



UvA-DARE (Digital Academic Repository)

General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the United States

Nolte, S.; Liegl, G.; Petersen, M.A.; Aaronson, N.K.; Costantini, A.; Fayers, P.M.; Groenvold, M.; Holzner, B.; Johnson, C.D.; Kemmler, G.; Tomaszewski, K.A.; Waldmann, A.; Young, T.E.; Rose, M.; EORTC Quality of Life Group

DOI

[10.1016/j.ejca.2018.11.024](https://doi.org/10.1016/j.ejca.2018.11.024)

Publication date

2019

Document Version

Final published version

Published in

European Journal of Cancer

License

CC BY-NC-ND

[Link to publication](#)

Citation for published version (APA):

Nolte, S., Liegl, G., Petersen, M. A., Aaronson, N. K., Costantini, A., Fayers, P. M., Groenvold, M., Holzner, B., Johnson, C. D., Kemmler, G., Tomaszewski, K. A., Waldmann, A., Young, T. E., Rose, M., & EORTC Quality of Life Group (2019). General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the United States. *European Journal of Cancer*, 107, 153-163. <https://doi.org/10.1016/j.ejca.2018.11.024>

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the library <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.



Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejancer.com



Original Research

General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the United States



S. Nolte^{a,b,*}, G. Liegl^a, M.A. Petersen^c, N.K. Aaronson^d,
A. Costantini^e, P.M. Fayers^f, M. Groenvold^{c,g}, B. Holzner^h,
C.D. Johnsonⁱ, G. Kemmler^h, K.A. Tomaszewski^j, A. Waldmann^{k,l},
T.E. Young^m, M. Rose^{a,n} on behalf of the EORTC Quality of Life Group

^a Department of Psychosomatic Medicine, Center for Internal Medicine and Dermatology, Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany

^b Population Health Strategic Research Centre, School of Health and Social Development, Deakin University, Burwood, VIC, Australia

^c Department of Palliative Medicine, Bispebjerg Hospital, Copenhagen, Denmark

^d Division of Psychosocial Research & Epidemiology, The Netherlands Cancer Institute, Amsterdam, the Netherlands

^e Psycho-Oncology Unit, Sant'Andrea Hospital Sapienza, University of Rome, Rome, Italy

^f Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom

^g Department of Public Health, University of Copenhagen, Copenhagen, Denmark

^h Department of Psychiatry, Psychotherapy and Psychosomatics, Innsbruck Medical University, Innsbruck, Austria

ⁱ University of Southampton, Southampton, United Kingdom

^j Health Outcomes Research Unit, Department of Gerontology, Geriatrics, and Social Work, Faculty of Education, Ignatianum Academy, Krakow, Poland

^k Institute of Social Medicine and Epidemiology, University of Luebeck, Luebeck, Germany

^l Ministry for Health and Consumer Protection, Hamburg Cancer Registry, Hamburg, Germany

^m East & North Hertfordshire NHS Trust Including Mount Vernon Cancer Centre, Northwood, Middlesex, United Kingdom

ⁿ Quantitative Health Sciences, Outcomes Measurement Science, University of Massachusetts Medical School, Worcester, MA, USA

Received 7 November 2018; accepted 10 November 2018

Available online 19 December 2018

DOI of original article: <https://doi.org/10.1016/j.ejca.2018.11.023>.

* Corresponding author: Sandra Nolte, PhD, Department of Psychosomatic Medicine, Center for Internal Medicine and Dermatology, Charité - Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany.

E-mail address: sandra.nolte@charite.de (S. Nolte).

<https://doi.org/10.1016/j.ejca.2018.11.024>

0959-8049/© 2018 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

KEYWORDS

Quality of life;
EORTC QLQ-C30;
self-report;
patient-reported
outcomes;
General population;
norm data;
normative data;
survey;
Europe;
Canada;
USA

Abstract Objective: The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 health-related quality of life questionnaire is one of the most widely used cancer-specific health-related quality of life questionnaires worldwide. General population norm data can facilitate the interpretation of QLQ-C30 data obtained from cancer patients. This study aimed at systematically collecting norm data from the general population to develop European QLQ-C30 norm scores and to generate comparable norm data for individual countries in Europe and North America.

Methods: We collected QLQ-C30 data from the general population across 11 European Union (EU) countries, Russia, Turkey, Canada and United States ($n \geq 1000/\text{country}$). Representative samples were stratified by sex and age groups (18–39, 40–49, 50–59, 60–69 and ≥ 70 years). After applying weights based on the United Nations population distribution statistics, we calculated QLQ-C30 domain scores to generate a ‘European QLQ-C30 Norm’ based on the EU countries. Further, we calculated QLQ-C30 norm scores for all 15 individual countries.

Results: A total of 15,386 respondents completed the online survey. For the EU sample, most QLQ-C30 domains showed differences by sex/age, with men scoring somewhat better health than women, while age effects varied across domains. Substantially larger differences were seen in inter-country comparisons, with Austrian and Dutch respondents reporting consistently better health compared with British and Polish respondents.

Conclusions: This study is the first to systematically collect EORTC QLQ-C30 general population norm data across Europe and North America applying a consistent data collection method across 15 countries. These new norm data facilitate valid intra-country as well as inter-country comparisons and QLQ-C30 score interpretation.

© 2018 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

The importance of including the patients’ voice in clinical practice and research has been recognised widely for several decades [1,2]. In more recent years, patient-reported outcomes (PROs) have also been increasingly acknowledged in drug development and regulatory decision-making [3–5]. Given this growing relevance of PROs, it is not surprising that efforts are undertaken to standardise PRO data, with several initiatives worldwide tackling the issue in different ways. One possible approach—as taken by the International Consortium for Health Outcomes Measurement (ICHOM)—is to define standard sets of existing PRO instruments to enable comparison of outcomes across health-care providers and geographies [6]. A more elaborate approach is to measure PROs by applying modern test theory methods where items measuring the same latent construct are calibrated on the same metric. This serves as the foundation of the application of computer-adaptive tests (CATs) [7–9].

