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Confirmatory Factor Analysis of the Quality of Life in Patients Premalignant and Malignant Cervix Pathology

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Abstract

The concept of quality of life (QOL) become a used notion in the medical research and is considered a dynamic, multidimensional and subjective construct. There is no universal instrument for evaluating all the QOL facets by populations, pathologies and treatments, the choice of certain measurement instruments is done according to the objectives and outcomes of the research. The aim of this study was to to test the factorial structure, reliability and convergent validity of health related quality of life scale using EORTC QLQ-C30 instrument for the Romanian population of patients with pre-malignant and malignant cervical pathology. Data from a convenience sample consisted of 102 women of reproductive age, treated at "Prof. Dr. Ion Chiricuta" Institute of Oncology (IOCN), Cluj-Napoca, during 2007-2012, for premalignant and malignant pathology of the cervix, namely high grade dysplasia and microinvasive carcinoma with conservative surgery (cervical conization) were analyzed by confirmatory factor analysis. Two alternative measurement models were tested for statistical model fit to the sample data. The fit of models was analyzed by χ^2 goodness-of-fit test and descriptive goodness-of-fit indices. Both models showed an acceptable fit to data and a good reliability and convergent validity. Confirmatory factor analysis brought two new measurement HRQOL models.

Keywords: Confirmatory factor analysis; Structural equation modeling; Quality of life; Cervix pathology.

Introduction

In recent years, the concept of quality of life (QOL) has become a key notion in the medical community and has been accepted as a unique construct consisting of two fundamental components: multidimensionality and subjectivity [1]. Multidimensionality refers to the inclusion of at least four categories of variables in the definition of this concept such as physical, psychological, cognitive and social functioning [2-4] while subjectivity means that this concept should be understood from the patients' perspective.

Although there is a general consensus regarding to the potential value of using the QOL concept as an outcome variable, there is no general agreement as regards the definition thereof. Multiple definitions can be assigned to it, which also include other concepts such as that of well-being, satisfaction, expectations, or health-related quality of life (HRQOL) [5,6].

The HRQOL concept was adopted in the context in which the QOL is deemed to be also influenced by social and economic factors of no importance upon evaluating the evolution of pathology. Revicki et al. [7] defined HRQOL as "the subjective evaluation of disease and treatment impact in physical, psychological, social and somatic dimensions of functionality". In the literature they are considered interchangeable concepts but each of them has its own definition. The QOL construct is considered as a broader concept, referring to all aspects of life, while HRQOL is centered on the effects of pathology or of a specific treatment on quality of life [8].

The evaluation of the QOL and HRQOL may be performed at general level by means of an item of the following type: "How would you evaluate the quality of your life in general in the last week?", to which either ill or healthy subjects may answer, the outcomes being compared afterwards. Because many of the aspects of quality of life (QOL) or health-related quality of life (HRQOL) cannot be measured directly, they are generally evaluated according to the traditional procedures of item-measurement theory [9]. This theory involves that there is a true score of quality-of-life, that cannot be measured directly, but it can be measured indirectly by a set of questions known as "items," each of them means the same true concept or construct (interchangeable items). The items response scores of patient are then transformed to numerical scores and are combined to obtain "scale scores" or "domain scores". If the items are representative, the measurement scores of scale, should differ from the corresponding true value only by random error of measurement. This type of assessment may be applied to any subject with or without certain pathology and includes physical, psychological or social facets of quality of life.

The EORTC QLQ-C30 developed by the European Organization for Research and Treatment of Cancer is one of the widely used tools for assessing quality of life in cancer patients [10]. It is a core questionnaire which assesses the physical, social and emotional aspects common to patients regardless of their cancer specific diagnosis. In addition, this type of cancer-oriented instrument includes items that describe the symptoms of the disease as well as the adverse effects of the treatment.

The EORTC QLQ-C30 questionnaire incorporates in total 9 multi-items scale and 6 single items. Although the EORTC QLQ-C30 can be easily administered, some psychometric and format difficulties were revealed. It was considered that the psychometric problems were due more to how the items were formulated and how the patients responded than a deficiency in the construct (scale) formulation [11].

Unlike other QOL measurement instruments such Short Form-36 (SF-36) [12], Functional Assessment of Cancer Therapy-Generic (FACT-G) [13] or World Health Organization Quality of Life Assessment (WHOQOL) [14] that using a total score for quality of life construct, the EORTC QLQ-C30 did not povide an overall summary score of "quality of life" even it provides summary scores for each of the functional and symptom scales [15].

There is an interest in developing a global QOL or HRQOL score that can be useful in clinical oncology research by simplifying the analysis of QOL concept, minimization Type I statistical errors due to multiple comparisons or representing the QOL concept as a composite variable measured with greater accuracy than by multiple variables each measured with a smaller precision.

