

Spanish General Population Normative Data Analysis for the EORTC QLQ-C30 and Relationships Between Sex, Age, and Health Conditions

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Research

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Abstract

Purpose

General population normative data for the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire facilitates interpretation of data assessed from cancer patients. This study aimed to present normative data of the Spanish general population.

Methods/Patients

Data were obtained from a prior larger study collecting EORTC QLQ-C30 norm data across 15 countries. Data were stratified by sex and age groups (18–39, 40–49, 50–59, 60–69 and >70 years). Sex and age distribution were weighted according to population distribution statistics. Sex- and age-specific normative values were analysed separately, as were participants with versus those without health conditions. Multiple linear regression was used to estimate the association of each of the EORTC QLQ-C30 scales with the determinants age, sex, sex-by-age interaction term, and health condition.

Results

1165 Spanish individuals participated in the study. Differences were found by sex and age. The largest sex-related differences were seen in fatigue, emotional functioning, and global QoL (Quality of Life), favouring men. Largest age differences were seen in emotional functioning, insomnia, and pain, with middle-aged groups having the worst scores. Those >60 years scored better than those <60 years on all scales except for physical functioning. Participants with no health conditions scored better in all QLQ-C30 domains.

Conclusions

The present study highlights differences in HRQoL between specific sex/age strata and especially between persons with and without a health condition in the Spanish general population. These factors must be considered when comparing general population HRQoL data with that of cancer patients.

Background

Health-related quality of Life (HRQoL) is a key outcome in oncology that is widely assessed in clinical studies of patients with cancer [1] and it is now frequently integrated into treatment evaluation in clinical practice [2]. HRQoL is typically assessed with standardized questionnaires whose scores are to be appropriately interpreted to obtain clinically relevant information [3]. The availability of reference data from general population samples improves the interpretability of the data. Population norms are useful in clinical work to assess individual patients' needs, use as target values for patients, and interpret the results of clinical studies and clinical trials [4, 5].

A true HRQoL baseline assessment is always missing prior to diagnosis and frequently prior to starting treatment in studies of patients with cancer [1, 5, 6], as newly diagnosed patients may already have physical or emotional symptoms. Therefore, reference values from population norms may be useful to substitute missing baseline values.

The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Group (QLG) developed the HRQoL core questionnaire—QLQ-C30—more than 25 years ago [7]. This 30-item instrument is one of the most widely used cancer-specific HRQoL questionnaire [4, 8–10], covering key cancer symptoms and aspects of functional health. More recently, a summary score was developed [11]. This EORTC QLQ-C30 Summary Score was introduced to supplement the detailed 15-scale profile of the QLQ-C30.

Several supplements have been developed to facilitate interpretation of QLQ-C30 scores: reference values manual for cancer patients that also included data from the general population [12], thresholds for clinical interpretation of QLQ-C30 scales [13], as well as definition of minimal important differences (MID) [14]. Additionally, general population norms from the QLQ-C30 have been obtained for specific Northern and Central European countries—Denmark [5, 15], Norway [16, 17], Sweden [18, 19], Germany [20–22], the Netherlands [1, 23], Slovenia [6]—as well as South Korea [24] and Colombia [25]. However, the QLQ-C30's normative data for countries in Southern Europe—except Croatia [26]—is lacking. Reference HRQoL data from that region may differ from that of other areas due to possible cross-cultural differences [27].

Basic participant characteristics, such as age, sex, and health conditions, may also impact general-population HRQoL scores; hence, they should be considered when interpreting HRQoL results [5]. For example, older patients constitute the largest group of oncology patients [28], and maintaining HRQoL is a key aim of their treatment [29]. Furthermore, studies indicate men report better functioning and fewer symptoms than women [21, 25], and that the presence and severity of symptoms increase while function declines with age [21]. Furthermore, health conditions, such as chronic pain or diabetes, may also impact the areas measured by the QLQ-C30 [5, 6, 21, 24].

A recent study provided EORTC QLQ-C30 general population normative data pooled from 15 countries: 11 within the European Union (including Spain) plus Russia, Turkey, Canada, and United States [30]. Substantial variation in mean QLQ-C30 scores across countries were observed in this study, thereby underscoring the need of country-specific normative values. Therefore, we aimed to report HRQoL normative data for the Spanish general population, including age- and sex-specific values plus values for persons with versus those without health conditions.

Material And Methods

Sampling

For this study, data was collected via an online survey managed by GfK SE, a market research company experienced in online panels. The population sample was stratified by sex and age, including 100 women and 100 men per pre-specified age stratum (18–39, 40–49, 50–59, 60–69 and ≥ 70 years). The sampling was also stratified based on household size and geographic region, allowing for sufficient sample sizes per group to establish normative values of age- and sex-specific subgroups. However, stratification resulted in a non-representative age- and sex-distribution; thus, post-hoc weighting of the data was required. Weighting was done according to the sex and age distributions indicated in the United Nations official 2015 population distribution statistics report [31].

