Therefore we decided to access the problem from the general perspective of the universe of somatic and mental illnesses in the large psychiatric institution. We thought that the eventual evidence of such an independent association would represent a new kind of argument for the need for an integral approach to somatic and mental illness.

SUBJECTS AND METHODS

Study design and setting

This nested cross-sectional study enrolled patients during May 2016. It was nested within the prospective cohort study "Somatic comorbidities in psychiatric patients (SCPP)" which expected completion date is June 2017. The study was done at Psychiatric hospital "Sveti Ivan", Zagreb, Croatia. The study protocol was registered at ClinicalTrials.gov (NCT02773108). The study protocol has been approved by Psychiatric hospital "Sveti Ivan" Ethics Committee. All participants gave informed consent for participation. Participants' anonymity was protected. The study was designed and executed in accordance with World Medical Association Declaration of Helsinki 2013 (Anon 2013).

Subjects

Targeted population was general population of patients treated in specialized psychiatric hospital. Inclusion criteria were: both genders, age 18t years, diagnosed with a psychiatric illness (ICD-10: V Mental and behavioral disorder; F00-F99), patients' ability to answer the questionnaire by themselves, understanding of the Croatian language. Exclusion criteria were acute suicidality, dementia, moderate, severe or profound mental retardation, acute psychosis, intoxication, inability to answer the questionnaire by themselves. We chose a consecutive sample of outpatients by the order of their arrival at the exam, and all patients who were hospitalized or examined in daily hospital during the enrollment period.

Needed sample size

Power analysis was done before the start of the enrollment period and independently of the power analysis for the main prospective cohort study. A logistic regression of a binary response variable (the lowest 25% results on the SF-36 General health subscale) on a binary independent variable (somatic comorbidity) with a final sample size of 453 observations (of which 50% have and 50% don't have a somatic comorbidity) achieves 80% power at a 0.05 significance level to detect a change in probability of lowest 25% result on the SF-36 General health subscale from the baseline value of 0.5 to 0.67. This change corresponds to an odds ratio of 2.00 that we considered clinically relevant. An adjustment was made since a multiple regression of the somatic comorbidities on other sociodemographic and clinical variables (age, sex, education, duration of primary psychiatric diagnosis) in the logistic regression obtained an R2 of 0.40. Anticipating up to 20% of incorrectly collected data we decided to initially enroll 567 patients. Data needed for the calculation was taken from Topic at al 2013 (Topic et al. 2013). Power analysis was done in PASS 14 Power Analysis and Sample Size Software (2015). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass.

Outcomes

Our primary outcome was the lowest 25% results on the SF-36 General health sub-scale, indicating the worst HRQoL. We used SF-36 version 2.0 (Ware 2000) translated and validated in Croatian general population (Masliü Sersiü & Vuletiü 2006). SF-36 is not disease-specific instrument containing 36 questions each relating to only one of eight scales. General health scale was constructed according to SF-36 RAND scoring manual, based on five items: ″In general, would you say your health is: excellent, very good, good, fair, poor″; ″I seem to get sick a little easier than other people″, ″I am as healthy as anybody I know″, ″I expect my health to get worse″, ″My health is excellent″; with following answer options: definitely true, mostly true, don't know, mostly false, definitely false. In the first step, original items were rescaled to the scale ranging from 0 to 100. In the second step the arithmetic mean of these scores was calculated. We used a generic HRQoL instead of diagnosis-specific HRQoL instrument to be able to compare our findings to the results of studies focusing on particular somatic and psychiatric illnesses.

Independent variables (predictors)

Our predictors were all somatic illnesses recorded by a psychiatrist during the exam and verified by medical history.

Possible confounders

Possible confounders and effect modifiers whose effect we tried to control by multivariate analysis were: sex, age, education, marital status, number of household members, work status, monthly income per household members (measured by paper questionnaire for patients' self-administration), Body mass index (kg/m2), waist circumference (measured by a medical nurse during the exam). Primary psychiatric diagnosis, duration of primary psychiatric illness, illness severity measured by Clinical global impression - severity (CGI-S) scale and improvement since diagnosis measured by Clinical global impression - improvement (CGI-I) scale, treatment by antipsychotic or antidepressants were recorded by a psychiatrist.