The possibility to calculate a global score of HRQOL with equal or unequal weight of items can be tested by a confirmatory factor analysis method [16-17]. This method is a special case of structural equation modelling which allows the assessment of reliability and construct validity of a measurement model. It can also be used to examine the higher-order structure of a measurement model. From our knowledge, to date, there are a limited number of studies that have examined the higher-order structure of HRQOL factor with EORTC QLQ-C30 instrument. Models analyzed in these research articles were tested on patients with breast cancer, ovarian cancer, lung cancer, gastrointestinal malignancies or heterogeneous group of patients with various types of cancers [18-23]. None of the studies developed a HRQOL model for patients with premalignant and malignant pathology of the cervix, namely high grade dysplasia and microinvasive carcinoma with conservative surgery (cervical conization). The statistical methods used in developing models were the exploratory factor analysis, principal component analysis [18,22] and confirmatory factor analysis [17,20,21]. The aim of this study was to test the factorial structure, reliability and construct validity of health related quality of life scale in order to establish a measurement HRQOL model based on EORTC QLQ-C30 instrument for the Romanian population of patients with pre-malignant and malignant cervical pathology. The research objectives were: 1) to analyze the statistical fit of two higher order factor HRQOL measurement models by confirmatory factor analysis applied on a sample of women with pre-malignant and malignant diseases of the cervix assessed at one year after cervical conization surgery; 2) assessing the reliability coefficient and convergent validity of HRQOL based on the CFA method, items and scales of EORTC QLQ-C30 considered representative for our sample.

Material and Method

Sample and Procedure

The data used in this study come from a larger project that aimed to identify and ranking determinants of quality of life in a population of women of reproductive age, treated for premalignant and malignant pathology of the cervix with conservative surgery (cervical conization).

The convenience sample consisted of 102 women of reproductive age, treated at "Prof. Dr. Ion Chiricuta" Institute of Oncology (IOCN), Cluj-Napoca, during 2007-2012, for premalignant and malignant pathology of the cervix, namely high grade dysplasia and microinvasive carcinoma with conservative surgery (cervical conization). Inclusion criteria were: 1) adult patients aged between 18 and 41 years; 2) advanced dysplasia and microinvasive cervical carcinoma confirmed by biopsy 3) patients's consent for conization; 4) No further treatment was required and 5) all patients are under follow-up. Exclusion criteria included women with known psychoemotional disorders or patients who used medications that can affect sexual functioning.

Patients completed a self-administered questionnaire consisting of items related to demographic and clinical characteristics (such as age at questionnaire completion, age at time of surgery, type of complications arising after surgery), items of the questionnaire used in international scientific circuit for measuring quality of life construct [9], sexual functionality [24] and descriptors items of Attitudes and Beliefs Scale [25] and a visual analogue scale of distress. The patients filled the items of questionnaire, retrospectively, within the first year after surgery (cold knife conization for diagnosis and treatment of cervical dysplasia or microinvasive cervical carcinoma).

The QLQ-C30 instrument

European Organization for Research and Treatment of Cancer Quality of Life C30 (EORTC QLQ-C30) was used to assess a range of aspects (domains) of health related quality of life to patients included in the study. It comprised 30 items who described five functional domains (*Physical functionning* measured by 5 items, Social functionning measured by 2 items, *Fulfillment of social roles* defined by 2 items, *Mental/ emotional functionning* - 4 items and *Cognitive functionning* – 2 items), three symptom domains (*Fatique* measured by 3 items, *Pain* and *Nausea/vomiting* each described by 2 items), six domains with single items who described common symptoms reported by cancer patients (insomnia, constipation, diarrhea, loss of appetite and dyspnea) and financial problems due to the disease. The instrument also contained 2 items related to the subjective perception of overall health status and overall quality of life.

First 28 items used a 4-point Likert response scale („not at all", „a little", „quite a bit", „very much" denoted by 1, 2, 3 and 4), a high score of items related to functional domains representing a low level of functionality and a high score for a symptom item representing a high level of symptomatology. The last 2 items used 7-point response scale, ranging from "very poor" to "excellent", a high scores meaning a high level of overall quality of life /health status.

Because the variables used in this study are part of a larger questionnaire including many other items, the variables were presented with the original label of the questionnaire (item 37, item 38,…, Item 66. These variables were in the order they were listed, the 30 items of the original questionnaire (EORTC QLQ -C30). The items were introduced in the statistical analysis with original scores not with standardized scores proposed by EORTC QLQ-C30.

Measurement Models

The two hypothetical HRQOL alternative measurement models were chosen based on theoretical models [7,26] and empirically validated models in different populations [20,21], models generated from items and domains QLQ- C30 and tested by structural equation modeling. These models were fit to the data. The higher order CFA models were based on the modified model corresponding to the standard model with the original 13 QLQ C30 scales. Because the standard model fit was rejected on the data, the respecification of the model was made by examining the sample correlation matrix and the implied model correlation matrix. The final items used in the analysis of measurement models were listed in the following table (Table1).