The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group (QLG) has a long track record of developing and validating PRO instruments for use in oncology. Their quality of life (QoL) core questionnaire, the QLQ-C30, was developed more than 25 years ago and is one of the most widely used cancer-specific PRO instruments [10,11]. Regarding standardisation, use of the QLQ-C30

as part of clinical routine is frequently recommended in ICHOM standard sets for malignant neoplasms (e.g. [12,13]). Further, the EORTC QLG developed a QLQ-C30 CAT version, the EORTC CAT Core [8]. Through tailoring items to the individual respondent, CATs can achieve the same measurement precision as static instruments while using fewer items; CATs also minimise floor/ceiling effects [14].

While these initiatives are crucial steps toward improving quality and comparability of PRO data, data analysis and interpretation is further enhanced by using a sensible reference for comparative purposes. Depending on the objective of such comparison, a useful reference can be data obtained from cancer patients or norm data collected from the general population. If these data are not available, interpretation of PRO data may be arbitrary. For the comparison of QLQ-C30 scores with cancer-patient data, the EORTC QLG has published reference values generated for various cancer populations [15]. In addition, general population norm data have been collected in different countries over the last two decades, with European data available for Denmark [16,17], Germany [18–20], the Netherlands [21,22], Norway [23,24], Slovenia [25] and Sweden [26,27], with the latest German publication providing a European norm by collating data from different samples [20]. However, a major drawback of this work is that inter-country comparisons are hampered because of the lack of a common sampling methodology across studies.

Given the dearth of research regarding European QLQ-C30 general population norm data for use in inter-country comparisons, the EORTC QLG set out to systematically collect general population data in 13 European countries, Canada and the United States using a common methodology to generate norm data for the QLQ-C30 and the CAT Core [8]. This article presents European QLQ-C30 general population norm data and individual country norms for 15 countries.

2. Material and methods

2.1. Country selection

Country selection was based on several criteria, including population size and balance of geographical location, whilst considering budgetary constraints. The final selection included 11 European Union (EU) countries (Austria, Denmark, France, Germany, Hungary, Italy, the Netherlands, Poland, Spain, Sweden and United Kingdom). For comparative purposes, we also collected data in Russia, Turkey, Canada and the United States.

2.2. Item selection and sociodemographic data

The QLQ-C30 consists of 30 items covering five function subscales (physical, role, emotional, cognitive and social), nine symptom subscales/items (fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties) and a global health/QoL subscale. Further details of the full-scale survey are reported elsewhere [41]. A range of sociodemographic data were collected, including sex, age, education, employment, relationship status and presence of health conditions.

2.3. Translation and cultural adaptation of included variables

All QLQ-C30 items were available for the languages spoken in the selected countries. In contrast, the sociodemographic variables had to be developed and translated. During this process, assessment of educational attainment proved to be challenging. After a comprehensive consensus process, including review of the International Standard Classification of Education (2011), the final categorisation was deemed adequate by the study collaborators.

2.4. Sampling

To generate sufficiently large sample sizes for estimating stable norms for a range of subgroups, we stratified samples by sex and age group (18–39, 40–49, 50–59, 60–69 and ≥ 70 years) with sample sizes of $n = 100/\text{stratum}$, i.e. $n = 1000/\text{country}$. Sampling of an equal

distribution of sex and age groups provides norm data for purposes of comparing cancer-patient data with sex- and age-matched peers from the general population. Further details regarding the rationale for the sample size are reported elsewhere [41].

2.5. Data collection

To ensure a consistent data collection method and representative samples throughout, we subcontracted data collection to GfK SE (www.gfk.com), a panel research company experienced in multinational/multilanguage online surveys. These internet panels are representative for the general population (with internet access) in a given country in terms of sex, age, region, hometown size, household size and socioeconomic status. While GfK achieved most quotas via internet panels, $n = 290$ respondents (≥ 60 years) provided data via computer-assisted telephone interviews to achieve quotas in Turkey.

Data were collected in March/April 2017. As GfK panel members are registered voluntarily and generally participate when contacted, GfK attains response rates between 75 and 90%.

2.6. Establishing European norm data for the EORTC QLQ-C30

For the final definition of the ‘European QLQ-C30 Norm’, we included the 11 EU countries. We weighted data by respective country’s population size, sex and age distribution based on official 2015 population distribution statistics published by the United Nations [28].

2.7. Statistical analyses

We calculated mean scores and 95% confidence intervals (CIs) of the QLQ-C30 subscales ranging between 0 and 100 following the QLQ-C30 scoring manual [29]. We calculated norm scores for the sex/age strata of the combined EU sample weighted by country size and sex/age distribution. Given the large samples, we further divided the youngest age group into 18–29 and 30–39 years, respectively. Finally, we calculated national norm data for all 15 countries, weighted by respective country’s sex/age distribution. For all analyses, we used IBM SPSS Statistics®, version 25.

3. Results

Stratified quotas were achieved in all 15 countries, with $n \geq 100$ individuals completing the survey in each sex*age*country subgroup. Country sample sizes ranged between $n = 1000$ (the Netherlands) and $n = 1165$ (Spain), leading to a final sample size of $N = 15,386$ for the full and $n = 11,343$ for the EU sample (Table 1).

Table 1

Sociodemographic data of full sample (13 European countries, Canada, USA) and “EORTC QLQ-C30 Norm” sample (11 EU countries).