Sociodemographic data were collected, including sex, age, education, marital and employment status, and presence of self-reported health conditions, including cancer, via an online data form. Participants were asked to report only health conditions diagnosed by a doctor.

The EORTC QLQ-C30 Questionnaire

The EORTC QLQ-C30 [32] includes 30 items covering five ‘functioning’ scales (physical, role, social, emotional, and cognitive functioning), nine symptom scales (fatigue, pain, nausea/vomiting, dyspnoea, sleep disturbances, appetite loss, constipation, diarrhoea, and financial difficulties), and a global QoL scale. The questionnaire’s Spanish version has been validated for use in Spain [33]. All questions are answered on a 4-point Likert-type scale, except for two global QoL items using a 7-point scale. The questionnaire is scored on a 0–100 metric according to the standard EORTC scoring algorithm [34]. The recently introduced QLQ-C30 Summary Score was calculated as the mean of the combined 13 QLQ-C30 scale scores (excluding financial impact and Global QoL). Before calculating the mean, symptom scale scores are reversed, so that higher scores indicate lower symptom burden [11]. For the functioning scales, the global QoL scale and the summary score, a higher score indicates better health. For the symptom scales, a higher score indicates a higher level of symptom burden.

Statistical analyses

Normative values are given as means and standard deviations (SD) separately for women and men in five age groups (18–39, 40–49, 50–59, 60–69, and 70+ years) and in combined sex and age groups. Furthermore, we calculated normative scores for participants with and without health conditions within each group.

As in prior studies [16, 20, 35], we also used multivariable linear regression to estimate the association of each of the QLQ-C30 scales (dependent variable) with age (linear and quadratic term), sex (0 = men, 1 = women), sex-by-age interaction term, and health condition (0 = none, 1 = one or more). Since all participants were 18 years or older, we used an age variable by counting the years above 18 to estimate regression coefficients (i.e. participant age minus 18). The regression models predict normative scores for individuals or patient groups based on their sex, age and health conditions more precisely than the normative tables indicate. SPSS version 25.0 was used for all analyses.

Results

Participant characteristics

In total, 1165 Spanish individuals participated in the study. The raw (unweighted) data set included 54.2% men (weighted, 48.6%); mean age was 54.3 (SD 14.7) years (weighted, 48.1 [SD 16.5] years). The applied weights for the individual participants ranged from 0.36 to 3.52.

In the weighted data, 91.8% % of the sample had at least post-compulsory education, 70.9% were married/in a steady relationship, 52.7% were working, and 61.6% presented one or more health conditions. Detailed sample characteristics are presented in Table 1.

Normative data for the general Spanish population

Table 2 shows the EORTC QLQ-C30 reference values for the general population of Spain. The scores for the global sample in the functional scales ranged between 85.7 and 87.8, except for emotional functioning (77.1). Symptoms scores were > 20 points in fatigue, insomnia, and pain. The mean summary score was 84.8. For further details please see Table 2. Floor and ceiling effects for the EORTC QLQ-C30 scales (weighted data) are shown in Table 3.

Normative data by sex and age

Table 4 shows descriptive statistics by sex. In the weighted descriptive data, the largest mean differences by sex were fatigue (men 21.6 versus women 26.5 points), emotional functioning (men 79.2 vs women 75.0 points), and global QoL (men 68.4 vs women 65.3 points), with better QoL in men. Mean differences for physical functioning, dyspnoea, financial problems, and summary score were below 1 point (see tables 4 and 5).

The largest pairwise mean differences between age groups were observed for emotional functioning (age 40–49 years: 73.1 points vs. age 70+ years: 85.1), and insomnia (age 50–59 years: 28.3 points vs age 70+ years: 19.2), and pain (age 40–49 years: 26.6 points vs age 60–69 years: 17.6 points; see Table 2).

In an additional analysis, comparing participants above and below 60 years, participants ≥ 60 years old had better scores across all QLQ-C30 domains, including summary score, except physical functioning. The greatest mean differences were in emotional functioning (+ 8.7 points), insomnia (-7.3 points), financial impact (-6.5 points), social functioning (+ 5.8 points), and fatigue (-5.8 points).

In women, comparing age groups against the overall mean for women we found the five largest differences for: insomnia + 7.1 points (women aged 50–59 years), emotional functioning + 7.0 (women aged > 70 years), financial problems + 6.3 points (women aged 40–49 years), physical functioning - 5.9 points (women aged > 70 years), and pain + 5.7 (women aged 40–49 years). In men, the comparison of the age-group specific mean against the overall mean in men showed the five largest differences for: emotional functioning + 10.3 points, insomnia - 9.9 points, pain - 8.3 points, fatigue - 7.7 points (all in men aged > 70 years), and appetite loss + 6.6 points (men aged 18–39 years).