Table 1. Description of the items

Item no.	Item description
38	„Do you have any trouble taking a long walk?”
39	„Do you have any trouble taking a short walk outside of the house?”
40	„Do you need to stay in bed or a chair during the day?”
42	„During the past week: Were you limited in doing either your work or other daily activities?” (During the past week)
43	„During the past week: Were you limited in pursuing your hobbies or other leisure time activities?”
45	„During the past week: Have you had pain?”
46	„During the past week: Did you need to rest?”
47	„During the past week: Have you had trouble sleeping?”
48	„During the past week: Have you felt weak?”
49	„During the past week: Have you lacked appetite?”
54	„During the past week: Were you tired?”
55	„During the past week: Did pain interfere with your daily activities?”
56	„During the past week: Have you had difficulty in concentrating on things, like reading a newspaper or watching television?”
57	„During the past week: Did you feel tense?”
58	„During the past week: Did you worry?”
59	„During the past week: Did you feel irritable?”
60	„During the past week: Did you feel depressed?”
61	„During the past week: Have you had difficulty remembering things?”
62	„During the past week: Has your physical condition or medical treatment interfered with your family life?”
63	„During the past week: Has your physical condition or medical treatment interfered with your social activities?”

The first model was a one-dimensional HRQOL model also named second-order CFA model, a restrictive and parsimonious model in terms of estimated parameters. It assumed that all first-order latent factors loaded a single second-order latent factor called HRQOL.

The second model is similar in some aspects with the models of Fayers et al. [27,28] and Boehmer and Luszczynska [18]. The design of this model is a MIMIC model („multiple indicator, multiple cause”). In this type of model, the items corresponding to symptoms are considered formative or „causal” indicators for HRQOL because their presence can determine or “cause” a low level of HRQOL. In this type of model, it is not necessary that indicators are all intercorrelated. This involves that a low level of HRQOL not necessarily involve that patient suffers from all the symptoms represented in the model [29]. The choice of reflective and formative items was based on the “thought test” proposed by Bollen [30]. A change score in the latent variable produces a change in the score of the reflective indicator and, conversely. Also a modification of score in the latent variable “not necessarily” produces a change in the score of causal” or formative indicator but a change in the observed scores of items produces a change in the latent variable scores.

Statistical Analysis

The statistical method of the present study was a special case of structural equation modelling called confirmatory factor analysis (CFA). Its application was conditioned by the verification of the conceptual and statistical assumptions. The minimal condition of univariate normality was performed by Anscombe [31] and D’Agostino [32] tests described in the “moments” and “semTools” packages of the R v.3.03 statistical programming and graphical representation environment, while the verification of the multivariate normality was performed by the Shapiro and Mardia tests [33] applicable with the aid of MVN package from the same software. The CFA modelling was achieved by the aid of “lavaan” package [34]. As the data highlighted deviations from the normality condition, the Satorra-Bentler robust maximum likelihood correction method was used for test the fit of model and estimates the model parameters. The existence of the four-point Likert items suggested the verification of the model stability in terms of approximate fit indexes and Chi-square model test by the robust weighted least squares estimation method (WLSMV). The both estimation methods were considered robust for small sample size and deviation from normality [35,36].

The sufficient condition for an identified model, given by the rule of the 2 indicators, was fulfilled, each factor, except for 2 factors, being defined by means of at least 2 indicators. The factors measured by a single item, for reasons of model identification, were restricted with regard to the measurement error variances, which were fixed at 0.10 (value calculated based on the item variance and reliability, measured by means of the test-retest correlations reported in the literature [37]. Thus, all the tested models verified the necessary identification condition given by the counting rule: df (degrees of freedom) > 0.

The model fit was examined by the χ^2 test and approximate fit indexes. A good model fit should provide an insignificant result at a 0.05 significance level [38]. Because the Chi-square test was considered sensitive to sample size in rejecting the null hypothesis (the covariance matrix implied by the proposed model was identical to sample covariance matrix), we used the normed Chi-square (NC) as an alternative fit index. Although there is no consensus concerning a reasonable value of NC, recommendations specified a value ranging from 2 to 5 [39]. The approximate fit indexes were described by the absolute fit indexes represented by Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Square Residual (SRMR) or Weighted Root Mean Square Residual (WRMR) and incremental fit indexes as Nonnormed Fit Index (NNFI sau TLI), Comparative Fit Index (CFI), Goodness-of-fit Index (GFI) and Adjusted Goodness-of-Fit Index (AGFI). The rules of thumb are that a RMSEA value less than 0.05 indicates close approximate fit, values between 0.05 and 0.08 indicate acceptable fit, and values greater than 0.10 indicate poor approximate fit [40]. A value close to 0.90 for CFI or TLI indicates reasonable fit while a value close to 0.95 means a good fit of model to data [41]. The recommended reference value of GFI is 0.90 [42] and a value of AGFI greater than 0.85 indicates an adequate acceptable while higher values of 0.90 suggests a good fit to the data [43]. The scaled Chi-square difference test was used for comparison of the first- and second-order CFA models.