Sociodemographic variable	Full sample (15 countries) N = 15,386		EORTC QLQ-C30 Norm (11 EU countries) n = 11,343	
	n	%	n	%
Sex				
Female	7650	49.7	5623	49.6
Male	7736	50.3	5720	50.4
Age categories (years)				
18–29	1177	7.6	883	7.8
30–39	1902	12.4	1370	12.1
40–49	3049	19.8	2248	19.8
50–59	3059	19.9	2253	19.9
60–69	3138	20.4	2337	20.6
≥70	3061	19.9	2252	19.9
Education				
Less than compulsory education	183	1.2	95	0.9
Compulsory (left school at the minimum school leaving age)	1509	9.9	897	8.0
Some post compulsory (some school after reaching school leaving age without reaching university entrance qualifications (e.g., A-levels))	2050	13.5	1954	17.5
Post compulsory below university (e.g. reaching A levels)	4405	29.0	3408	30.5
University degree (bachelor’s degree or equivalent level)	3716	24.4	2689	24.1
Postgraduate degree (master’s degree, doctorate or equivalent level)	3337	22.0	2131	19.1
Prefer not to answer ^a	186	—	169	—
Employment status				
Employed full-time	5532	36.2	4087	36.3
Employed part-time	1256	8.2	984	8.7
Homemaker	795	5.2	485	4.3
Student	389	2.5	328	2.9
Unemployed	811	5.3	614	5.5
Retired	5238	34.3	3827	34.0
Self-employed	833	5.5	620	5.5
Other	422	2.8	305	2.7
Prefer not to answer	110	—	93	—
Relationship status				
Single/not in a steady relationship	2589	17.0	1951	17.4
Married or in a steady relationship	10,263	67.4	7640	68.1
Separated/divorced/widowed	2376	15.6	1633	14.5
Prefer not to answer	158	—	119	—
Health status^{b,c}				
No health condition/disease	5361	36.6	4204	39.0
Chronic pain	3582	24.5	2468	22.9
Heart disease	1226	8.4	804	7.5
Cancer (excluding basal cell carcinoma)	416	2.8	308	2.9
Depression	1452	9.9	903	8.4
Chronic obstructive pulmonary disease (COPD)	532	3.6	373	3.5
Arthritis	2114	14.4	1427	13.2
Diabetes	1546	10.6	1095	10.2
Asthma	924	6.3	658	6.1
Anxiety disorder	1218	8.3	785	7.3
Obesity	1513	10.3	1072	9.9
Drug/alcohol use disorder	153	1.0	96	0.9
Other	2634	18.0	1863	17.3
Prefer not to answer	631	—	486	—
Country				
Austria ^d	1002	6.5	1002	8.8
Canada	1004	6.5	—	—
Denmark ^d	1003	6.5	1003	8.8
France ^d	1001	6.5	1001	8.8
Germany ^d	1006	6.5	1006	8.9
Hungary ^d	1053	6.8	1053	9.3

Table 1 (continued)

Sociodemographic variable	Full sample (15 countries) N = 15,386		EORTC QLQ-C30 Norm (11 EU countries) n = 11,343	
	n	%	n	%
Italy ^d	1036	6.7	1036	9.1
The Netherlands ^d	1000	6.5	1000	8.8
Poland ^d	1024	6.7	1024	9.0
Russia	1007	6.5	—	—
Spain ^d	1165	7.6	1165	10.3
Sweden ^d	1027	6.7	1027	9.1
Turkey	1023	6.6	—	—
United Kingdom ^d	1026	6.7	1026	9.0
USA	1009	6.6	—	—

^a For the calculation of percentage distributions, the category “prefer not to answer” is treated as missing data.

^b The sample sizes were reduced by n = 114 (0.7%) in the full sample and n = 79 (0.7%) in the EU subsample, respectively, as respondents had provided implausible data to the question on presence of disease.

^c The sum of health conditions is larger than the total sample of N = 15,386 (full sample) and n = 11,343 (EU subsample), respectively, as respondents were able to check multiple response options.

^d Countries included in the calculation of the “EORTC QLQ-C30 Norm”.

Sociodemographic characteristics of the two samples were comparable. As per sampling, there was an equal distribution of females/males and age groups. Respondents' age ranged between 18 and 99 years, with mean age 53.6 years. Around 90% of respondents indicated to have at least some post-compulsory education. Across samples, 36% of respondents were working full-time; 34% were retired. About two-thirds reported being married/in a steady relationship. Finally, the most frequently reported diseases were chronic pain, arthritis, diabetes, obesity and depression, with 63% (full sample) and 61% (EU sample), respectively, reporting to have at least one health condition (Table 1).

As shown in Table 2, self-rated function in our EU sample was relatively high. Across subscales, sample mean scores ranged between 84.3 and 86.2 (on a 100-point scale), with 95% CIs between ± 0.50 and ± 0.65 . The only exception was emotional function, with a mean score of 74.2 (95% CI, ± 0.66). Women and men rated themselves similarly, except for emotional function where men rated themselves 4.7 points higher than women. Age effects varied. For physical and role function, women reported decreasing function with increasing age; men did not show age differences. For the remaining function subscales, age effects tended to be in the opposite direction, with older respondents reporting higher function than younger respondents. For some symptom subscales, marked floor effects were observed, with > 80% selecting the lowest/best score for nausea/vomiting, appetite loss, diarrhoea and financial difficulties. Scores ranged between 5.9 (nausea/vomiting) and 29.5 (fatigue), with 95% CIs between ± 0.48 and ± 0.79 . Men tended to rate themselves lower/better than women, with largest differences observed for insomnia, fatigue and pain. Age effects varied. For pain and dyspnoea, women reported more symptoms with increasing age. In contrast, for fatigue, nausea/vomiting

and appetite loss, older respondents tended to score lower/better than younger respondents; for diarrhoea and financial difficulties, this age effect was only seen in men. For global health/QoL, men reported higher scores than women (68.0 for men, 95% CI, ± 0.81 ; 64.3 for women, 95% CI, ± 0.74). Respondents aged 50–59 years reported lowest global health/QoL scores (65.8 for men; 62.6 for women; 95% CI, ± 1.63 each).

Compared with differences between sex/age groups, inter-country comparisons suggest larger group differences (Table 3, Fig. 1 and 2). Austrian and Dutch respondents reported the best scores, i.e. highest for function and lowest for symptoms. In contrast, Polish and British respondents for the EU sample and Russian, Turkish and United States respondents for the full sample regularly reported worse scores, with differences reaching or exceeding 10 points, a difference that is often applied to indicate clinical relevance [30]. On the global health/QoL subscale, differences between lowest (Poland, Russia, Turkey and United Kingdom) and highest scoring nations (Austria and Netherlands) again exceeded 10 points.