Statistical analysis

The level of statistical significance was set at $P<0.05$ and we gave all confidence intervals at 95% level. In all instances we used two-tailed tests. Before the analysis original SF-36 Global health sub-scale was transformed to the scale ranging from 0 to 100 where higher values indicate better HRQoL. The main analysis was done in two steps. In the first step we did a series of univariate binary logistic regression analysis. All variables that were significantly at $P<0.1$ associated with the poorest HRQoL were entered into the multivariate, adjusted model. As the standardized effect size we gave odds ratio (OR) with it's confidence intervals. Statistical data analysis was done by NCSS 10 (2015) and MedCalc version 15.6.1 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2015).

RESULTS

Total of 567 patients were enrolled. There were missing data for at least one SF-36 item needed for the calculation of General Health scale in 61 (10.8%) of patients. They were excluded from the analysis. The final sample consisted of 506 patients with median (interquartile range) of age: 45 (34-56) years (Table 1). The youngest patient was 19, and the oldest one was 86 years old. A similar number of patients was diagnosed with schizophrenia, schizotypal and delusional disorder (F20-F29), as with neurotic, stress-related and somatoform disorder (F40-F48) or mood (affective) disorders (F30-F39) (Table 2).

Somatic comorbidities were present at 236 (46.6%) of patients (Table 3). They were more prevalent in female, 138 (56.6%), than in male patients, 98 (37.5%)

Table 1. Patients´ sociodemographic and vital characteristics (n=506)

	n	(%)
Sex		
male	261	(51.7)
female	244	(48.3)
Age (years), median (IQR)	45	(34-56)
Age (years)		
□35	130	(26.0)
35-44	114	(22.8)
45-54	123	(24.6)
55-64	91	(18.2)
□65	42	(8.4)
Education		
primary	52	(10.3)
secondary	320	(63.6)
university	131	(26.0)
Marital status		
never married	216	(43.4)
married	174	(34.9)
widow	29	(5.8)
divorced	79	(15.9)
Number of household members		
living alone	88	(17.6)
one	140	(28.0)
two	167	(33.4)
three or more	105	(21.0)
Work status		
employed	240	(50.1)
unemployed	110	(23.0)
retired	129	(26.9)
Monthly income per household member (EUR), median (IQR)	401	(200-668)
Body mass index (kg/m2), median (IQR)	26	(23-30)
Body mass index (kg/m2)		
normal (<25.0)	201	(41.5)
overweight (25.0-29.9)	161	(33.3)
obese (□30.0)	122	(25.2)
Waist circumference (cm)		
normal	228	(46.3)
elevated (male >100 cm; female >90 cm)	264	(53.7)
Waist to hip ratio		
normal	255	(52.1)
elevated (male □1.0; female □0.85)	234	(47.9)

Data are presented as number (percentage) of participants if not stated otherwise; IQR = interquartile range; Data was not properly collected for sex 1 (0.2%), age 6 (1.2%) of participants, education 3 (0.6%), marital status 8 (1.6%), number of household members 6 (1.2%), work status 27 (5.3), monthly household income per household member 89 (17.6%), body mass index 22 (4.3%), waist circumference 14 (2.8%), waist to hip ratio 17 (3.4%) of participants

Table 2. Patients´ clinical characteristics and therapy (n=506)

