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Review

Quality of life in epilepsy—31 inventory (QOLIE-31) scores: A global comparison

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ABSTRACT

Quality of life is a pragmatic endpoint for understanding the experience of people with epilepsy (PWE) in low- and middle-income countries (LMICs), where > 80% of PWE reside. However, the literature is bereft of QOL in epilepsy (QOLIE) studies among LMICs and knowledge of the variation in QOLIE globally. We therefore performed a Medline search of original research studies using the quality of life in epilepsy—31 inventory (QOLIE-31) in a recent fifteen-year period (2000–2015). Each of the 194 countries listed by the World Health Organization (WHO) was individually included as search terms. Differences in QOLIE were tested across WHO world regions and World Bank country income group classifications. Sixteen percent of all countries (n = 31) reported on 7255 individuals, including only 8 LMICs. The global mean QOLIE-31 score was 59.8 (standard deviation (SD): 8.0), with a range from 42.1 (SD: 4.1) in the Russian Federation to 82 (SD: 32.8) in Canada. There was a statistically significant difference seen in the QOLIE-31 score by world region and income category, with lower country income level associated with worse QOL (test for trend, $p < 0.0001$). There exists substantial global variation in QOLIE, and country income level may play a role. Understanding what contributes to international differences in QOLIE can help reduce disparities in QOL among PWE worldwide.

1. Introduction

The impact of epilepsy on a person's quality of life (QOL) may be significant because of profound adverse social, physical, and psychological consequences of epilepsy and its treatments. The 31-item quality of life in epilepsy (QOLIE) inventory—QOLIE-31—is one instrument developed to assess the QOLIE, yielding a composite score from 0 to 100 that represents a person with epilepsy (PWE)'s overall wellness including cognitive impact and social functioning [1]. A higher score indicates a higher self-reported QOLIE. The QOLIE-31 inventory has been translated and validated in various languages spanning many continents [1–4].

In recent years, there has been increasing awareness of the disproportionate burden of epilepsy among low- and middle-income countries (LMICs)—where 80% of PWE reside [5]. The QOLIE seems to also be low in individual studies pertaining to LMICs [6–10]. However, systematic studies on QOLIE from LMICs continue to be sparse in the epilepsy literature. We are aware of one large systematic review of the predictors of QOLIE, published in 2011. In that study, 61 of 86 included reports derived from Europe or North America [11]. The available analysis provides no comparative framework to understand the extent of variation in the QOLIE across countries of differing gross national income (GNI) per capita levels. Two studies conducted to explore differences in QOLIE between countries were focused on Europe [12,13].

We conducted a literature search for available original research reports using the QOLIE-31 inventory published in the past 15 years. Currently, there are no published papers, to our knowledge, assessing the global variations in QOL in PWE, information that would inform existing and emerging interventions for enhancing epilepsy care worldwide.

2. Methods

We performed a search using Medline (PubMed) to identify studies related to QOL among PWE, using the QOLIE-31 inventory and published between Jan. 1, 2000 and Dec. 31, 2015. Searches were conducted as follows: ((“Quality of life”[Mesh] OR “QOLIE”[all fields] OR “QOLIE-31”[all fields] OR “QOLIE31”[all fields]) AND (“Epilepsy”[Mesh] OR “Seizures”[Mesh] OR “epilepsy”[all fields]) AND “[country name]”). Each of the 194 countries listed by the World Health Organization (WHO) in 2015 was included as a search term [14]. Countries were designated as low-, lower middle-, upper middle-, or high-income

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according to World Bank 2015 fiscal year classification [15]. If 2014 GNI per capita data were unavailable, data from the most recently available reporting year were used instead.

The title and abstract of each study were read by one physician reviewer (AS) to determine if it met inclusion criteria [16]. We limited our search to articles assessing QOL in PWE using the QOLIE-31 inventory and those that were published with at least an abstract in English. If the title or abstract was not clear, the full manuscript was read to determine the study's eligibility for inclusion. Studies that were narrow in their patient population were excluded, when participants were considered to be nonrepresentative and noncomparable across many countries. We then augmented the formal literature search by performing manual search engine queries to find additional articles, involving the country name and QOLIE as sole search terms.