4. Discussion

This study is the first to systematically collect European and individual country general population norm data for the EORTC QLQ-C30 using consistent data collection methods across 15 countries in Europe and North America. The ‘European QLQ-C30 Norm’ enables valid inter-country comparisons for cancer-patient data. Data from cancer patients can be compared with sex-/age-matched peers from the general population. In addition, the country-specific norm data for 15 countries, especially for those where no QLQ-C30 norm data yet existed, can be used for country-level comparisons.

Table 2

European EORTC QLQ-C30 general population norm data^a. Mean scores (M)/standard deviations (SD) by subscales stratified by sex and age weighted by sex, age and country according to the United Nations (UN), Department of Economic and Social Affairs population distribution statistics for the year 2015².

Domain	Total	Female							Male						
		All female	18-29 years	30-39 years	40-49 years	50-59 years	60-69 years	≥70 years	All male	18-29 years	30-39 years	40-49 years	50-59 years	60-69 years	≥70 years
Function subscales															
Physical function															
M	85.1	84.3	88.9	86.7	85.8	83.4	82.1	78.5	86.0	85.6	87.3	87.9	86.8	84.9	82.7
SD	18.9	18.5	14.5	18.0	18.8	18.8	18.7	19.8	19.3	21.6	19.0	18.0	18.2	18.3	19.6
Role function															
M	84.3	84.1	89.1	84.6	84.1	82.3	83.5	80.7	84.5	82.5	85.2	85.3	84.3	85.4	84.8
SD	24.6	24.6	20.2	24.6	25.1	25.5	25.3	26.4	24.5	26.3	23.4	24.5	25.1	23.5	22.7
Emotional function															
M	74.2	71.9	66.2	67.8	69.1	71.0	77.8	79.9	76.6	73.7	71.1	74.3	75.9	82.2	85.7
SD	24.7	25.3	28.2	26.8	26.4	24.1	21.9	19.8	23.8	26.4	26.5	24.0	23.5	18.9	15.5
Cognitive function															
M	84.8	84.3	82.8	82.9	82.7	83.2	87.9	86.6	85.2	81.3	84.5	85.7	86.4	87.9	87.7
SD	21.3	20.9	22.4	23.5	22.7	21.1	16.6	17.2	21.7	27.5	23.3	20.7	20.8	16.6	14.9
Social function															
M	86.2	85.7	86.1	83.7	83.2	83.8	88.1	89.0	86.7	84.4	84.8	85.3	87.6	89.8	90.2
SD	24.1	24.6	24.7	26.4	26.8	25.7	22.7	20.4	23.6	26.6	25.2	24.1	22.1	20.8	19.3
Symptom subscales/ items															
Fatigue															
M	29.5	31.7	34.4	34.6	33.9	32.1	26.6	28.1	27.1	30.7	29.6	27.5	26.7	23.5	21.9
SD	25.5	25.9	25.3	27.3	27.1	26.2	24.5	24.2	24.8	25.2	25.0	24.5	25.1	23.9	23.3
Nausea/vomiting															
M	5.9	5.7	7.2	8.5	6.3	4.9	3.7	3.3	6.1	11.9	9.4	5.2	3.4	2.3	1.2
SD	16.0	14.9	17.4	17.8	16.1	12.8	11.6	11.6	17.1	24.9	20.3	15.0	11.0	9.4	5.5
Pain															
M	23.5	25.3	20.6	23.3	25.2	28.7	25.4	28.8	21.6	21.3	22.1	21.4	22.9	22.1	19.7
SD	27.1	27.9	24.9	27.7	28.1	29.2	28.6	28.2	26.0	26.6	25.9	26.0	26.3	26.0	25.0
Dyspnoea															
M	15.9	16.3	12.6	16.1	16.2	17.0	16.6	19.3	15.5	16.2	15.1	14.0	14.6	16.9	16.4
SD	24.6	24.5	20.8	23.6	24.8	24.7	25.0	27.3	24.7	26.1	24.7	23.0	23.6	25.5	25.0
Insomnia															
M	26.6	29.3	26.0	28.9	30.4	35.2	29.2	27.1	23.6	20.4	27.1	26.0	25.6	22.3	20.3
SD	30.3	30.7	29.8	30.9	31.2	32.5	30.7	28.7	29.6	29.5	30.8	29.8	30.4	28.1	27.5
Appetite loss															
M	10.0	10.3	11.6	13.5	11.4	9.6	7.6	8.3	9.6	15.8	12.1	7.6	7.5	6.4	5.2
SD	21.6	21.6	23.2	24.8	23.1	19.7	18.7	18.7	21.6	28.4	22.6	18.1	19.2	17.2	15.8
Constipation															
M	12.5	14.1	14.1	17.8	14.7	14.1	11.8	12.3	10.9	13.6	12.9	10.0	8.6	9.0	10.1
SD	23.3	24.4	25.3	27.0	25.3	24.4	21.4	22.3	21.9	25.9	24.1	20.8	19.1	18.9	19.4
Diarrhoea															
M	9.5	9.0	9.0	12.5	8.8	9.4	6.5	7.7	10.0	14.3	13.5	10.3	8.7	5.9	4.4
SD	20.9	20.3	20.2	23.5	20.4	20.4	17.0	19.5	21.4	26.4	23.8	21.2	20.2	15.4	13.1
Financial difficulties															
M	10.6	10.9	9.5	12.9	13.6	12.5	9.3	8.0	10.4	13.6	12.8	11.0	8.9	8.0	5.7
SD	23.6	24.2	24.1	25.4	27.3	24.8	22.4	20.1	22.9	25.9	24.9	23.9	21.4	20.2	16.7
Global health / Quality of Life															
M	66.1	64.3	66.4	63.4	62.9	62.6	65.6	64.8	68.0	71.1	67.4	66.3	65.8	67.0	69.6
SD	21.7	21.8	20.5	21.7	22.9	22.5	22.3	20.9	21.4	21.7	20.9	21.1	22.7	20.8	20.3

^a The European norm scores for the EORTC QLQ-C30 are based on 11 EU countries (as listed in Table 1).