	n	(%)
Psychiatric diagnosis		
Schizophrenia, schizotypal and delusional disorders (F20-F29)	177	(35.9)
Neurotic, stress-related and somatoform disorders (F40-F48)	166	(33.7)
Mood (affective) disorders (F30-F39)	156	(31.6)
Disorders of adult personality and behavior (F60-F69)	111	(22.5)
Mental and behavioral disorders due to psychoactive substance use (F10-F19)	79	(16.0)
Organic, including symptomatic, mental disorders (F00-F09)	45	(9.1)
Behavioral syndromes associated with psychological disturbances and physical factors (F50-F59)	19	(3.9)
Mild intellectual disabilities (F70)	5	(1.0)
Behavioral and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98)	2	(0.4)
Disorders of psychological development (F80-F89)	1	(0.2)
Duration of illness (years), median (IQR)*	4	(1-11)
Duration of psychiatric illness (years)*		
□1	167	(34.3)
2-4	94	(19.3)
5-9	85	(17.5)
□10	141	(29.0)
Clinical global impression - severity scale (CGI-S)		
up to mildly ill	109	(22.1)
moderately ill	190	(38.5)
significantly ill	141	(28.6)
severely ill	53	(10.8)
Clinical global impression - improvement since diagnosis (CGI)-I)		
significant improvement	219	(44.6)
minimal improvement	176	(35.8)
no change	59	(12.0)
worsening	37	(7.5)
Antipsychotics		
no antipsychotics	218	(43.6)
atypical	231	(46.2)
typical	99	(19.8)
clozapine	37	(7.4)
Number of antipsychotics		
no antipsychotics	218	(43.1)
monotherapy	164	(32.4)
combination	124	(24.5)
Antidepressants		
no antidepressants	200	(39.5)
selective serotonin reuptake inhibitors (SSRI)	182	(36.0)
serotonin-norepinephrine reuptake inhibitors (SNRI)	61	(12.1)
noradrenergic and specific serotonergic (NaSSA)	33	(6.5)
other†	27	(5.3)
Number of antidepressants		
no antidepressants	200	(39.5)
monotherapy	282	(55.7)
combination	24	(4.7)
Mode of treatment		
outpatients	240	(47.6)
hospitalized	185	(36.7)
daily hospital	79	(15.7)

Data are presented as number (percentage) of participants if not stated otherwise; IQR = interquartile range;
Data was not properly collected for diagnosis 13 (2.6%), duration of psychiatric illness 19 (3.8%), clinical global impression - severity scale 13 (2.6%); clinical global impression - improvement since diagnosis (CGI-I) 15 (3.0%) of participants;
* Duration of primary psychiatric diagnosis; † Drugs recommended to <5% of patients: tricyclcic (TCA) 15 (3.0%), serotonin modulator and stimulator (SMS) 8 (1.6%), tetracyclic (TeCA) 3 (0.6%), reversible inhibitor of monoamine oxidase A (RIMA) 1 (0.2%)

Table 3. Somatic comorbidities (n=506)

	n	(%)	(95% CI)
IV Endocrine, nutritional and metabolic diseases (E00-E90)	111	(21.9)	(18.4-25.8)
IX Diseases of the circulatory system (I00-I99)	103	(20.4)	(17.0-24.2)
XI Diseases of the digestive system (K00-K93)	52	(10.3)	(7.8-13.3)
XIII Diseases of the musculoskeletal system and connective tissue (M00-M99)	36	(7.1)	(5.0-9.7)
VI Diseases of the nervous system (G00-G99)	31	(6.1)	(4.2-8.6)
X Diseases of the respiratory system (J00-J99)	25	(4.9)	(3.2-7.2)
III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)	18	(3.6)	(2.2-5.6)
XIV Diseases of the genitourinary system (N00-N99)	10	(2.0)	(1.0-3.6)
II Neoplasms (C00-D48)	7	(1.4)	(0.6-2.9)
XII Diseases of the skin and subcutaneous tissue (L00-L99)	5	(1.0)	(0.3-2.3)
XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)	5	(1.0)	(0.3-2.3)
XIX Injury, poisoning and certain other consequences of external causes (S00-T98)	4	(0.8)	(0.2-2.0)
I Certain infectious and parasitic diseases (A00-B99)	3	(0.6)	(0.1-1.7)
VII Diseases of the eye and adnexa (H00-H59)	3	(0.6)	(0.1-1.7)
VIII Diseases of the ear and mastoid process (H60-H95)	2	(0.4)	(0.0-1.4)
XXI Factors influencing health status and contact with health services (Z00-Z99)	1	(0.2)	(0.0-1.1)
Number of somatic comorbidities, $\bar{x}$ (SD)	1.13	(1.47)	(1.03-1.22)
Number of somatic comorbidities			
none	270	(53.4)	(48.9-57.8)
1	110	(21.7)	(18.2-25.6)
2	48	(9.5)	(7.1-12.4)
3	38	(7.5)	(5.4-10.2)
□4	40	(7.9)	(5.7-10.6)