The model with a good fit was interpreted in relation to the standardised coefficients which were used to analyse the importance of each indicator within the construct, their values being an estimator of the effect size. Thus, the values around the threshold value of 0.30 indicated a moderate effect, while the values greater than 0.50 indicated a large effect [44].

The measurement models were then tested for the reliability and convergent validity. The measure of reliability for the first order factor was assessed by McDonald’s coefficient omega [45] not by Cronbach’s coefficient alpha considered to underestimate factor reliability in congeneric models (models with different loading coefficients in the same construct). The reliability of the second-order factor was assessed by the coefficient omega at level 1, which describes the proportion of the total variance observed scores due to the second-order factor, coefficient omega at level 2, which describes proportion of the total variance of the first-order factors explained by the presence of the second-order factor, and partial coefficient omega at level 1, which determines the variance proportion of the observed scores due to the second-order factor after the elimination of the uniqueness effect of the first-order factors.

Results

The descriptive statistics of the items analyzed were presented in Table 2. The patients reported a moderate level of functionality (physical, cognitive, emotional and social), high level of symptomatology and an overall good level of QOL.

Table 2. Arithmetic mean and standard deviation of EORTC QLQ-C30 items

Item	mean±standard deviation	Item	mean±standard deviation
37	1.51±0.89	52	1.39±0.73
38	1.24±0.57	53	1.11±0.34
39	1.05±0.22	54	1.84±0.85
40	1.49±0.71	55	1.33±0.65
41	1.03±0.22	56	1.24±0.53
42	1.32±0.72	57	1.72±0.78
43	1.35±0.75	58	1.95±0.86
44	1.34±0.61	59	1.80±0.78
45	1.44±0.64	60	1.53±0.71
46	1.84±0.82	61	1.54±0.65
47	1.48±0.81	62	1.28±0.60
48	1.59±0.74	63	1.32±0.65
49	1.14±0.40	64	1.32±0.73
50	1.28±0.60	65	5.17±1.28
51	1.20±0.51	66	5.26±1.26

The statistically significant associations (correlations) between the variables were between 0.22 and 0.94. The correlation coefficients exceeding 0.90 between several items suggested the problem of a possible multicollinearity if these items had been associated to different constructs (Table 3).

Regarding the multivariate distribution of the 30 items, there were found deviations from the normal multivariate distribution (Mardia test. estimated multivariate kurtosis coefficient=525.39, Z statistic=40.21, $p<0.05$, Shapiro test: W statistic = 0.28 $p<0.001$). Most of the univariate skewness coefficients were positive, with a range of (absolute) values between 0.75 and 3. The univariate kurtosis coefficients of most of the items were positive, with value net above the reference value 3. The analysis of the significance showed that the unvariate distributions of the items (except for items 58 and 65) are asymmetric (test D'Agostino $p<0.05$) and are characterized by (except for the distribution of items 46. 54. 57. 58. 59. 60. 65) a kurtosis coefficient significantly different from the value 3 (test Anscombe-Glynn, $p<0.05$).

After elimination of irrelevant items based on the absence of correlation between the items of the same construct, the modified factorial model including 20 items, model based on the standard model, demonstrated a good fit to data (Chi-square test. $\chi^2=166.697$, df=136, p=0.04 normed Chi-square=1.23 RMSEA=0.047 (90% CI [0.022−0.066]) SRMR=0.068, CFI=0.92 TLI=0.88, GFI=0.95 AGFI=0.92).

Table 3. Pearson's correlation matrix within items

Item	38	39	40	42	43	45	46	47	48	49	54	55	56	57	58	59	60	61	62
38	1																		
39	0.48*	1																	
40	0.43*	0.29#	1																
42	0.55*	0.31+	0.34*	1															
43	0.53*	0.29#	0.32*	0.65*	1														
45	0.31+	0.18	0.42*	0.23†	0.30+	1													
46	0.44*	0.16	0.60*	0.40*	0.47*	0.43*	1												
47	0.20±	0.16	0.17	0.05	0.19	0.25##	0.26##	1											
48	0.37*	0.20±	0.39*	0.38*	0.45*	0.43*	0.62*	0.45*	1										
49	0.16	0.19	0.09	0.20†±	0.24†	0.25##	0.22++	0.11	0.29#	1									
54	0.39*	0.13	0.48*	0.24†	0.31+	0.24†	0.61*	0.28##	0.42*	-0.05	1								
55	0.38*	0.31+	0.26##	0.33**	0.31+	0.50*	0.33**	0.30+	0.35*	0.20±	0.31**	1							
56	0.37*	0.13	0.13	0.20±	0.25##	0.24†	0.18	0.28##	0.30#	0.16	0.24†	0.26##	1						
57	0.28#	0.18	0.28##	0.13	0.15	0.26##	0.41*	0.26##	0.35*	0.21++	0.49*	0.31**	0.45*	1					
58	0.37*	0.17	0.30+	0.24†	0.22++	0.34*	0.44*	0.27##	0.36*	0.14	0.53*	0.38*	0.45*	0.69*	1				
59	0.20±	-0.05	0.22++	0.11	0.15	0.30+	0.36*	0.27##	0.35*	0.18	0.35*	0.26##	0.37*	0.59*	0.70*	1			
60	0.13	-0.03	0.27##	0.002	0.10	0.29#	0.28#	0.25##	0.40*	0.08	0.30+	0.27##	0.39*	0.46*	0.56*	0.66*	1		
61	0.16	0.10	0.27##	0.02	0.01	0.04	0.15	0.16	0.22++	-0.02	0.23±	0.11	0.46*	0.48*	0.50*	0.46*	0.47*	1	
62	0.13	0.01	0.09	0.16	0.10	0.17	0.09	0.12	0.11	0.11	0.20±	0.29#	0.50*	0.37*	0.32**	0.30+	0.24†	0.27##	1
63	0.43*	0.34**	0.33**	0.33**	0.28‡	0.24†	0.25##	0.10	0.21±	0.22++	0.24†	0.37*	0.40*	0.34**	0.36*	0.23†	0.31+	0.13	0.61*