^b United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision, DVD Edition.

To generate these norm data, we subcontracted data collection via online surveys to a panel research company (GfK). Such internet panels are an efficient and cost-effective method to generate norm data, and there is evidence from a comparable study carried out in the context of the United States Patient-Reported Outcomes

Measurement Information System (PROMIS) initiative that data are representative of the general population provided that scores are weighted [31], which is consistent with the methods we applied. As 15 individual samples, however, are more heterogenous compared with aforementioned single-country survey, we

Table 3

Country general population norm data for the EORTC QLQ-C30. Mean scores (M)/standard deviations (SD) by subscales weighted by individual country weights and sex and age distributions according to the UN Department of Economic and Social Affairs population distribution statistics for the year 2015^a.

Domain		AUT ^b	CAN	DNK	FRA	DEU	HUN	ITA	NLD	POL	RUS	ESP	SWE	TUR	GBR	USA
Function subscales																
Physical function																
	M	89.7	85.4	84.2	89.1	82.8	89.1	85.2	90.7	81.3	76.3	86.8	88.9	75.8	81.8	80.8
	SD	13.9	19.3	20.4	15.9	21.2	14.0	17.0	14.9	16.5	16.4	16.8	14.6	16.7	23.5	25.2
Role function																
	M	88.9	83.7	82.4	87.8	80.8	87.5	86.1	89.1	83.4	81.0	86.1	88.0	82.3	80.2	81.7
	SD	20.3	25.6	25.9	22.4	27.2	20.5	22.2	21.5	22.1	21.0	21.5	21.4	22.4	29.1	28.2
Emotional function																
	M	78.1	75.5	79.2	76.7	73.9	72.1	73.5	82.3	68.3	68.1	77.1	76.7	65.8	71.0	73.3
	SD	22.3	23.5	25.1	24.3	24.7	22.9	22.7	21.2	25.0	23.7	22.4	21.7	25.5	28.4	28.0
Cognitive function																
	M	89.1	84.7	83.7	86.7	83.9	87.4	87.0	90.3	81.2	79.5	85.7	87.1	75.5	80.5	80.9
	SD	17.8	20.8	22.6	19.5	22.7	17.7	18.6	17.1	22.0	19.0	19.4	18.6	23.2	25.2	25.6
Social function																
	M	92.2	84.9	86.5	90.5	84.8	90.2	88.1	91.9	80.8	83.3	87.8	91.4	83.1	80.3	81.6
	SD	17.1	26.3	24.2	20.8	25.5	19.4	20.6	19.0	25.4	23.7	22.5	19.1	23.6	29.4	29.4
Symptom subscales/ items																
Fatigue																
	M	24.1	29.1	29.9	27.7	31.5	30.2	28.5	23.7	35.9	41.5	23.9	25.6	39.4	32.2	31.9
	SD	22.7	24.1	26.7	26.2	27.2	22.6	23.9	23.0	22.7	23.9	22.7	22.2	24.0	27.6	27.8
Nausea/vomiting																
	M	2.0	6.7	7.9	4.1	6.0	3.8	6.5	3.5	7.4	7.4	4.9	4.0	11.3	8.1	10.9
	SD	8.3	16.6	18.3	13.5	17.2	11.9	15.9	11.8	17.5	15.2	14.5	11.2	18.9	18.9	22.6
Pain																
	M	20.0	24.4	23.4	19.6	27.6	23.5	20.2	17.7	26.0	27.1	22.7	20.4	24.9	26.7	27.5
	SD	24.3	27.2	26.5	24.7	30.9	23.8	23.9	22.9	23.7	23.9	24.0	25.0	22.9	31.2	30.2
Dyspnoea																
	M	10.9	16.3	13.7	14.4	18.7	9.1	15.7	9.5	13.4	23.1	12.4	28.1	18.2	19.5	19.9
	SD	20.6	24.5	23.5	23.8	27.3	19.1	23.0	19.7	21.4	25.0	20.7	26.8	24.8	27.9	28.5
Insomnia																
	M	20.0	30.8	28.5	25.9	27.6	22.1	22.9	21.3	28.6	31.3	25.2	21.8	31.6	32.6	30.8
	SD	27.8	30.6	31.2	30.6	33.1	27.4	27.1	26.1	28.3	29.7	28.0	27.6	28.5	32.8	33.2
Appetite loss																
	M	4.4	11.3	11.8	8.0	10.1	8.0	8.5	4.9	13.0	13.8	9.5	7.6	19.2	14.2	14.1
	SD	16.1	22.8	24.2	19.7	23.3	18.4	19.0	15.1	23.2	22.7	19.9	17.6	24.6	25.2	25.3
Constipation																
	M	6.2	14.6	10.8	11.1	9.6	10.3	14.2	4.9	18.8	14.7	15.3	6.7	23.2	14.7	18.6
	SD	17.3	25.0	23.0	21.2	22.3	20.7	23.4	13.6	26.2	24.4	24.1	17.0	28.6	26.2	28.6
Diarrhoea																
	M	7.5	11.1	10.7	7.3	10.4	9.6	9.3	6.9	12.0	12.2	7.8	7.9	13.5	11.2	13.7
	SD	18.7	21.1	22.0	18.8	22.7	20.2	19.5	17.8	23.3	21.9	18.1	17.2	22.3	23.0	27.1
Financial difficulties																
	M	5.0	12.7	12.2	6.7	11.3	14.8	9.7	4.9	15.5	20.5	9.5	5.8	17.6	14.5	17.5
	SD	17.6	27.0	26.2	19.3	25.0	26.2	21.6	17.1	24.9	29.0	20.7	18.2	25.8	28.7	30.8
Global health / QoL																
	M	75.6	65.9	67.0	68.2	67.0	66.3	64.9	77.4	60.0	59.7	66.8	69.2	60.7	62.3	63.9
	SD	20.0	20.6	23.4	20.1	21.8	20.4	20.3	19.8	20.6	19.7	21.5	22.1	22.7	23.7	22.9

^a United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision, DVD Edition.