Data are presented as number (percentage) of participants if not stated otherwise; $\bar{x}$= arithmetic mean; SD = standard deviation

(OR=2.17; 95% CI 1.52-3.09; P<0.001). As expected, the prevalence of somatic comorbidities increases with the patients' age from 5/35 (14.3%) in the group of patients younger than 25 years up to 13/15 (86.7%) in the group of patients □75 years old. The most prevalent somatic comorbidities were endocrine, nutritional and metabolic diseases (E00-E90), and diseases of the circulatory system (I00-I99).

Our key outcome, the lowest HRQoL quartile comprised the SF-36 General health sub-scale results from 0 to 30. Median (IQR) General health sub-scale result of the lowest HRQoL quartile was 25 (15-30). Median (IQR) General health sub-scale result of the rest of the sample (the highest 75% results) was 62 (45-72).

Series of univariate binary logistic regression analyses revealed significantly more often the poorest perceived HRQoL in female and in older patients, in patients whose highest education was a primary school, who were widowed and retired, with lower monthly income per household member (Table 4). Duration of primary psychiatric illness was not significantly associated with the poorest HRQoL, but illness severity and improvement since diagnosis were. Being treated by antidepressants or being treated in outpatient's office instead of being hospitalized, univariately decreased odds for having the poorest HRQoL. Four somatic comorbidities were univariately associated with the poorest HRQoL: endocrine, nutritional and metabolic diseases (E00-E90), diseases of the circulatory system (I00-I99), diseases of the respiratory system (J00-J99) and diseases of the musculoskeletal system and connective tissue (M00-M99) (Table 4). The highest association was noticed in the latter case. Diseases of the digestive system (K00-K93) were on the edge of statistical significance.

After controlling by multivariate, binary logistic regression for all monitored sociodemographic and clinical factors, three somatic comorbidities remained independently associated with the poorest HRQoL: endocrine, nutritional and metabolic diseases (E00-E90) (OR=2.42; 95% CI 1.16-5.05; P=0.019), diseases of the respiratory system (J00-J99) (OR=5.73; 95% CI 1.28-25.71; P=0.023), and diseases of the musculoskeletal system and connective tissue (M00-M99) (OR=5.85; 95% CI 1.78-19.22; P=0.004) (Table 4). In addition to these three somatic comorbidities, the poorest HRQoL was independently associated with the result of Clinical global impression - severity scale and treatment with antidepressants. Patients who were severely ill had almost 12 times higher odds for having the poorest HRQoL.

Table 4. Prediction of the worst HRQoL defined as lowest quartile of SF-36 General HRQoL scale results; only variables that were univariately significant at P<0.1