The mean QOLIE-31 scores, which were presented in the studies identified, were according to the various sample sizes. Differences in QOLIE were then tested for trends across WHO world region and World Bank country income group classification using an extension of the developed Wilcoxon Rank-Sum test [17].

3. Results

3.1. Search results

The literature search yielded 188 articles in the 15-year timeframe of interest (Fig. 1). Languages of reports were English (n = 165 articles), Spanish (n = 10), Hungarian (n = 3), Russian (n = 2), Dutch (n = 2), German (n = 2), Norwegian (n = 2), Japanese (n = 1), and Polish (n = 1). None of the articles excluded because of language were from LMICs. Articles were excluded if the population of PWE was too narrow (e.g., refractory epilepsy, neurooncology patients, surgical patients, patients with neurocysticercosis) (n = 35 articles), included only pediatric or adolescent populations (n = 32), used scales other than the QOLIE-31 (n = 34), focused on issues other than QOLIE (e.g., cost, medication adherence, driving, marriage, sexual dysfunction) (n = 35), or were irrelevant to the study question (e.g., use of QOLIE in patients with narcolepsy) (n = 5). One additional article of potential relevance could not be accessed through Harvard University's Library system or through attempts to reach the corresponding author.

Twenty-three articles were included from the search. An additional 17 articles were added via hand searching the literature. The majority of all articles were from European countries (n = 3219, 11 countries), followed by the Western Pacific (n = 1481, 6 countries), the Americas (n = 815, 5 countries), Africa (n = 954, 4 countries), Southeast Asia (n = 642, 4 countries), and the Eastern Mediterranean (n = 144, 1 country). Some studies covered multiple countries. In total, 15% of all countries (n = 31) reported on a total of 7255 individuals. Of these, only 8 are classified as low- or middle-income by the World Bank (25% of all reporting countries in the literature search). The findings are presented in Table 1.

3.2. Synthesis of QOLIE across countries

The global mean QOLIE-31 score was 59.8 (SD: 8.0) (n = 7255 people). The QOLIE-31 scores were 57.2 (SD: 7.8) for African countries, 58.3 (8.4) for the Americas, 59.9 (8.2) for Europe, 52.7 (0.6) for the Eastern Mediterranean, 59.7 (8.1) for Southeast Asia, and 62.7 (6.1) for the Western Pacific. The international range in QOLIE scores was from 42.1 (SD: 4.1) in Russia to 82 (SD: 32.8) in Canada. Excluding these two endpoints, the range of QOLIE globally becomes narrower: 48.7 (10.8) in Russia to 70.8 (13.3) in Spain.

There was a statistically significant difference by high-, upper-middle-, lower-middle-, and low-income countries with higher-income countries reporting higher mean QOLIE overall (test for trend, $p < 0.0001$). The QOLIE-31 subscale scores were not available for all countries to conduct secondary analyses on regional or country income status differences on subscales of the QOLIE battery.

4. Discussion

The present analysis provides an overview of the global variation in the QOL in PWE worldwide based on the QOLIE-31 inventory and highlights the need for further studies in LMICs. Even though LMICs are disproportionately burdened by epilepsy, in our reviewed literature, QOLIE-31 scores were available from only eight LMICs. Interestingly, limiting inclusion to articles in English did not exclude any articles from LMIC contexts, further highlighting the relative absence of LMICs in QOLIE literature, at least in large search engines, and the need for