Normative data by sex and age, and health conditions

In the total sample, the largest differences between participants with and without health conditions were found for pain (30.6 points vs 10.1), global QoL (59.1 vs 79.3), and fatigue (30.3 vs 13.5). In men, the largest differences were observed for global QoL (61.2 vs 80.0), pain (28.4 vs 10.6), and role functioning (79.8 vs 94.2). In women the largest differences were found for pain (32.6 vs 9.6), global QoL (57.2 vs 78.6), pain (32.6 vs 9.6). All of these differences were in favour of participants without health conditions. For further details please see Table 5.

Regression models for prediction of normative scores

To predict scores for each of the QLQ-C30 scales for an individual or a group, we developed regression models based on age, sex (0 = men, 1 = women), and health conditions (0 = none, 1 = one or more). Details on the regression models are given in Supplementary Table S1.

The regression model uses years above 18 as age variable (i.e. participant age minus 18). To give an example, for a female participant aged 50 years, and suffering from one or more health conditions, the predicted score for Physical Functioning can be obtained via the following equation:

Physical Functioning (predicted) = $86.085 + \text{sex} * 2.514 + (\text{age}-18) * 0.529 + (\text{age}-18)^2 * -0.006 + \text{sex} * (\text{age}-18) * -0.003 + \text{health condition} * -11.426$.

Physical Functioning (predicted) = $86.085 + 1 \text{ (female)} * 2.514 + (50 - 18) * 0.529 + (50 - 18)^2 * -0.006 + 1 * (50 - 18) * -0.003 + 1 \text{ (one or more health conditions)} * -11.426 = 87.861$

Discussion

In this article, we have reported a detailed analysis of normative data for the EORTC QLQ-C30 in the Spanish general population. While we observed age- and sex-specific differences, the most important aspect with a substantial negative impact on all EORTC QLQ-C30 domains was the presence of a health condition. Scores in the QLQ-C30 for the overall sample were generally high, in line with the scores from the international study's global sample [30]. Comparing the results from this analysis against the global sample published previously [14], differences between Spanish data and the global sample were trivial or small. Regarding summary score, Spain ranked 6th among the 13 European countries analysed in the international study, with only two countries outperforming Spain by more than 1 point (Austria + 3.2 points, Netherlands + 3.9 points). The summary score in our study aligns with that of a study from Croatia [26] but is much lower (7 points) than in the study from The Netherlands [1].

Fayers [36] has suggested possible reasons for these differences among countries including health habits and cultural effects: communities may perceive their HRQoL differently due to variations in expectations. Other reasons could involve selection bias or differences in the interview systems [22], although this is not likely in the overall sample as the selection process was standardised across the different countries.

Our EORTC QLQ-C30 scores were aligned with those in the EORTC Reference Values manual for the general population [12]. Further, similar to our results, small differences by sex for emotional functioning and fatigue [14] were also found in the main general population study [30], other studies performed in Europe [1, 6, 17–19, 23, 26], and various other countries [25, 37]. Contrary to ours, however, most of those studies found differences in various HRQoL domains. One exception was a study performed in Denmark, where differences in other scale items were found (small differences, as in ours). The Danish authors indicate that differences by sex among various countries could be related to health and lifestyle differences [5].

Our HRQoL results are in keeping with an Australian study that showed that older adults have higher overall HRQoL (highest scores for 11 QLQ-C30 domains [37]. Contrary to our data, some other studies have reported substantially lower HRQoL in older participants [1, 4–6, 16, 23]; in others, age effects were weak [22, 26]. Nevertheless, some differences we found with sex and increasing age are aligned with results of the main general population study [30] and other QLQ-C30 studies [1, 6, 17] as well as the reference values study of the EuroQoL-5D-5L for Spain [38].

Our higher item/scale scores for older adults could be related to people being better at adapting to situations as they age [39]. Also, older adults in Spain tend to have good health and life expectancies among the highest in Europe: 86.1 years for women; 81.6 years for men [40]. Our results could also reflect the fact that patients > 80 years old were underrepresented in our sample (1.3 % of participants), and a decline in HRQoL could be expected at this age [1, 5, 21].

Other QLQ-C30 studies have indicated declines in HRQoL in people with chronic health conditions [1, 5, 18, 21, 23]. Thus, the results of this and other studies highlight the importance of accounting for this variable in HRQoL studies of both cancer patients and the general population. In view of this finding, HRQoL of patients with cancer may be impacted more by comorbidities than by late-stage treatment effects [6, 23, 41]. The presence of other health conditions could be one reason some studies have found lower HRQoL in older adults [6].