^b Country codes: AUT = Austria, CAN=Canada, DNK = Denmark, FRA=France, DEU = Germany, HUN=Hungary, ITA=Italy, NLD=Netherlands, POL=Poland, RUS = Russia, ESP = Spain, SWE=Sweden, TUR = Turkey, GBR = United Kingdom, USA=United States of America.

compared our sample characteristics with official population statistics where available. For example, in our EU sample, 6.8% of respondents indicated that they were unemployed (weighted data, not shown), which

matches the official 2017 EU unemployment rate of 6.7% for individuals older than 25 years [32]. Further, 64.4% of respondents reported being married/in a steady relationship, which is slightly higher than the EU

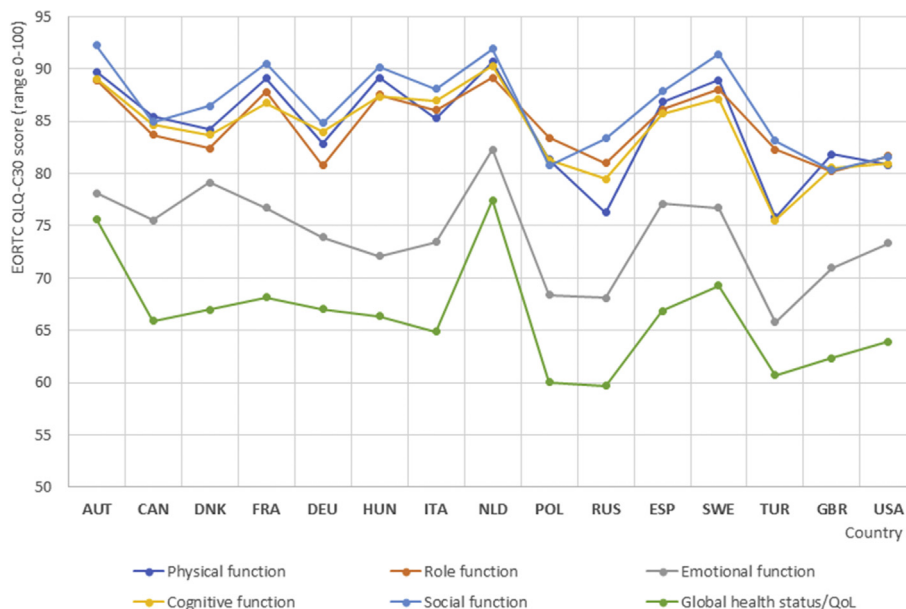


Fig. 1. EORTC QLQ-C30 country reference values for function subscales and global health status/quality of life (for country codes, please refer to Table 3). EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life core.

average of 59.3% [33]. Finally, self-reported prevalence of several health conditions is largely in-line with prevalence rates published in the literature [34–36]. In contrast, individuals with lower educational levels appear underrepresented in our EU sample, with around 90% reporting at least some post-compulsory education. This is generally lower than in most European countries; however, percentage distribution varies widely by country [37].

Some observed subgroup and country differences warrant further discussion. For example, in emotional function, several symptom subscales and overall QoL, men reported somewhat better scores than women, a finding also observed in other QLQ-C30 norm data studies [20]. Further, in some instances, older respondents reported remarkably high function. For physical function, further subgroup analyses within our oldest age group suggest that decline in self-reported

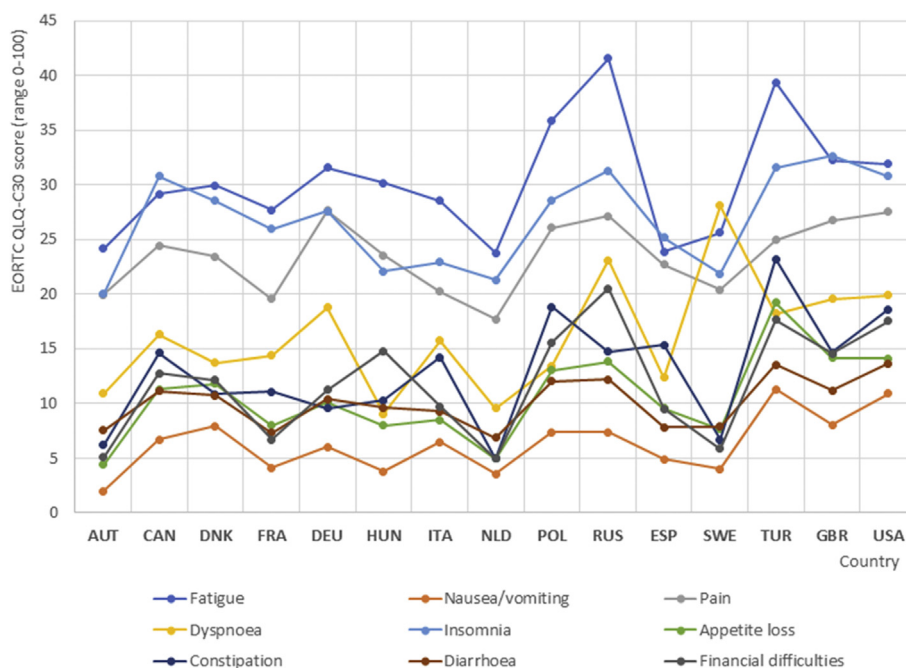


Fig. 2. EORTC QLQ-C30 country reference values for symptom subscales/items (for country codes, please refer to Table 3). EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life core.

physical function occurs primarily from ≥ 80 years (data not shown). Unfortunately, we did not have sufficient numbers in this age group, as our oldest stratified age group was ≥ 70 years. Also, older respondents' self-reported cognitive function appears high. This finding may be explained by people adjusting health expectations with increasing age. Research also suggests that older persons value different factors compared with younger persons when assessing their health and that younger persons' health perceptions are more affected by health limitations than those of older persons [38]. Additionally, given that in the oldest age group, over 90% were retired, everyday demands on cognitive function may be lower than that of younger respondents, especially those in the workforce. Hence, the construct we are trying to measure may differ depending on respondents' age. The high cognitive function reported by older respondents may also reflect some degree of selection bias, given that respondents had to have internet access and some computer skills. Finally, several reasons might explain the observed country differences. It is conceivable that items and/or response scales have different meanings in different cultures; however, given EORTC's long-standing experience with translations/linguistic validations, it is unlikely that this explains observed differences [39]. It is more likely that differences are indeed true differences between countries and that factors such as the welfare state characteristic [40] play a role in people's self-reported health.

