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PatientsLikeMe® Online Epilepsy Community: Patient characteristics and predictors of poor health-related quality of life

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ABSTRACT

Objective: The online PatientsLikeMe® Epilepsy Community allows patients with epilepsy to record, monitor, and share their demographic, disease, and treatment characteristics, providing valuable insights into patient perceptions and understanding of epilepsy. The objective of this retrospective analysis was to characterize the profile of users and their disease and identify factors predictive of poor health-related quality of life (HRQoL), while assessing the platform's potential in providing patient-reported data for research purposes.
Methods: Data recorded (January 2010–November 2011) by Epilepsy Community members, with an epilepsy diagnosis and who reported >1 seizure, included the following: sociodemographic and disease characteristics, treatments, symptoms, side effects perceived as medication-related, seizure occurrence, and standardized questionnaires (Quality of Life in Epilepsy Inventory [QOLIE-31/P], EuroQoL 5-Dimensions Scale, 3 Levels [EQ-5D-3L], and Hospital Anxiety and Depression Scale [HADS]). Univariate and multivariate logistic regressions were conducted to identify predictors of poor HRQoL.
Results: During the study period, the Epilepsy Community comprised 3073 patients, of whom 71.5% were female, had a mean age of 37.8 years, and had a mean epilepsy duration of 17.7 years. The most frequently reported moderate/severe symptoms (n = 2135) included memory problems (60.2%), problems concentrating (53.8%), and fatigue (50.0%). Medication-related side effects (n = 639) included somnolence (23.2%), fatigue (17.2%), and memory impairment (13.8%). The QOLIE-31/P scores (n = 1121) were significantly worse in patients who experienced a recent seizure. For QOLIE-31/P, highly predictive factors for poor HRQoL included the following: mild/moderate problems concentrating, depression, memory problems, treatment side effects, occurrence of tonic–clonic seizures, and epilepsy duration ≤1 year. For EQ-5D-3L, highly predictive factors for poor HRQoL included the following: pain, depression, and comorbidities. Patients on newer AEDs were less likely to report poor HRQoL (QOLIE-31/P).
Significance: These findings move further towards supporting the feasibility and usefulness of collecting real-world, anonymized data recorded by patients online. The data provide insights into factors impacting HRQoL, suggesting that a holistic treatment approach beyond seizure control should be considered in epilepsy.

1. Introduction

Health-related quality of life (HRQoL) describes an individual's self-perception of well-being, which includes physical, mental, emotional, and social domains of life [1,2]; HRQoL focuses on the impact health status has on quality of life. In epilepsy, the occurrence of seizures has a negative impact on the HRQoL of those living with epilepsy [3], with higher seizure frequency and severity resulting in decreased patient HRQoL [4]. Other factors also contribute to poor HRQoL among patients with epilepsy, such as the occurrence of side effects associated with

Abbreviations: AED, antiepileptic drug; EQ-5D-3L, EuroQoL 5-Dimensions Scale, 3 Levels; HADS, Hospital Anxiety and Depression Scale; GTC, generalized tonic–clonic; HRQoL, health-related quality of life; NEWQOL, Quality of Life in Newly Diagnosed Epilepsy Instrument; PRO, patient-reported outcome; QOLIE-31/P, Quality of Life in Epilepsy Inventory; SD, standard deviation.

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antiepileptic drug (AED) treatment [5]; psychiatric comorbidities, such as depression and anxiety [3,6]; the perceived stigma of epilepsy [7]; and a reduced level of independence (e.g., not being able to drive) [8]. Improving the HRQoL of patients with epilepsy is an important component of contemporary disease management strategies [9], in addition to treating or preventing the occurrence of seizures.

Disease management and patient support strategies have evolved significantly over the past decade, with many patients now taking a more active role in collaborating with their healthcare provider(s) [10,11]. The popularity of networking sites, online communities, and virtual forums, where patients can discuss their health concerns and exchange information, is growing, especially for those living with chronic diseases [11]. PatientsLikeMe® (http://www.patientslikeme.com) is an online health data-sharing platform for patients with life-changing diseases. The main goals of the website are to provide patients with the tools to record, track, and share their disease characteristics and outcomes; to help patients learn how to improve their care through peer-to-peer interactions; and to enhance understanding of how the disease and its treatment can potentially impact their lives [10,11]. The PatientsLikeMe Epilepsy Community, launched in the United States in January 2010, was developed in partnership with UCB Pharma. The perceived benefits reported by patients using the system include the ability to connect with others experiencing the same symptoms, having a better understanding of their seizures, learning more about symptoms or treatments [11], and improvement in patient self-management and self-efficacy [12].