As mentioned above, the use of normative data is only one way to facilitate interpretation of PRO scores. Unlike the concept of MID's that support interpretations of PRO score differences between groups or time points, normative data is primarily applicable for interpreting cross-sectional data from individual patients or patient groups. In this regard, normative data provides a different perspective than thresholds (cut-offs). Thresholds allow for categorisation of patients according to clinically relevant criteria [13]; they can also be linked to clinical actions and allow calculations of prevalence rates. However, they provide almost no detailed information of severity levels. PRO scores using normative data maintains the level of information conveyed by scores, adding further information by linking them to normative populations. Normative data can be integrated into the scoring of a PRO instrument itself, as usually done by calculating T-scores [42], but they can also be a key component of graphical result presentations [43], such as heat maps or reference lines in graphical charts. A key consideration when using normative data is the selection of the reference population. We consider general population data the most appropriate comparator when interpreting PRO scores of cancer survivors, or when estimates of pre-disease levels of symptoms or functional health are required. For populations of patients undergoing active anti-cancer treatment, it may be more appropriate to rely on reference data from cancer patient populations that share essential disease and treatment characteristics.

This study has several limitations. It would have been interesting to include a higher number of people older than 80 years to study the effect of aging on HRQoL in this group.

However, the authors of the main general population study [30] have indicated obtaining a larger sample of this hard-to-reach group was outside the scope of their study as it would have substantially increased the budget for GfK which was financially no viable

Also, our sample was relatively highly educated. This plus the lack of elderly persons could be a consequence of conducting the surveys online. The effect of comorbidity on HRQoL has been studied in organising participants into just two groups based on the presence/absence of comorbidities. It might be interesting to have a future study in which comorbidities can be studied in more detail.

In conclusion, Spanish normative data presented in this article will enhance outcome interpretation in future studies, by providing benchmark data against which study findings from the EORTC QLQ-C30 could be compared. Our results highlight that age, sex and comorbid health conditions must be considered when comparing HRQoL data from the general population with that of cancer patients [24, 36]. Easier interpretation of scores from PRO instruments is key to fostering their wider use in clinical research and daily practice.

Declarations

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Conflicts of interest/Competing interests

The authors report no conflicts of interest

Ethics approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate: Informed consent was obtained from all individual participants included in the study

Consent for publication All authors have consented to submission of this article for publication

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Tables

Table 1: Participants' demographic characteristics (N = 1165)

		Unweighted data	Weighted data
Sex N (%)	Male	632 (54.2%)	567 (48.6%)
	Female	533 (45.8%)	598 (51.4%)
Age	M (SD)	54.3 (14.7)	48.1 (16.5)
	Median [IQR]	56 [43-66]	48 [34-61]
Education N (%)	Less than compulsory education	14 (1.2%)	15 (1.3%)
	Compulsory school	83 (7.2%)	79 (6.8%)
	Some post-compulsory school	132 (11.4%)	117 (10.1%)
	Post-compulsory below university	360 (31.1%)	334 (28.8%)
	University degree (Bachelor)	374 (32.3%)	392 (33.9%)
	Postgraduate Degree	196 (16.9%)	220 (19.0%)
	Prefer not to answer	6	8
Marital status N (%)	Single/not in steady relationship	120 (10.3%)	188 (16.2%)
	Married or in a steady relationship	854 (73.6%)	823 (70.9%)
	Separated/divorced/widowed	187 (16.1%)	150 (12.9%)
	Prefer not to answer	4	3
Employment status N (%)	Full-time employed	437 (37.6%)	507 (43.7%)
	Part-time employed	87 (7.5%)	104 (9.0%)
	Homemaker	88 (7.6%)	85 (7.3%)
	Student	14 (1.2%)	38 (3.3%)
	Unemployed	109 (9.4%)	112 (9.7%)
	Retired	352 (30.3%)	245 (21.1%)
	Self-employed	59 (5.1%)	49 (4.3%)
	Other	17 (1.5%)	19 (1.6%)
	Prefer not to answer	2	4
Comorbidity N (%)	None	391 (34.8%)	429 (38.4%)
	One or more	733 (65.2%)	688 (61.6%)
	Chronic Pain	252 (22.4%)	239 (21.4%)
	Heart Disease	55 (4.9%)	42 (3.7%)
	Cancer	31 (2.8%)	26 (2.3%)
	Depression	110 (9.8%)	113 (10.1%)
	COPD	47 (4.2%)	35 (3.1%)
	Arthritis	103 (9.2%)	96 (8.6%)
	Diabetes	135 (12.0%)	113 (10.1%)
	Asthma	59 (5.2%)	74 (6.6%)
	Anxiety disorder	97 (8.6%)	100 (9.0%)
	Obesity	148 (13.2%)	142 (12.7%)
	Drug/alcohol disorder	4 (0.4%)	6 (0.6%)
	Other	208 (18.5%)	180 (16.1%)
	Prefer not to answer	35	42
	Missing	6	6