This study has several limitations that should be noted. First, as indicated above, targeting older age groups, i.e. ≥ 80 years, could provide further insight into changes in QoL as a consequence of aging. It was beyond the scope of our study to collect these data as costs are disproportionately high because of the need to often conduct personal/telephone interviews instead of online surveys in older age groups. Second, we observed marked floor effects for several symptoms. Such effects are unavoidable when data are obtained from the general (i.e. relatively healthy) population, especially if fixed-length questionnaires, including some single-item subscales, are used. One possible solution to reduce floor/ceiling effects is the use of CAT such as the EORTC CAT Core [8]. Finally, while our norm data are assumed to be representative of the general population, our sample was relatively highly educated. In our EORTC CAT Core norm data article [41], we explore the influence of educational level on scores. While significant differences were found, with more highly educated respondents reporting better health, the practical relevance of these differences was very small as indicated by small effect sizes. Also, it was difficult to harmonise educational levels across countries; hence, it is plausible that 'post-compulsory' has different meanings in different countries. Despite all of these limitations, online surveys represent an efficient, cost-effective method of obtaining large, representative general population samples. While it

comes with disadvantages such as difficulty with reaching older age groups, as seen with the Turkish sample, there are many convincing advantages to this method over personal and telephone interviews (e.g. higher response rates and avoidance of interviewer bias). With the steadily increasing use of the internet in recent years, this method is gaining in popularity [31]. Using internet panels, we were able to obtain a large sample of $N = 15,386$ persons generating norm data for 15 countries, thereby providing a valuable resource for studies using the QLQ-C30. These general population norm scores are robust, even for stratified analyses, as is evidenced by the generally very small 95% CIs.

5. Conclusions

This study generated European (and North American) and individual country norm data for the EORTC QLQ-C30 based on a common sampling strategy and survey design. We recommend that the 'European QLQ-C30 Norm' be used to compare self-reported health-related quality of life of cancer patients with general population data, especially in multinational projects.

Ethical statement

Ethical approval was not sought as this study is solely based on panel research data. As opposed to medical research where medical professional codes of conduct apply, there is widespread agreement that health research involving volunteers from the general population is not subject to ethical approval. Both the European Pharmaceutical Market Research Association (EphMRA) and the NHS Health Research Authority specify that this type of research does not require ethical approval as long as the research conforms to ethical guidelines. Our online survey was carried out by the panel research company GfK SE which is member of EphMRA. The multinational survey conformed to the required ethical standards by obtaining informed consent from all participants and collecting data completely anonymously. Any identification of the respondents through the authors is impossible.

Acknowledgements

This research was funded by the European Organisation for Research and Treatment of Cancer Quality of Life Group (grant number 001 2015). The work of Bernhard Holzner was partially funded by the Austrian Science Fund (FWF #P26930). The authors thank the many translators who kindly volunteered their time to embark on the task of standardising the sociodemographic variables across languages and cultures. In addition to the collaborators of this project, special thanks go to Susan Bartlett for making the variables in

English and French suitable for the Canadian context; Eveline Bleiker, Jacobien Kieffer, Marieke van Leeuwen for Dutch; Thierry Conroy for French; Agnes Czimbalmos for Hungarian; Alice Iuso for Italian; Tatyana Ionova for Russian; Juan Ignacio Arraras for Spanish; Eva Hammerlid, Yvonne Brandberg for Swedish; Deniz Yüce for Turkish; and Claire Snyder for English for the U.S.-American context.