Through this research, data collected from PatientsLikeMe Epilepsy Community members were utilized to help characterize demographic and epilepsy characteristics in this patient population, including symptoms and medication-related side effects, and to identify factors predictive of poor HRQoL. In addition, the potential of the platform for collecting patient-reported data suitable for research purposes was assessed, as were the validated and standardized instruments used to record HRQoL-related data from patients with epilepsy.

2. Methods

2.1. Study population

PatientsLikeMe Epilepsy Community members, who logged in to the website between January 2010 and November 2011, reported a diagnosis of epilepsy, and had experienced more than one seizure during their lifetime, were included in the analysis. Initially, the community was only accessible to users in the United States; however, from April 2011, it became available worldwide (English language only). Members and users of the site became aware of the opportunity to join PatientsLikeMe through online advertising (e.g., on Google and Facebook), media partnerships, press coverage, word of mouth, and physician referral.

All members of the PatientsLikeMe Epilepsy Community agreed to be contacted for research as a condition of joining the community and were free to opt in or out, allowing for them to only disclose information they were willing to share. It was made clear that there would be no adverse consequences if members elected not to participate.

Institutional review board approval was not sought because of the noninterventional nature of the analysis.

2.2. Data collection

Patients (or their caregiver [parent or guardian]) were able to record information on sociodemographic characteristics and a range of epilepsy and treatment-related characteristics. Patients could record the occurrence and severity of symptoms (none, mild, moderate, severe) using a predefined checklist (Supplementary Fig. 1A). The symptom checklist was developed by a panel of epilepsy experts and included symptoms considered likely to occur frequently among patients with epilepsy (anxiety, depression, fatigue, headache, insomnia, memory problems, pain, problems concentrating, and somnolence). Patients could also document their treatment history and current treatment(s) and specify any side effects they perceived to be related to their treatment (medication-related side effects; assessed as mild, moderate, or severe) (Supplementary Fig. 1B). Side effects were not prespecified. However, a drop-down box listing side effects previously reported by users of the PatientsLikeMe site was available and appeared once the user began typing in his/her side effects. The user could also include verbatim side effects where applicable. Side-effect terms were classified according to the Medical Dictionary for Regulatory Activities coding [13] version 14.1. In line with adverse event reporting regulations, a pharmacovigilance system was employed during the data collection period to identify, record, evaluate, and report medication-related side effects attributed to UCB products.

Patients also had the opportunity to complete and review their information for a number of validated, standardized patient-reported outcome (PRO) instruments, namely, the Quality of Life in Epilepsy Inventory (QOLIE-31/P) [14], the Hospital Anxiety and Depression Scale (HADS) [15], and the EuroQoL 5-Dimensions Scale, 3 Levels (EQ-5D-3L) [16]. These instruments were selected as QOLIE-31/P is the most widely used assessment of HRQoL in epilepsy trials, HADS captures varying levels of anxiety and depression and is widely referenced in the literature, and the EQ-5D-3L is in widespread use for health technology assessments by agencies such as the National Institute for Health and Care Excellence (NICE). The QOLIE-31/P is an epilepsy-specific HRQoL instrument, which comprises 30 items grouped into seven multi-item subscales, assessing seizure worry, overall quality of life, emotional well-being, energy/fatigue, cognitive function, medication effects, and social function. It requests that participants take into consideration the last 4 weeks when responding. It also includes an additional, overall health status item [14,17] not included in the total score calculation. The QOLIE-31/P total score is calculated as a weighted average of the subscale scores and ranges from 0 to 100, with 100 representing the best HRQoL [14,17]. The HADS instrument assesses the presence and severity of anxiety and depression and requests that the previous week be considered when responding. It consists of 14 items, scored on a 4-point severity scale. An anxiety score and a depression score are calculated, each ranging from 0 to 21, with levels of anxiety and depression classified as follows: normal (0–7), mild (8–10), moderate (11–14), and severe (15–21) [15]. The EQ-5D-3L is a generic instrument assessing health status that enables comparison with other diseases [16]. It includes five items covering key dimensions of life, including the following: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, which are rated as follows: no problem, some/moderate problems, or extreme problems [16]. These dimensions are used to determine the patient's health state, which is mapped to a utility score anchored at 0 and 1, with 1 representing full health [16]. The overall health status item is measured on a visual analog scale from 0 to 100, with 100 representing full health. The EQ-5D-3L instrument requests that participants take into consideration 'your own health state today' when responding. The EQ-5D-3L utility score was calculated using US weights taken from the general population [18].