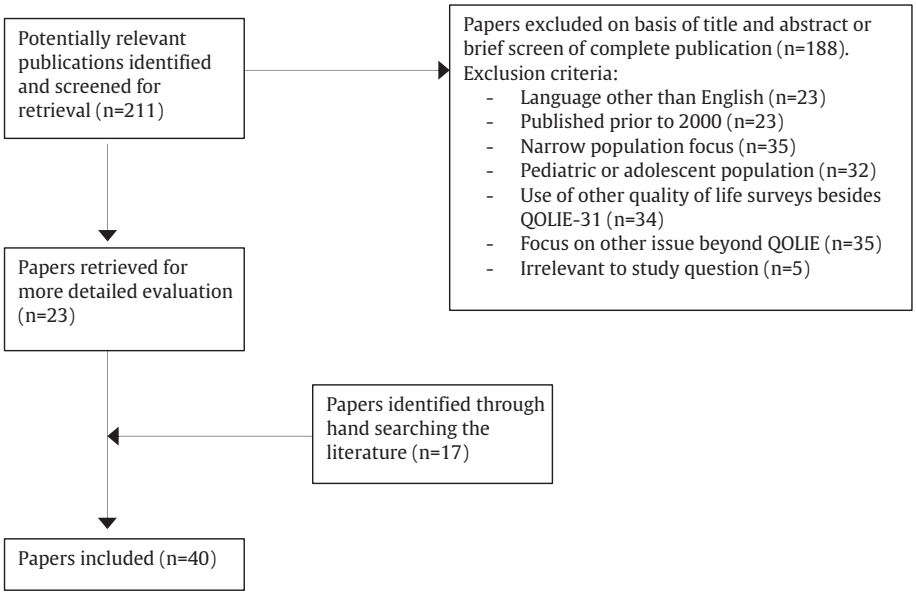

Fig. 1. Study selection for global comparison of QOLIE-31 scores.

Table 1
Global comparison of QOLIE-31 scores.