*p<0.001; ** p=0.001; + p=0.002; # p=0.003; ‡ p=0.005; ##p=0.01; †p=0.02; ++ p=0.03; ±p=0.04;
numbers without any sign are not statistically significant (p<0.05)

The Second Order QOL Model with Reflective Items

The number of the information units on sample representing variances and covariances was equal to q(q+1)/2=210, where q represented the number of the indicators. The number of the estimated parameters was equal to 47, these being 11 loadings coefficients, 18 measurement error variances, 9 residual variances 8 loadings coefficients of first order factor, 1 second-order factor variances. The number of degrees of freedom (df) was equal to 163. The MLM estimation procedure was convergent after 70 iterations, respectively 47 iteration by the WLSMV method.

The second-order HRQOL model had the adjusted Chi-square statistics with Satorra-Bentler correction equal to 214.650, df=163, p=0.004. Because of the sensitivity of the χ^2 test to increased sample size, the observed significance level was also calculated by Bollen-Stine-type bootstrap method with a number of re-sampling equal to 1000, obtaining the value p=0.19>0.05. The observed significance level obtained by the WLSMV method was lower than 0.001 to the same number of degrees of freedom.

Using the MLM and WLSMV methods was found that: χ^2/df= 1.32 for MLM and 1.61 for WLSMV, the RMSEA= 0.057 (90% CI RMSEA [0.040−0.071] respectively RMSEA=0.07 (90% CI RMSEA [0.06−0.09]). According to the value of GFI index obtained by the two estimation methods,. the covariance matrix reproduced by the tested model explained 94% respectively 97% of the total variability in the sample covariance matrix. From the values of the CFI index was found a relative improvement by 86% respectively 91% in the fit of the tested model compared to the one of the independence model (model with all variables supposed uncorrelated). The rest of fit indexes also had values within the recommended limits: SRMR=0.09, TLI=0.83, AGFI=0.91 respectively WRMR=0.98, TLI=0.90; AGFI=0.96 for WLSMV method.

The final model had all indicators with significant loadings coefficients with a large effect size (standardized value) superior to 0.50, except for one item. As for the 1st order factors, the standardized loadings coefficients indicated a large effect size comprised between 0.50-0.92. The standardized estimates of model parameters were presented in the Figure 1.

It was found that the second-order HRQOL factor was best measured by the first order factors presented in their order of relevance: PH (Physical functionality), FA (Fatique), PA(Pain), Emotional functionality (EF), SR (Social role accomplishment), SF (Social functionality), CF (Cognitive functionality), LA (Lack of appetite) and IN(Insomnie).

Concerning the amount of variance in the indicator explained by the common factors (communality) it has been found that PH factor explained 38% of the total variance of Item38, 16% of variance in Item39 and 55% of the variability of Item40. The SR factor explained 71% of the total variance in Item42 and 72% of the variance of Item43. The CF factor explained 79% of the total variance of Item56 and 40% of the Item 61 and the SF factor explained 51% of the variability of Item62 and 83% of the Item63 variance. The EF factor explained 62% of the Item57 variance and 75% of the Item58 variation, 62% of the Item59 and 49% of the Item60. The FA defined by 3 items, explained 74%, 56% and 56% of their variability while the PA factor defined by 2 items, explained 47% and 70% of their variance. The proportion of the total variance of the 1st order factors explained by the 2nd order HRQOL factor was comprised between 23% and 82% with the largest effect on factors: PF, FA, PA and SR. The proportion of unexplained variance of indicators varied from 16% and 65% for most of the indicators (except for one item whose proportion of unique variance was greater than 80%).

All the unstandardized estimated parameters obtained by the MLM method were statistically significant. The standardized estimates of model parameters of seconder order CFA model were presented in the Figure 1.