Table 2: EORTC QLQ-C30 reference values for the general population of Spain

	All		18–39 years		40–49 years		50–59 years		60–69 years		≥ 70 years	
	N = 1165		N = 406		N = 227		N = 197		N = 146		N = 189	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Physical Functioning	86.8	16.8	87.1	16.5	87.0	17.9	87.9	15.1	88.9	14.9	83.4	18.7
Role Functioning	86.1	21.5	85.6	21.1	84.3	22.5	86.7	21.4	89.5	20.3	86.0	22.0
Emotional Functioning	77.1	22.4	74.7	24.6	73.1	22.7	75.9	21.8	80.9	19.9	85.1	16.8
Cognitive Functioning	85.7	19.4	85.6	21.2	83.5	20.6	85.7	21.1	87.3	16.2	87.2	13.3
Social Functioning	87.8	22.5	86.5	24.4	83.9	24.3	88.2	21.0	92.8	17.7	91.4	19.5
Global QOL	66.8	21.5	67.0	21.1	63.0	20.8	67.6	22.4	70.9	20.3	67.3	22.4
Fatigue	23.9	22.7	25.4	23.9	26.1	21.7	25.0	23.1	18.8	21.0	20.4	21.0
Nausea / Vomiting	4.9	14.5	7.4	18.2	5.7	14.7	4.0	12.5	2.6	10.3	1.4	7.3
Pain	22.7	24.0	21.9	24.0	26.6	24.8	24.6	24.2	17.6	21.6	21.6	23.8
Dyspnoea	12.4	20.7	13.1	21.1	13.7	21.4	12.4	20.3	10.8	21.4	10.5	18.7
Insomnia	25.2	28.0	26.3	29.1	28.1	27.7	28.3	28.9	21.0	26.0	19.2	25.2
Appetite loss	9.5	19.9	12.7	22.9	9.4	19.0	8.0	17.2	6.4	17.4	6.8	17.5
Constipation	15.3	24.1	16.4	26.0	14.4	22.2	15.3	24.9	14.1	21.3	15.1	23.0
Diarrhoea	7.8	18.1	10.4	20.8	8.9	18.2	7.0	16.9	5.5	13.7	3.7	14.6
Financial Problems	9.5	20.7	10.9	21.7	13.4	24.9	10.0	21.8	5.3	15.6	4.5	12.5
Summary Score	84.8	15.1	83.5	17.3	83.0	14.7	84.6	14.2	87.9	12.8	87.3	12.3

Table 3: Floor and ceiling effects in the EORTC QLQ-C30 scales (weighted data)

	Lowest possible score (0 points)	Highest possible score (100 points)
Physical Functioning	0.4%	36.9%
Role Functioning	0.9%	61.0%
Emotional Functioning	1.1%	25.2%
Cognitive Functioning	1.1%	50.8%
Social Functioning	1.5%	69.7%
Global QOL	0.9%	8.5%
Fatigue	26.2%	1.4%
Nausea / Vomiting	85.7%	0.6%
Pain	37.4%	2.0%
Dyspnoea	69.3%	1.1%
Insomnia	46.3%	4.2%
Appetite loss	77.9%	1.1%
Constipation	64.8%	2.9%
Diarrhoea	81.1%	1.1%
Financial Problems	79.0%	1.7%
Summary Score	0.3%	4.7%

Table 4: EORTC QLQ-C30 reference values for men in the general population of Spain