Conflict of interest statement

None declared

References

- [1] Snyder CF, Aaronson NK. Use of patient-reported outcomes in clinical practice. *Lancet* 2009;374(9687):369–70.
- [2] Blazeby JM, Avery K, Sprangers M, Pikhart H, Fayers P, Donovan J. Health-related quality of life measurement in randomized clinical trials in surgical oncology. *J Clin Oncol* 2006; 24(19):3178–86.
- [3] Basch E, Dueck AC. Patient-reported outcome measurement in drug discovery: a tool to improve accuracy and completeness of efficacy and safety data. *Expert Opin Drug Discov* 2016;11(8): 753–8.
- [4] Shields AL, Hao Y, Krohe M, Yaworsky A, Mazar I, Foley C, et al. Patient-reported outcomes in oncology drug labeling in the United States: a framework for navigating early challenges. *Am Health Drug Benefits* 2016;9(4):188–97.
- [5] Kluetz PG, O'Connor DJ, Soltys K. Incorporating the patient experience into regulatory decision making in the USA, Europe, and Canada. *Lancet Oncol* 2018;19(5):e267–74.
- [6] Porter ME, Larsson S, Lee TH. Standardizing patient outcomes measurement. *N Engl J Med* 2016;374(6):504–6.
- [7] Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. *Med Care* 2007;45(5 Suppl 1): S3–11.
- [8] Petersen MA, Aaronson NK, Arraras JI, Chie WC, Conroy T, Costantini A, et al. The EORTC CAT Core-The computer adaptive version of the EORTC QLQ-C30 questionnaire. *Eur J Canc* 2018;100:8–16.
- [9] Fischer HF, Rose M. www.common-metrics.org: a web application to estimate scores from different patient-reported outcome measures on a common scale. *BMC Med Res Methodol* 2016;16(1):142. <https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/s12874-016-0241-0>.
- [10] Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85(5):365–76.
- [11] Fayers P, Bottomley A. On behalf of the EORTC quality of life group and of the quality of life unit. Quality of life research within the EORTC-the EORTC QLQ-C30. *Eur J Canc* 2002;38(Suppl 4): S125–33.
- [12] Zerillo JA, Schouwenburg MG, van Bommel ACM, Stowell C, Lippa J, Bauer D, et al. An international collaborative standardizing a comprehensive patient-centered outcomes measurement set for colorectal cancer. *JAMA Oncol* 2017;3(5): 686–94.
- [13] Ong WL, Schouwenburg MG, van Bommel ACM, Stowell C, Allison KH, Benn KE, et al. A standard set of value-based patient-centered outcomes for breast cancer: the international Consortium for health outcomes measurement (ICHOM) initiative. *JAMA Oncol* 2017;3(5):677–85.
- [14] Revicki DA, Cella DF. Health status assessment for the twenty-first century: item response theory, item banking and computer adaptive testing. *Qual Life Res* 1997;6(6):595–600.
- [15] Scott NW, Fayers PM, Aaronson NK, Bottomley A, de Graeff A, Groenvold M, et al. EORTC QLQ-C30 reference values. 2008. Brussels, Belgium.
- [16] Klee M, Groenvold M, Machin D. Quality of life of Danish women: population-based norms of the EORTC QLQ-C30. *Qual Life Res* 1997;6(1):27–34.
- [17] Juul T, Petersen MA, Holzner B, Laurberg S, Christensen P, Gronvold M. Danish population-based reference data for the EORTC QLQ-C30: associations with gender, age and morbidity. *Qual Life Res* 2014;23(8):2183–93.
- [18] Schwarz R, Hinz A. Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. *Eur J Canc* 2001;37(11):1345–51.
- [19] Waldmann A, Schubert D, Katalinic A. Normative data of the EORTC QLQ-C30 for the German population: a population-based survey. *PLoS One* 2013;8(9). e74149.
- [20] Hinz A, Singer S, Brahler E. European reference values for the quality of life questionnaire EORTC QLQ-C30: results of a German investigation and a summarizing analysis of six European general population normative studies. *Acta Oncol* 2014; 53(7):958–65.
- [21] van de Poll-Franse LV, Mols F, Gundy CM, Creutzberg CL, Nout RA, Verdonck-de Leeuw IM, et al. Normative data for the EORTC QLQ-C30 and EORTC-sexuality items in the general Dutch population. *Eur J Canc* 2011;47(5):667–75.
- [22] Mols F, Husson O, Oudejans M, Vlooswijk C, Horevoorts N, van de Poll-Franse LV. Reference data of the EORTC QLQ-C30 questionnaire: five consecutive annual assessments of approximately 2000 representative Dutch men and women. *Acta Oncol* 2018:1–11.
- [23] Hjermstad MJ, Fayers PM, Bjordal K, Kaasa S. Health-related quality of life in the general Norwegian population assessed by the european organization for research and treatment of cancer core quality-of-life questionnaire: the QLQ=C30 (+ 3). *J Clin Oncol* 1998;16(3):1188–96.
- [24] Hjermstad MJ, Fayers PM, Bjordal K, Kaasa S. Using reference data on quality of life – the importance of adjusting for age and gender, exemplified by the EORTC QLQ-C30 (+3). *Eur J Canc* 1998;34(9):1381–9.
- [25] Velenik V, Secerov-Ermenc A, But-Hadzic J, Zadnik V. Health-related quality of life assessed by the EORTC QLQ-C30 questionnaire in the general slovenian population. *Radiol Oncol* 2017; 51(3):342–50.
- [26] Michelson H, Bolund C, Nilsson B, Brandberg Y. Health-related quality of life measured by the EORTC QLQ-C30-reference values from a large sample of Swedish population. *Acta Oncol* 2000;39(4):477–84.
- [27] Derogar M, van der Schaaf M, Lagergren P. Reference values for the EORTC QLQ-C30 quality of life questionnaire in a random sample of the Swedish population. *Acta Oncol* 2012;51(1):10–6.
- [28] United Nations Department of Economic and Social Affairs Population Division. World population Prospects: the 2017 revision. DVD Edition 2017.
- [29] Fayers P, Aaronson N, Bjordal K, Groenvold M, Curran D, Bottomley A, et al. The EORTC QLQ-C30 scoring manual. 3rd ed. Brussels: European Organisation for Research and Treatment of Cancer; 2001.
- [30] Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. *J Clin Oncol* 1998;16(1):139–44.
- [31] Liu H, Cella D, Gershon R, Shen J, Morales LS, Riley W, et al. Representativeness of the patient-reported outcomes measurement information System internet panel. *J Clin Epidemiol* 2010; 63(11):1169–78.

- [32] OECD. Harmonised Unemployment Rates (HURs). OECD - updated: june 2018. 2018.
- [33] OECD. SF3.3. Cohabitation rate and prevalence of other forms of partnership. 2016.
- [34] Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 2006;10(4):287–333.
- [35] Gallus S, Lugo A, Murisic B, Bosetti C, Boffetta P, La Vecchia C. Overweight and obesity in 16 European countries. *Eur J Nutr* 2015;54(5):679–89.
- [36] Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jonsson B, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuro-psychopharmacol* 2011;21(9):655–79.
- [37] eurostat. Share of the population by level of educational attainment, by selected age groups and country. 2016. 2017.
- [38] Idler E, Cartwright K. What do we rate when we rate our health? Decomposing age-related contributions to self-rated health. *J Health Soc Behav* 2018;59(1):74–93.
- [39] Scott NW, Fayers PM, Bottomley A, Aaronson NK, de Graeff A, Groenvold M, et al. Comparing translations of the EORTC QLQ-C30 using differential item functioning analyses. *Qual Life Res* 2006;15(6):1103–15. discussion 1117-20.
- [40] Bergqvist K, Yngwe MÅ, Lundberg O. Understanding the role of welfare state characteristics for health and inequalities – an analytical review. *BMC Publ Health* 2013;13:1234. 1234.
- [41] Liegl G, Petersen MA, Groenvold M, Aaronson NK, Costantini A, Fayers PM, et al. Establishing the European Norm for the health-related quality of life domains of the computer-adaptive test EORTC CAT Core. *Eur J Canc* 2018 (in this issue).