	WHO region	GNI per capita (USD)	Mean QOL (SD)	Number of participants (n)	Mean age (SD)	Age range (years)	Location of study
WHO income level							
Low							
Benin	Africa	810	52.1 (33.4)	215	30 (10)	18+	Rural areas [7]
Cambodia	Western Pacific	1020	50.0 (10.4)	96	24 (13.6)	3–70	Prey Veng province [9]
Togo	Africa	570	49.5 (7.4)	281	32 (10)	18+	Rural areas [7]
Uganda	Africa	680	58.1 (13.1)	175	26.6 (11.1)	15+	Mental clinics at Mulago & Butabika national referral hospitals [8]
Lower middle							
Bhutan	Southeast Asia	2390	48.9 (16.7)	204	27.5 (10.9)	14–75	Jigme Dorji Wangchuck National Referral Hospital [6]
India	Southeast Asia	1570	59.53 (17.6)	31	33.7 (11.2)	18–65	Psychiatric Centre Campus, Jaipur [10]
			68 (15.8)	112	31.2 (10.7)	17–60	Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum [18]
			64.6 (9.0)	60	30.2 (10.1)	18+	Tertiary care teaching hospital, Nagpur, Maharashtra [19]
Indonesia	Southeast Asia	3630	67.6 (14.6)	145	31.41 (9.8)	18–60	Department of Neurology—Cipto Mangunkusumo Hospital [20]
Nigeria	Africa	2970	72 (15.1)	93	34 (14.6)	18+	University College Hospital, Ibadan, Nigeria [21]
			67.1 (13.7)	102	32.5 (15)	18+	Neurology department of Olabisi Onabanjo University Teaching
			65.2 (14.51)	88	31.8 (13.6)	18+	Hospital, Sagamu [22,23]
Upper middle							
Brazil	Americas	11,530	50.4 (23.8)	150	32 (10.5)	18+	Hospital Sao Paolo [2]
Bulgaria	Europe	7420	56.8 (18.9)	106	37.2 (11.5)	18–60	Clinics of Neurology of the University Hospital in Varna; eight neurological practices [24]
China	Western Pacific	7380	60.7 (16.9)	247	27	18+	Neurology Department of Huashan Hospital [25]
Tibet		NA	42.2 (17.6)	37	28 (12)	10–54	Lhasa and Chamdo cities, rural areas [26]
Jamaica	Americas	5220	61.6 (18.5)	101	41 (15.4)	18+	Kingston Public Hospital & Epilepsy Centre of Jamaica [27]
Iran	Eastern Mediterranean	6,840	53.4 (22.8)/ 52.2 (14.6)	60/ 84	32.6 (9.2)	18-65/ 18-60	Teaching hospital in Zanjan / Tehran [28,29]
Malaysia	Western Pacific	10,760	68.9 (15.9)	106	31.8 (11)	18–62	Hospital Universiti Sains Malaysia, urban [3]
			52.6 (17.5)	60	27.5	18–65	Hospital Sultanah Nur Zahirah, Kuala Terengganu [30]
Mexico	Americas	9860	55.7 (14.9)	401	32.2 (11.6)	18+	National Institute of Neurology and Neurosurgery of Mexico [31]
Serbia	Europe	5820	70.6 (17.7)	203	37.9 (13.6)	18–65	Department of Epilepsy and Clinical Neurophysiology of the Institute of Mental Health in Belgrade [32,33]
Thailand	Southeast Asia	5370	57.7 (15.8)	90	32.5	15–50	Tertiary referral medical center [34]
Turkey	Europe	10,840	56.4 (17.3)	148	32.5 (10.7)	17–65	Sivas and Istanbul [4]
High							
Czech Republic	Europe	18,970	65.6 (18.3)	221	40.6 (14.9)	18–81	University Hospital Hradec Kralove [35]
Canada	Americas	51,690	82 (32.8)	80	34.9 (9.6)	16+	University of Calgary [36]
France	Europe	43,070	61.9 (19)	190	40.8 (15.5)	16+	University Hospital of Montpellier [37]
Germany	Europe	47,640	54.5 (18.5)	509	35.4 (12.3)	17–77	Bethel Epilepsy Center [38]
Greece	Europe	22,090	69.6 (18.1)	223	35.2 (13.2)	18+	University Hospital of Alexandroupolis, the First Neurology Department of AHEPA hospital in Thessaloniki and the Department of Neurology at Aiginitio Hospital in Athens [39]
Hong Kong	Western Pacific	40,320	64.3 (16.2)	247	38.8 (12.6)	18–76	Prince of Wales Hospital [40]
			70 (9.2)	186	37.8 (12.5)	18+	Prince of Wales Hospital [41]
Hungary	Europe	13,470	53.9 (28.5)	170		16+	5 Hungarian epilepsy centers [42]
Japan	Western Pacific	42,000	68.2 (18.3)	102	45.8 (15.7)	18–82	Nagoya City University clinic [43]
Italy	Europe	34,280	63.9 (18.2)	484	37	14–80	44 Italian referral centers [44]
Russia	Europe	13,210	48.7 (10.8)	208	31.5 (13.2)	18–74	Moscow/Moscow regions [45]
			42.1 (4.1)	242	35.9 (17.6)		Moscow [46]
South Korea	Western Pacific	27,090	63.1 (15.8)	400	32.9 (9.4)	19–64	10 epilepsy centers [47]
Spain	Europe	29,940	61.8 (17.3)	252	33.6 (12.3)	18–65	Neurology Service of the Hospital Clinic de Barcelona [48]
			70.8 (13.3)	263	46.5 (13.9)	18+	Multiple centers [49]
United States	Americas	55,200	58 (16)	83	45.2 (12.5)	18+	Seattle—Metropolitan area [50]

Legend: GNI = gross national income.

supporting research endeavors in LMICs to enhance understanding of global gaps in epilepsy care.

The QOLIE-31 scores differed among countries based on their income level and world region. We were not able to determine whether income category versus WHO regional category was a stronger determinant of QOLIE-31 scores as there is not a reliable statistical technique to test trend over unranked categories such as the WHO categories versus ranked categories (income level). The overall mean global QOLIE was relatively low at 59.8 and spanned widely in range. The world region differences could be mostly attributable to the higher QOLIE-31 scores in one region in particular—the Western Pacific. To better appreciate the differences that may be due to study methodology or, more likely, differences in the actual experience of epilepsy, there is a need for more data on QOL in PWE in LMICs. Further studies could assess which factors most contribute to these global differences. Our finding that QOLIE is generally lower in LMICs focuses attention to the potential role of economic conditions and available resources within each country on the patients' lived experiences with epilepsy but does not exclude other possibilities such as geography, culture, and health system infrastructure. Economic conditions can influence the availability of neurologists; the training of primary care providers who can treat epilepsy; the availability and cost of medications; access to prevention, treatment, and follow-up care; and public educational campaigns addressing risk factors or stigma of epilepsy [5].