	Men												Women					
	Total		18–39 years		40–49 years		50–59 years		60–69 years		≥ 70 years		Total		18-39 years		40-4	
	N = 567		N = 206		N = 115		N = 98		N = 70		N = 78		N = 598		N = 201		N =	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Physical Functioning	86,8	18,2	84,8	19,0	86,0	20,7	89,8	14,9	89,8	15,5	87,0	17,4	86,8	15,4	89,5	13,2	88,1	14,9
Role Functioning	84,9	22,7	81,8	23,3	83,0	24,7	86,3	22,4	89,7	19,9	89,7	19,0	87,2	20,3	89,4	17,8	85,6	20,3
Emotional Functioning	79,2	21,8	75,6	25,2	76,5	20,8	79,1	19,6	83,0	18,9	89,5	13,1	75,0	22,9	73,9	24,0	69,7	23,9
Cognitive Functioning	86,9	19,2	85,9	22,5	84,8	20,2	89,5	16,7	87,8	16,6	89,0	12,0	84,5	19,6	85,4	19,9	82,1	19,9
Social Functioning	88,9	21,7	86,4	25,5	85,6	22,2	90,7	18,4	93,7	17,4	94,0	15,1	86,8	23,1	86,5	23,2	82,1	23,2
Global QOL	68,4	20,5	68,2	20,4	64,0	19,4	67,7	22,3	73,3	17,9	72,4	20,7	65,3	22,3	65,7	21,8	62,0	21,8
Fatigue	21,0	21,6	25,1	22,9	23,1	21,0	19,5	19,5	16,4	21,3	13,3	19,4	26,5	23,3	25,8	25,0	29,3	25,0
Nausea / Vomiting	5,8	16,8	9,6	22,6	6,8	16,9	3,0	8,5	2,3	10,2	0,7	4,0	4,1	11,9	5,1	11,7	4,5	11,7
Pain	21,8	23,9	25,7	25,7	24,1	24,7	21,9	23,4	16,0	20,7	13,5	18,2	23,5	24,0	18,0	21,4	29,2	21,4
Dyspnoea	12,5	21,3	13,2	21,3	14,9	22,6	12,6	21,6	10,6	20,2	8,8	19,8	12,2	20,1	13,0	20,8	12,3	20,8
Insomnia	24,1	27,1	28,8	30,8	24,8	24,5	23,1	25,4	21,0	25,3	14,2	21,2	26,2	28,7	23,7	27,1	31,5	27,1
Appetite loss	10,6	21,2	17,2	26,4	9,2	18,2	6,3	14,6	5,7	16,7	5,1	16,2	8,5	18,5	8,0	17,6	9,6	17,6
Constipation	14,3	23,3	16,7	26,5	14,9	21,7	12,0	21,9	13,4	21,4	10,5	19,4	16,3	24,8	16,1	25,7	13,9	25,7
Diarrhoea	8,4	18,6	12,9	24,0	8,6	16,0	5,1	12,9	6,4	14,1	2,3	11,4	7,3	17,5	7,8	16,4	9,3	16,4
Financial Problems	9,9	21,5	13,2	24,7	11,4	22,6	9,0	22,0	5,2	14,8	4,3	11,2	9,1	20,0	8,5	17,8	15,4	17,8
Summary Score	85,2	16,1	81,9	19,7	83,8	15,8	87,1	12,4	88,6	12,3	90,8	10,0	84,3	14,1	85,2	14,2	82,2	14,2
THE FIVE LARGEST PAIRWISE DIFFERENCES TO OVERALL MEAN ARE COLORED; SEPARATELY FOR MEN AND WOMEN																		
Physical Functioning			-2,0		-0,8		3,0		3,0		0,2				2,7		1,3	
Role Functioning			-3,1		-1,9		1,4		4,8		4,8				2,2		-1,6	
Emotional Functioning			-3,6		-2,7		-0,1		3,8		10,3				-1,1		-5,3	
Cognitive Functioning			-1,0		-2,1		2,6		0,9		2,1				0,9		-2,4	
Social Functioning			-2,5		-3,3		1,8		4,8		5,1				-0,3		-4,7	
Global QOL			-0,2		-4,4		-0,7		4,9		4,0				0,4		-3,3	
Fatigue			4,1		2,1		-1,5		-4,6		-7,7				-0,7		2,8	
Nausea / Vomiting			3,8		1,0		-2,8		-3,5		-5,1				1,0		0,4	
Pain			3,9		2,3		0,1		-5,8		-8,3				-5,5		5,7	

Dyspnoea	0,7	2,4	0,1	-1,9	-3,7	0,8	0,1
Insomnia	4,7	0,7	-1,0	-3,1	-9,9	-2,5	5,3
Appetite loss	6,6	-1,4	-4,3	-4,9	-5,5	-0,5	1,1
Constipation	2,4	0,6	-2,3	-0,9	-3,8	-0,2	-2,4
Diarrhoea	4,5	0,2	-3,3	-2,0	-6,1	0,5	2,0
Financial Problems	3,3	1,5	-0,9	-4,7	-5,6	-0,6	6,3
Summary Score	-3,3	-1,4	1,9	3,4	5,6	0,9	-2,1

Table 5: EORTC QLQ-C30 reference values for general population of Spain by age, sex, and health condition