The Second Order MIMIC Model

The estimated parameters number was equal to 53: 11 loadings coefficients of the 1st order factors. 18 measurement errors variances, 5 residual variances (disturbances) of the 1st order factors, 1 residual variances (disturbances) of the 2nd order factors, 4 loadings coefficients of the 2nd order factors, 4 path coefficients of formative indicators, 4 variances and 6 covariances of exogenous factors. The number of freedom degree (df) was equal to 157. The assessment procedure was convergent after 78 MLM iterations and 64 WLSMV iterations.

In the first step of MIMIC model testing, the fully saturated structural model was estimated. This model showed acceptable fit to the data (*SB* $\chi2$ =209.261; *df*=157; p-value=0.003; CFI=0.86, TLI=0.82; GFI=0.94, RMSEA=0.057 (90% CI RMSEA [0.039−0.073]). In the next step, the model was trimmed by constraining the non-significant paths to zero. The trimmed MIMIC model showed an acceptable fit by both estimation methods (MLM: *SB* $\chi2$=211.878; *df*=159; $p<0.003$; TLI=0.82; RMSEA=0.057 (90% CI RMSEA [0.039−0.073]) respectively WLSMV: $\chi2$=254.732; *df*=159; $p<0.001$; TLI=0.90; RMSEA=0.07; 90%CI RMSEA [0.059–0.09]). The normed Chi-square index (χ^2/df) was equal to 1.33 for MLM and 1.60 for WLSMV. According to the GFI index values obtained through both estimation methods, the implied model covariance matrix explained 94% and 97% of the sample covariance matrix. Amongst the CFI index values, a relative improvement of by 85% respectively 92% in the fit of the tested model compared to the one of the independence model. The rest of fit indexes also had values within the recommended limits: SRMR=0.09, AGFI=0.91 respectively WRMR=0.96. AGFI=0.96 for WLSMV method.

The statistical significance of the estimated parameters has been the same for both methods. The loadings coefficient values associated to the 1st order factors have been the same with the second order CFA measurement for HRQOL construct. The final MIMIC model had a global effect size (R^2) for the endogenous factor HRQOL equal to 0.94. It was found that the second-order HRQOL factor was best measured by the first order factors: PH, EF, SR, SF and CF. Concerning formative indicators, only fatique and pain showed a positive direct effect on HRQOL (γ=0.65. p<0.001 respectively γ=0.41, p=0.023).

The path diagram of the final model was presented in the Figure 2.

After evaluation the models on the basis of goodness-of-fit test and indexes, it was analyzed the reliability of first and second order latent factors.The reliability coefficients of the first order latent factors varied from 0.67 to 0.87 showing a good reliable indicators of them. Both models have revealed an acceptable reliability of the second order latent factor (Table 3).

Table 4. The reability coefficients of second order latent factor (HRQOL)

	Omega L1	Omega L2	Partial Omega L1
Second order CFA model	0.84	0.88	0.94
Second order MIMIC model	0.71	0.80	0.90