Patients were able to update their profile at any time and were asked to complete the battery of PRO instruments at least once. Before the completion of the PRO instruments, patients were prompted to update their profile and were required to provide information about their seizure experience during the last 4 weeks (experience/no experience of simple partial, complex partial, or generalized tonic–clonic seizure). The PRO instruments were provided in the following order: QOLIE-31/P, HADS, and EQ-5D, and all questions per page had to be answered in order to progress to the next page or to the next PRO instrument. Data were collected from the first completion of each of the PRO instruments. The results of the PRO instruments completed by each patient were available for the patient to view personally on the PatientsLikeMe

website, as well as being compiled anonymously with other patients' data.

For a further understanding of the interface of the PatientsLikeMe site, Wicks et al. (2012) [11] could be consulted.

2.3. Analysis

All data were anonymized and retrospectively analyzed. The population with epilepsy was defined as all patients who recorded a diagnosis of epilepsy and more than one seizure during their lifetime. Patients from the population with epilepsy who had also completed the predefined symptom checklist at least once comprised the population with symptoms, and those who also completed the PRO instruments at least once comprised the PRO population. The population with side effects comprised those patients from the population with epilepsy who also recorded at least one medication-related side effect.

The demographic and epilepsy characteristics recorded at the time of first completion of the online assessments were summarized descriptively. Similarly, descriptive analysis of current symptoms data, including symptom severity and HRQoL, utilized data recorded by each patient at first completion.

To determine the association between the occurrence of seizures and HRQoL, PRO scores were compared between subgroups of patients who had or had not experienced seizures within the preceding 4 weeks before the assessment (no seizures, ≥1 generalized tonic–clonic seizure [GTC, which included primary or secondarily generalized tonic–clonic seizures], ≥1 non-GTC seizure [which included any seizure not classified as a GTC seizure]).

To assess the association between anxiety and depression levels (as measured by HADS) and HRQoL (as measured by QOLIE-31/P total score), univariate linear regression analysis of the QOLIE-31/P total score on anxiety and depression, respectively, was conducted and Pearson's correlation coefficients were calculated.

Univariate and stepwise multivariate logistic regression analyses were undertaken to identify factors associated with poor HRQoL (QOLIE-31/P total and EQ-5D-3L utility scores), using data from patients in the PRO population who had completed the symptom checklist. Poor HRQoL was defined as having a QOLIE-31/P or EQ-5D-3L score, respectively, in the lowest quartile. Initially, univariate logistic regression was performed on a number of variables to identify those to be included in the multivariate analyses (see Supplementary Table 1). Variables assessed in the univariate analyses included the following: sociodemographic characteristics (age, gender, body mass index), disease characteristics (duration since diagnosis, type of epilepsy syndrome), occurrence of seizures in the 4 weeks preceding the assessment, severity of each symptom from the symptom checklist, AED treatment ongoing at the time of assessment (monotherapy or polytherapy; older AEDs [introduced before 1993] or newer AEDs [introduced after 1993]), medication-related side effects perceived by patients to be related to their treatment (recorded within the 4 weeks before assessment), and current comorbidities. Variables were selected for inclusion if results from the univariate analysis showed a p-value < 0.05. Results are presented as odds ratios with 95% confidence intervals (CIs). Only variables with $p < 0.05$ are presented. Factors highly predictive of poor HRQoL were defined as those with an odds ratio of >2 (positive predictor) or <0.5 (negative predictor).