	The worst HRQoL		Univariate		Multivariate, adjusted		
			OR	P	OR	(95% CI)	P
Sex							
male	62	(23.8)	1		1		
female	76	(31.1)	1.45	0.063	1.66	(0.87-3.16)	0.123
Age (years), median (IQR)	52	(42-58)	1.03	<0.001	1.00	(0.96-1.03)	0.877
Education							
primary	20	(38.5)	1		1		
secondary	93	(29.1)	0.66	0.174	0.79	(0.28-2.18)	0.643
university	23	(17.6)	0.34	0.003	0.73	(0.23-2.29)	0.584
Marital status							
never married	42	(19.4)	1		1		
married	59	(33.9)	2.13	0.001	1.11	(0.45-2.74)	0.822
widow	11	(37.9)	2.53	0.027	1.28	(0.19-8.63)	0.802
divorced	23	(29.1)	1.70	0.078	1.25	(0.44-3.59)	0.675
Work status							
employed	48	(20.0)	1		1		
unemployed	30	(27.3)	1.50	0.130	0.93	(0.42-2.08)	0.862
retired	54	(41.9)	2.88	<0.001	1.83	(0.75-4.45)	0.185
Monthly income per household member (EUR)							
<200	30	(33.0)	1		1		
200-599	54	(29.3)	0.85	0.540	0.88	(0.40-1.92)	0.746
□600	26	(18.3)	0.46	0.012	0.50	(0.20-1.25)	0.139
Psychiatric illness							
Duration of psychiatric illness (years)*							
□1	40	(24.0)	1		1		
2-4	20	(21.3)	0.86	0.622	0.71	(0.29-1.72)	0.442
5-9	23	(27.1)	1.18	0.590	0.80	(0.31-2.06)	0.641
□10	50	(35.5)	1.75	0.028	0.99	(0.43-2.28)	0.986
Clinical global impression - severity scale (CGI-S)							
up to mildly ill	6	(5.5)	1		1		
moderately ill	46	(24.2)	5.48	<0.001	4.95	(1.45-16.87)	0.011
significantly ill	56	(39.7)	11.31	<0.001	10.47	(2.56-54.34)	0.002
severely ill	23	(43.4)	13.16	<0.001	11.78	(2.56-54.34)	0.002
Clinical global impression - improvement since diagnosis (CGI)-I)							
significant improvement	31	(14.2)	1		1		
minimal improvement	65	(36.9)	3.55	<0.001	1.71	(0.80-3.62)	0.165
no change	23	(39.0)	3.88	<0.001	2.66	(0.97-7.32)	0.058
worsening	11	(29.7)	2.57	0.021	2.79	(0.91-8.55)	0.073
Antipsychotics							
no	85	(30.1)	1		1		
yes	51	(23.4)	0.71	0.093	0.71	(0.35-1.44)	0.346
Antidepressants							
no	102	(33.4)	1		1		
yes	36	(17.9)	0.43	<0.001	0.27	(0.13-0.55)	<0.001
Mode of treatment							
outpatients	46	(19.2)	1		1		
hospitalized	63	(34.1)	2.18	0.001	0.94	(0.44-1.99)	0.871
daily hospital	29	36.7)	2.45	0.002	2.32	(0.99-5.45)	0.053

Data are presented as number (percentage) of participants if not stated otherwise; IQR = interquartile range;
OR = odds ratio; 95% CI = 95% confidence interval; P = statistical significance of OR, binary logistic regression;
* Duration of primary psychiatric diagnosis

Table 4. Continous

	The worst HRQoL		Univariate OR	P	Multivariate, adjusted OR	(95% CI)	P
Somatic comorbidities							
IV Endocrine, nutritional and metabolic diseases (E00-E90)							
no	85	(21.5)	1		1		
yes	53	(47.7)	3.33	<0.001	2.42	(1.16-5.05)	0.019
IX Diseases of the circulatory system (I00-I99)							
no	97	(24.1)	1		1		
yes	41	(39.8)	2.09	0.002	0.82	(0.35-1.94)	0.657
X Diseases of the respiratory system (J00-J99)							
no	126	(26.2)	1		1		
yes	12	(48.0)	2.60	0.021	5.73	(1.28-25.71)	0.023
XI Diseases of the digestive system (K00-K93)							
no	118	(26.0)	1		1		
yes	20	(38.5)	1.78	0.058	0.99	(0.38-2.60)	0.984
XIII Diseases of the musculoskeletal system and connective tissue (M00-M99)							
no	113	(24.0)	1		1		
yes	25	(69.4)	7.18	<0.001	5.85	(1.78-19.22)	0.004

Data are presented as number (percentage) of participants if not stated otherwise; IQR = interquartile range;
OR = odds ratio; 95% CI = 95% confidence interval; P = statistical significance of OR, binary logistic regression;
* Duration of primary psychiatric diagnosis

DISCUSSION

Our study has shown that diseases of the musculoskeletal system and connective tissue (M00-M99), respiratory diseases (J00-J99) and endocrine, nutritional and metabolic disease (E00-E90) are associated with the poorest HRQoL independently of the sex and age, education, work and marital status, household impact per household member, duration of primary psychiatric illness, treatment with antipsychotics and antidepressants as hospitalized patient or being treated in hospital, in daily hospital or in outpatients' office.

Prevalence of chronic somatic diseases in our study was significantly lower (47%) than in study done by Topic et al. (2013). In their research, 75% of patients had somatic comorbidity. A plausible explanation is that our targeted population was much more diverse. Topic at al. focused on the recurrent depressive disorder.