Male																		
	18-39 years				40-49 years				50-59 years				60-69 years				70+ years	
	one or more health conditions N=94		no health condition N=99		one or more health conditions N=75		no health condition N=34		one or more health conditions N=59		no health condition N=33		one or more health conditions N=43		no health condition N=25		one or more health conditions N=59	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	
Physical Functioning	81,8	15,9	88,6	21,6	81,4	21,9	98,1	4,3	87,2	16,4	96,3	6,9	85,3	17,6	96,8	7,6	84,2	
Role Functioning	74,9	21,3	89,9	22,5	77,0	25,4	98,9	4,2	80,3	25,6	97,8	6,9	84,9	23,2	97,1	9,6	87,1	
Emotional Functioning	67,4	25,9	83,6	23,0	72,5	23,7	85,8	10,3	73,9	20,3	88,2	15,6	78,4	20,3	90,6	13,6	88,0	
Cognitive Functioning	78,5	22,7	91,5	21,6	79,9	22,4	94,1	10,1	86,1	19,2	95,2	9,4	84,9	18,2	93,0	12,1	87,1	
Social Functioning	78,8	27,9	93,5	22,0	79,7	24,7	98,9	6,0	86,8	21,3	97,4	9,9	90,2	20,7	99,0	8,1	92,8	
Global QOL	58,4	21,1	77,8	15,6	56,4	17,5	80,6	11,8	60,9	22,3	79,4	18,8	66,8	18,4	84,1	11,1	68,0	
Fatigue	32,8	21,4	17,4	22,5	29,1	21,7	9,0	12,6	26,0	20,8	7,9	10,3	23,0	23,6	5,6	11,4	16,2	
Nausea / Vomiting	14,8	25,3	5,7	20,4	9,3	19,8	1,6	6,6	4,5	10,3	0,4	2,7	2,7	11,2	1,7	8,8	0,6	
Pain	37,0	23,2	14,5	23,0	31,9	25,5	6,5	10,2	28,1	24,0	9,2	12,7	21,8	22,8	6,3	12,3	15,5	
Dyspnoea	16,4	19,4	10,4	23,3	20,6	25,1	3,2	10,0	16,9	24,9	4,4	11,4	15,4	23,1	3,4	11,8	11,0	
Insomnia	38,5	31,0	21,9	29,4	30,4	25,6	12,9	16,5	27,4	27,2	14,9	20,1	28,5	26,6	8,7	17,0	16,3	
Appetite loss	24,0	27,3	10,3	23,2	12,3	20,7	2,2	8,3	7,0	14,9	3,5	10,4	8,8	20,4	0,5	4,1	6,4	
Constipation	25,0	29,2	9,5	22,3	19,1	23,2	5,4	12,4	16,4	25,6	5,3	12,3	17,1	23,6	7,7	16,5	13,3	
Diarrhoea	18,7	26,1	8,6	22,0	10,3	17,5	6,5	13,4	6,5	14,5	2,6	9,1	8,5	15,4	3,4	11,8	2,7	
Financial Problems	20,9	26,0	6,5	22,5	16,2	26,1	1,1	6,0	13,4	26,7	0,9	5,4	7,7	17,3	1,4	9,0	5,7	
Summary Score	74,9	17,5	88,4	20,3	79,0	17,2	94,5	5,4	83,2	13,6	94,4	6,1	84,5	12,8	95,3	7,9	89,0	
Female																		
	18-39 years				40-49 years				50-59 years				60-69 years				70+ years	
	one or more health conditions N=88		no health condition N=102		one or more health conditions N=69		no health condition N=40		one or more health conditions N=65		no health condition N=32		one or more health conditions N=49		no health condition N=24		one or more health conditions N=88	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	
Physical Functioning	84,2	15,5	93,5	9,4	83,2	16,1	96,6	5,5	83,1	16,0	91,5	12,0	84,3	16,0	94,4	6,9	77,4	
Role Functioning	80,6	20,9	96,3	10,9	79,1	22,2	97,4	7,2	83,3	22,7	94,9	13,1	84,2	24,1	98,6	6,2	79,7	
Emotional Functioning	65,1	25,6	81,9	20,2	64,4	24,4	80,6	17,1	68,6	24,9	81,9	16,0	74,8	22,7	87,5	14,0	80,6	
Cognitive Functioning	79,6	20,4	89,4	19,0	77,4	23,0	91,5	12,0	76,2	27,4	92,6	10,1	83,1	17,5	93,5	9,2	85,0	
Social Functioning	76,1	26,7	95,0	15,9	75,4	28,9	94,9	11,6	81,7	26,3	94,4	12,0	88,4	21,5	99,1	3,9	86,9	
Global QOL	53,4	21,9	76,2	16,1	52,6	19,5	78,8	15,9	61,5	22,5	80,3	16,9	61,4	22,6	82,4	13,4	59,0	
Fatigue	36,6	27,2	17,3	19,8	38,5	20,9	12,8	12,9	37,0	26,1	17,3	17,9	27,5	21,7	9,0	11,6	28,4	
Nausea / Vomiting	9,7	15,3	1,6	5,7	6,7	14,2	0,9	5,3	6,7	18,1	1,9	7,8	4,6	12,9	0,0	0,0	2,3	
Pain	30,7	23,7	8,4	12,6	38,1	24,9	13,2	15,8	33,1	25,3	15,3	20,1	26,9	23,6	4,6	9,5	33,1	
Dyspnoea	23,2	23,6	5,5	14,5	18,9	22,6	1,7	7,4	16,2	20,9	3,7	10,6	16,4	26,2	0,9	5,6	14,3	