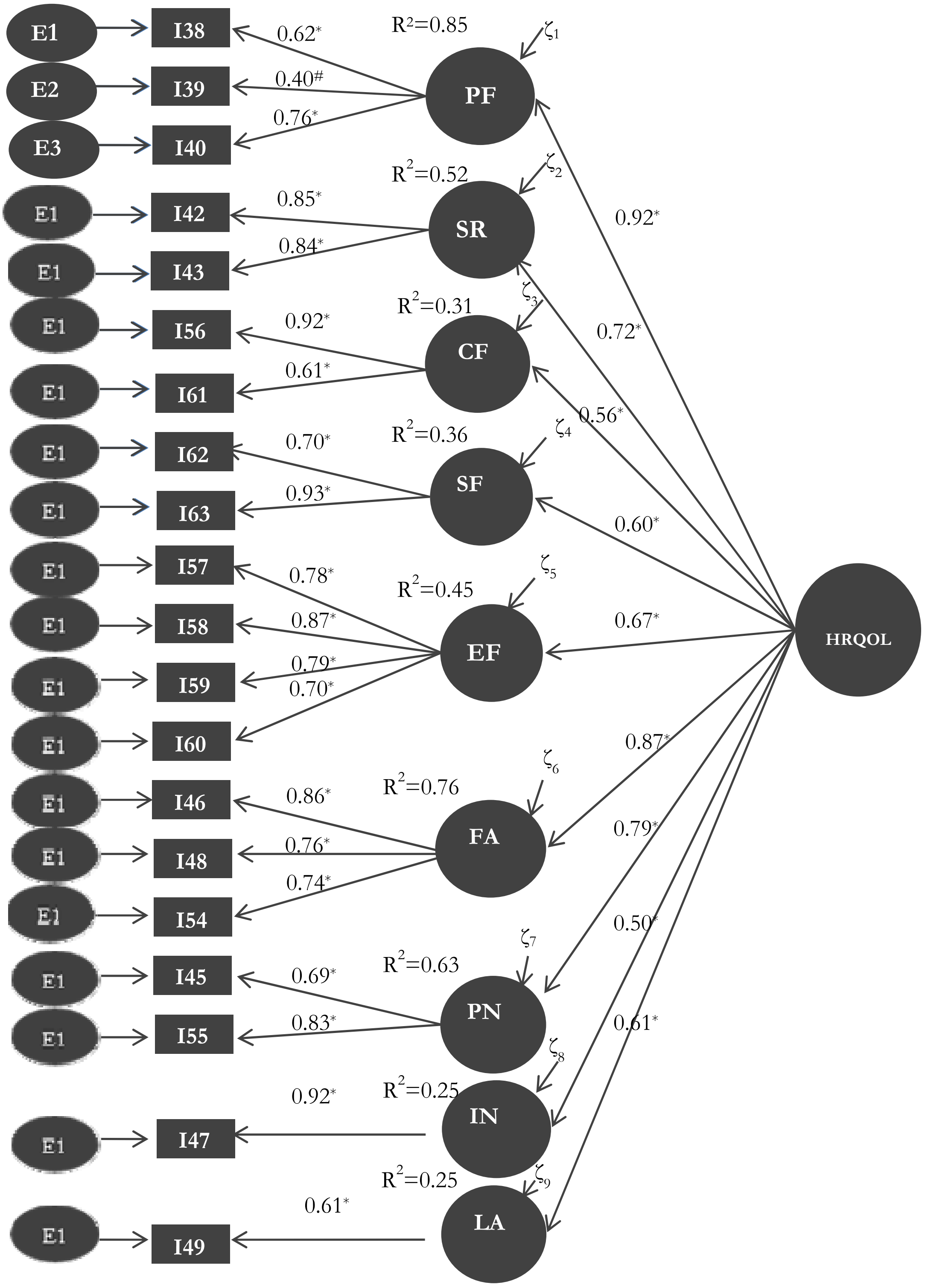

Figure 1. Standardized estimated parameters values for the second-order CFA model

N.B. Rectangles indicate observed variables (items); ellipses indicate latent factors. Latent factors: *Physical functionning* (PF); *Fulfillment of social roles* (SR); *Cognitive Confidence* (CF); *Social functionning* (SF); *Emotional functioning* (EF); *Cognitive functionning* (CF); *Fatique* (FA); Pain (PN); *Insomnia* (IN); *Lack of appetite* (LA). Figures show standardized loadings coefficients and their significance: *p<0.001; # p<0.05*. Errors Variances were not shown for the sake of clarity.

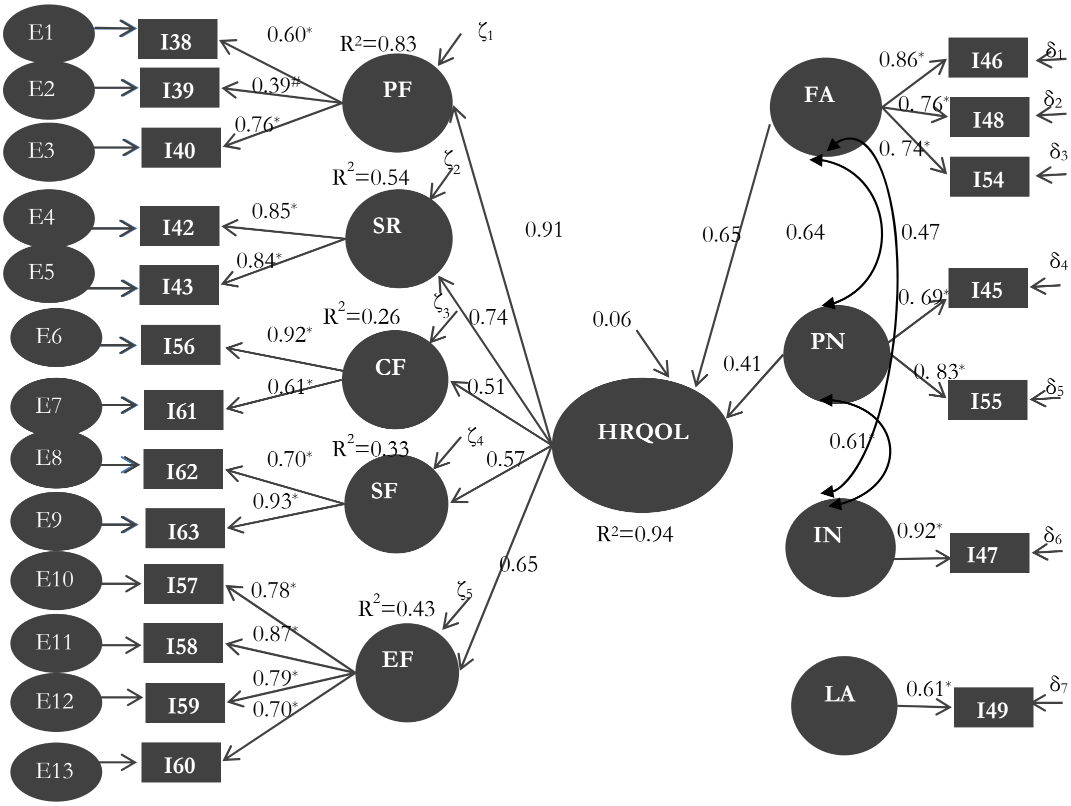

Figure 2. Standardized estimated parameters values for the second-order MIMIC model