There are limitations to this exploratory study. Primarily, this is a topical review rather than a systematic review, and we did not search databases other than Medline (PubMed). It is well recognized that many academic articles are not indexed in PubMed, and thus, potentially relevant papers may have been overlooked. We also acknowledge that the search strategy may have missed publications because of our

MESH term selection and search string strategy being overly selective. We only included one physician reviewer. Our sample size of published reports on QOLIE worldwide is nevertheless the largest analyzed so far, including 31 countries and >7000 participants in total.

Furthermore, our study may be replicated with inclusion of other QOLIE batteries. It is uncertain but valuable to know how the various QOLIE inventory results can be compared with each other internationally. One study suggests that QOLIE-10 and QOLIE-31 results are comparable [50], but there is little comparison among other inventories, including QOLIE-89. Other scales of interest are not focused on QOL or epilepsy specifically, such as the Washington Psychosocial Seizure Inventory (WPSI) and Short-Form (SF)—36 [51,52]. There is also the uncertainty about the applicability of these QOL inventories in LMIC contexts, as the inventories were developed in North America or Europe. For example, in a previously published study by the authors assessing the QOLIE in Bhutan using QOLIE-31 [6], the QOL question relating to driving was eliminated since a minority of the cohort drove motor vehicles. The importance of driving as a QOL facet is highly culturally specific, and in some cases, "transportation" may be a more appropriate but less precise question in LMICs. Other culturally specific domains that can be negatively affected include education, employment, and social relationships such as propensity to marry and have children.

The various studies comprising this global comparison are also variable in their methodological approach, which questions the generalizability of the studies to QOL among PWE in the entire country. For example, the sample sizes ranged from 31 to 509 participants; the study populations are either rural or urban without this factor often being taken into account as a potential confounder; and certain educational levels—such as illiteracy—serve as exclusion criteria [39], which could dampen how representative the findings are, especially given that PWE may be limited in their educational attainment in some locations. Ultimately, while this study uses QOLIE-31 scores to comment about trends of global variation in QOLIE, particularly as it pertains to differences in GNI, we acknowledge that this can be a crude representation of the lived experiences of PWE in these countries; neither the QOLIE-31 inventory nor its application in an investigative study is uniform across differing languages, cultures, or study designs. We assume a certain degree of representativeness in reporting by country, e.g., that QOLIE is lowest in Russia and highest in Canada. However, a particular published report may indeed be uncharacteristic of the reporting country, with either inflated or deflated QOLIE results due to study-specific factors that may be unrecognized or unreported. Future collaborative efforts with larger teams internationally could expand our comparative understanding of QOLIE studies globally.

In conclusion, while it is known that there is substantial global variation in the burden of epilepsy, we demonstrate here that there is also substantial variation in QOLIE, and country income level may play a contributing role. Low- and middle-income countries are still underrepresented in epilepsy literature despite an increasing awareness of global epilepsy disparities. In order to address global disparities in the epilepsy treatment gap, lower-income countries' investigators could engage in QOLIE studies. Comparing QOLIE across countries may increase our understanding of what factors determine QOL among PWE and thereby reduce the potentially damaging social consequences and poor health outcomes associated with poor QOLIE.

Author contributions

Dr. Altaf Saadi: drafting/revising the manuscript for content, including medical writing for content; acquisition of data; and analysis or interpretation of data.

Mr. Bryan Patenaude: statistical analysis and analysis or interpretation of data.

Dr. Farrah J. Mateen: drafting/revising the manuscript for content, study concept or design, analysis or interpretation of data, acquisition of data, and study supervision.

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Disclosures

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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