Insomnia	35,9	26,9	14,9	23,7	41,8	31,4	13,7	18,3	37,0	32,4	24,1	26,0	27,9	29,5	9,3	15,2	25,3
Appetite loss	15,1	22,8	2,7	9,2	12,9	23,2	4,3	11,3	13,0	22,1	3,7	10,6	10,0	21,4	1,9	7,8	9,7
Constipation	20,5	27,1	9,9	20,1	14,9	22,7	12,8	23,7	20,8	30,4	13,9	20,2	16,0	23,1	12,0	18,2	19,4
Diarrhoea	14,5	20,9	2,2	8,3	12,4	23,8	3,4	10,2	8,8	20,2	6,5	13,4	5,9	15,1	2,8	9,4	5,9
Financial Problems	13,2	21,0	3,9	13,2	22,9	31,4	3,4	10,2	15,3	24,4	1,9	11,1	8,2	19,9	0,0	0,0	5,9
Summary Score	76,9	14,6	91,8	10,1	76,6	13,3	92,2	6,6	78,5	17,1	89,9	7,8	83,0	14,6	94,8	4,2	82,4

Total																	
18-39 years				40-49 years				50-59 years				60-69 years				70+ years	
	one or more health conditions N=182		no health condition N=201		one or more health conditions N=144		no health condition N=74		one or more health conditions N=124		no health condition N=66		one or more health conditions N=92		no health condition N=49		one or health condition N=146
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean
Physical Functioning	83,0	15,7	91,1	16,7	82,2	19,3	97,3	5,0	85,0	16,3	93,9	10,0	84,8	16,7	95,7	7,3	80,1
Role Functioning	77,7	21,3	93,2	17,8	78,0	23,8	98,1	6,0	81,9	24,1	96,4	10,5	84,6	23,6	97,8	8,0	82,7
Emotional Functioning	66,2	25,7	82,8	21,6	68,6	24,3	82,9	14,6	71,1	22,9	85,1	16,0	76,5	21,6	89,1	13,7	83,5
Cognitive Functioning	79,0	21,6	90,5	20,3	78,7	22,6	92,7	11,2	80,9	24,3	93,9	9,8	83,9	17,8	93,3	10,7	85,9
Social Functioning	77,5	27,3	94,2	19,1	77,6	26,8	96,7	9,6	84,1	24,1	95,9	11,0	89,2	21,1	99,1	6,3	89,3
Global QOL	56,0	21,6	77,0	15,8	54,6	18,5	79,7	14,1	61,2	22,3	79,8	17,8	63,9	20,8	83,2	12,2	62,6
Fatigue	34,7	24,4	17,3	21,1	33,6	21,8	11,1	12,8	31,8	24,2	12,5	15,2	25,4	22,6	7,3	11,5	23,5
Nausea / Vomiting	12,4	21,1	3,6	15,0	8,1	17,3	1,2	5,9	5,6	14,9	1,1	5,8	3,7	12,1	0,9	6,2	1,6
Pain	33,9	23,6	11,4	18,7	34,8	25,3	10,1	13,9	30,7	24,7	12,2	16,9	24,5	23,2	5,5	10,9	26,1
Dyspnoea	19,7	21,8	7,9	19,4	19,8	23,9	2,4	8,7	16,5	22,8	4,1	11,0	15,9	24,7	2,2	9,3	13,0
Insomnia	37,3	29,0	18,3	26,8	35,9	29,0	13,3	17,4	32,4	30,3	19,4	23,5	28,1	28,0	9,0	16,0	21,7
Appetite loss	19,7	25,6	6,4	17,9	12,6	21,8	3,3	10,0	10,1	19,1	3,6	10,4	9,5	20,8	1,2	6,2	8,4
Constipation	22,8	28,3	9,7	21,2	17,1	23,0	9,4	19,6	18,7	28,2	9,5	17,1	16,5	23,2	9,8	17,3	16,9
Diarrhoea	16,7	23,7	5,4	16,8	11,3	20,7	4,8	11,8	7,7	17,7	4,5	11,5	7,1	15,2	3,1	10,6	4,6
Financial Problems	17,2	23,9	5,2	18,4	19,4	28,8	2,3	8,6	14,4	25,4	1,4	8,7	8,0	18,7	0,7	6,4	5,8
Summary Score	75,9	16,2	90,1	16,0	77,8	15,4	93,2	6,2	80,7	15,6	92,2	7,3	83,7	13,8	95,1	6,3	85,1

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