N.B. Rectangles indicate observed variables (items); ellipses indicate latent factors. Latent factors: *Physical functionning* (PF); *ulfillment of social roles* (SR); *Cognitive Confidence* (CF); *Social functionning* (SF); *Emotional functioning* (EF); *Cognitive functionning* (CF); *Fatique* (FA); Pain (PN); *Insomnia* (IN); *Lack of appetite* (LA). Figures show standardized loadings coefficients and their significance: *p<0.001, $^{\#}$p<0.05*. Errors variances not shown for the sake of clarity.

We also analyzed the convergent validity of first order latent factors in order to confirm the measurement models. Based on the standardized loadings indicators, the average variance extracted values were comprised between 0.58 and 0.72 except for PH factor. The construct reliability omega coefficients were greater than average variance extracted values for the all first order latent factors.

Discussion

The aim of our study (to test the factorial structure of HRQOL in order to find his reliable dimensions and measures for patients with cervix pre-malign and malign pathology to the reproducibility age) was achieved. The studied items are able to measure what it is intended to measure.

We built the HRQOL as a latent factor described in two ways: by reflective and formative indicators. With the second-order MIMIC model, we succeeded in certainly separating the „sources" and the consequences of the health related quality of life and the higher order CFA, all indictors (including symptomatology) were considered as facets or aspects of HRQOL. Unfortunately, the Chi-square difference test cannot be used to compare these two alternative non nested models, but reported to fit indices, both showed a good fitting to data. The model with formative indicators associated to HRQOL construct was studied by Boehmer and Luszczynska [18] on a heterogeneous number of patients suffering from different types of cancer. The MIMIC model studied in the present work confirmed the plausibility of formative indicators for HRQOL construct and extended it to other pathology with formative indicators representing specific symptomatology.

The advantage to test some superior order measurement model for HRQOL concept is the possibility to calculate the global score (index) of HRQOL with equal or unequal weights of items for the patients presenting the studied pathology. The global score based on the scores of reflective indicators is considered much more reliable than the obtained score answering to a simply question: "How would you assess your health related quality of life?", question with no stable reference framework which leaves some place of various interpreting. The weight of the reflective indicators scores for the achievement of a summary score has no practical relevance [16] but for the formative ones the establishment of some weight would be important because they affect independently HRQOL. The HRQOL models found in literature commonly ignored aspect of the existence of formative indicators that affect HRQOL in a different way from reflective indicators.

The confirmatory factor analysis is the optimal method for study the structure of a set of items. The exploratory factor analysis (EFA) was also used to examining the structure of QOL instruments [19,27] but it has several disadvantages: i) it is an exploratory not "theory-driven" technique that can generate different models of which can be selected the most sensitive model for research purposes; ii) it use only reflective indicators; iii) it not allows representation of not perfectly reliable measures (indicators with errors).

A limitation of this study has been the models choice which was not at all exhaustive we used an alternative model approach; there is the possibility to exist other theoretical alternative models generalization of the two models.

The second limitation consists to the small sample size which could reduce the result generalizability; the modelling by structural equations generally needs large samplings. Even there is no general rule valid in any case relative to the reference value defining a large sample we should always consider the dependence between the variables distribution, the model complexity and the psychometric properties of the indicators. Even the simulation studies [46] recommended a sample size equal to 100 subjects for the model with 3-4 indicators per factor, there are studies claiming that the models created for small and medium sample can be tested if there are no convergence issues improper solutions such as negative variance (Heywood cases) or simply there is no possibility to study the pattern on a large sample [47]. For the present study, there have been no convergence problems of estimation method or improper solutions but the future researches should consider the reply of obtained results on large sample to assure the cross-validation of measurement models.

Conclusion

The confirmatory factor analysis revealed the existence of the two measurement HRQOL models that could be applied to the patients with premalignant and malignant cervical pathology, models for evaluate the level of the health related quality of life.

List of abbreviations

QOL = quality of life concept
HRQOL = health related quality of life concept
WLSMV = weighted least squares estimation adjusted for mean and variance
RMSEA=Root Mean Square Error of Approximation, Standardized Root Mean Square
SRMR=Standardized Root Mean Square Residual
WRMR= Weighted Root Mean Square Residual
NNFI= Nonnormed Fit Index
CFI= Comparative Fit Index
GFI= Goodness-of-fit Index
AGFI= Adjusted Goodness-of-Fit Index

PF= Physical functionning
SR= Fulfillment of social roles
SF= Social functionning
EF= Emotional functioning
CF= Cognitive functionning
FA=Fatique
PN=Pain
LA=Lack of appetite
IN=Insomnia

Conflict of Interest

The authors declare that they have no conflict of interest.

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