Our results were consistent with Baumeister et al. (2005) review findings on the significant negative effect of mental and somatic illnesses comorbidities on patients' quality of life. Connell et al. (2014) in their qualitative study got the strong indication of physical comorbidities importance for psychiatric patients´ subjective quality of life. However, in their review of qualitative research from 2012 they concluded that physical well-being was "not a strong theme" within the reviewed studies (Connell et al. 2012). This was not surprising as they excluded studies where physical health was primary to mental health problems. Their major criticism of EQ-5D, another generic Quality of life questionnaire, was aiming this generic quality of life focus on physical rather than mental health. In a way, our findings are in accordance with theirs, but our conclusions are different. As our study found the independent association of three somatic comorbidities with the poorest HRQoL, we concluded they should be treated multidisciplinary and by an integral approach. This approach should be different to the currently dominant approach with separation between physical and mental, primary and secondary healthcare (Fleischhacker et al. 2008, Smith et al. 2013). Abraham at al. (2014) found that number of medical comorbidities was the strongest independent predictor of SF-36 physical health dimension in patients diagnosed with bipolar disorder after adjustment for various sociodemographic and psychographic variables. It was not significantly predictive for SF-36 mental health dimension, and they did not publish results of SF-36 general health subscale. Besides much narrower targeted population, the most important difference from our study was the usage of number of comorbidities instead of particular somatic diseases. Findings and conclusions by Miller at al. (2013) were comparable to ours.

Limitations of the study

Our study was done in one center. Therefore our results are not representative for the entire Croatian population. The center is the second largest psychiatric hospital in the highly urbanized country capital. It is possible that the population of patients is different in psychiatric wards of small county hospitals and in other clinical settings. Lacking the empirical studies we can only speculate that the prevalence of somatic comorbidities and their association with patients' HRQoL may be different in different centers. Further

studies are needed for clarification of this potential source of bias. Due to the cross-sectional nature of our study we were not able to infer on the eventual causal relationship between somatic comorbidities and the poorest HRQoL. As this study has been nested within the prospective cohort study, we will do the internal validation of our results, and examine the covariation of somatic comorbidities and changes in HRQoL during 12 months. The quality of life is a subjective concept and the validity of SF-36 General health sub-scale is less than perfect. Moreover, SF-36 is the generic instrument that may be less sensitive for changes in HRQoL in psychiatric patients.

Future research should focus on understanding the eventual causal relationships between somatic co-morbidities of mental disorders and HRQoL. As randomization is not an option in research of this subject, future studies should be properly powered to be able to control numerous confounders by multivariate analysis.

CONCLUSIONS

Musculoskeletal system and connective tissue, respiratory and endocrine, nutritional and metabolic diseases in psychiatric patients are associated with the poor HRQoL independently of different sociodemographic, vital and clinical factors. This implies the need for a multidisciplinary and integral approach to patients diagnosed with mental illness. Somatic comorbidities in psychiatric patients should be treated seriously and integrally with mental aspects of HRQoL. Early comorbidities detection and adequate pharmacological and psychotherapeutic treatment, as well as the prevention of risk factors, may improve the quality of life and reduce morbidity and mortality of psychiatric patients. Findings confirmed in this study motivated us to organize and implement a new project at Psychiatric hospital "Sveti Ivan": Center for Integrative Psychiatry - CIP. The project will have three consecutive steps: first step is prevention, detection and treatment of physical comorbidity, the second step includes a personalized pharmacotherapy and psychotherapy, the third step is education of mental patients, caregivers and healthcare professionals.

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Conflict of interest:

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Contribution of individual authors:

Igor Filipþiü & Ivona Šimunoviü Filipþiü designed the study, wrote protocol and participated in the writing and multiple edits of the manuscript drafts; *Katarina Matiü & Vanja Lovretiü* managed data collection; *Ena Iveziü* reviewed the manuscript drafts; *Žarko Bajiü* performed the statistical analyses and data interpretation; *Vladimir Grošiü & Slobodanka Keziü* were involved in data collection; *Branka Restek Petroviü* reviewed the manuscript drafts; *Aleksandar Vþev* reviewed the manuscript drafts.

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