3. Results

3.1. Patient characteristics

The PatientsLikeMe population with epilepsy comprised 3073 users who registered and completed data online between January 2010 and November 2011. Of these, 69.5% were included in the population with symptoms, and 36.5% completed all three PRO questionnaires (QOLIE-31/P, HADS, and EQ-5D-3L) at least once and comprised the PRO population (Table 1). Overall, 36.2% completed both the predefined symptom checklist and the PRO instruments. A total of 20.8% of patients recorded ≥1 side effect that they perceived as being related to their medication and were included in the population with side effects (Table 1).

In the population with epilepsy, 71.5% of patients were female. The mean (SD) age of patients in the population with epilepsy was 37.8 (12.7) years; 7.3%, 76.3%, and 16.4% of patients were aged 0–20 years, 21–50 years, and >50 years, respectively, with 96.4% aged ≥18 years. The mean time since diagnosis was 17.7 (14.1) years (Table 1). In total, 79.1% (2412/3049) of patients who recorded information about their diagnosing and/or treating physician had been diagnosed by a pediatric neurologist/neurologist, and 73.4% (2034/2770) were currently managed by a pediatric neurologist/neurologist. Diagnostic tests had been carried out on 99.2% (2953/2978) of patients, with the most frequent being magnetic resonance imaging (88.3%; 2607/2953), electroencephalography (85.6%; 2528/2953), and computed tomography (71.8%; 2120/2953). Of the patients who recorded a comorbid condition (n = 2271), more than half (53.9%) recorded at least one, most frequently migraine (28.1%), anxiety disorder (17.6%), major depressive disorder (13.9%), and hypertension (10.5%) (Table 1). Of the patients who recorded an AED therapy (n = 1773), similar proportions recorded monotherapy (51.4%) and polytherapy (48.6%); the majority (56.4%) were treated with newer AEDs only (as monotherapy or as part of a combination therapy). Approximately half of the patients (51.3%; 1488/2900) did not drive, with 84.8% (1261/1487) of these patients citing epilepsy as the reason for not driving.

Overall, the demographic characteristics of the different subpopulations appeared similar to those of the population with epilepsy, with the exception of the percentage of patients who recorded unknown seizure types (24.7%, 9.2%, 0.6%, and 4.2% for the population with epilepsy, population with symptoms, PRO population, and population with side effects, respectively).

3.2. Symptoms and medication-related side effects

Of the patients in the population with symptoms (n = 2135), 87.5% recorded at least one moderate or severe symptom from the predefined symptom checklist (36.2%: 1–3, 35.9%: 4–6, and 15.4%: 7–9). Symptoms most frequently recorded as moderate or severe were memory problems (60.2%), problems concentrating (53.8%), fatigue (50.0%), and excessive daytime sleepiness (somnolence: 41.4%) (Fig. 1).

Among the patients who recorded medication-related side effects that they perceived to be associated with their treatment (20.8% of the overall population with epilepsy), 6.7% (43/639) recorded one, 28.3% (181/639) recorded two, and 64.9% (415/639) recorded three or more medication-related side effects. The most frequently reported medication-related side effects (in ≥10% of patients) were somnolence (23.2%), fatigue (17.2%), memory impairment (13.8%), dizziness (11.6%), and abnormal weight gain (10.5%).

3.3. HRQoL

In the PRO population, overall mean (SD) QOLIE-31/P total score was 51.5 (19.0), indicating a moderate level of HRQoL. The occurrence of seizures during the 4 weeks preceding the QOLIE-31/P assessment was found to negatively affect HRQoL across all domains (Fig. 2). Patients recording ≥1 non-GTC seizure had significantly worse QOLIE-31/P scores, compared with those not recording any seizures. These findings were more pronounced among patients experiencing ≥1 GTC seizure during the 4 weeks preceding QOLIE-31/P assessment. Seizures affected all QOLIE-31/P domains in a similar manner for those experiencing either a GTC or non-GTC seizure within the past 4 weeks versus those who did not experience seizures. The greatest impact of

Table 1
Baseline demographic and epilepsy characteristics.

Parameter[a]	Population with epilepsy (n = 3073)	Subpopulation		
		Population with symptoms (n = 2135)	PRO population (n = 1121)	Population with side effects (n = 639)
Gender, n	2929	2107	1121	639
Female, %	71.5	73.2	72.2	73.4
Age, n	2909	2095	1120	633
Mean (SD), years	37.8 (12.7)	37.6 (12.6)	37.8 (12.3)	38.6
Age class, n	2909	2095	1120	633
0–20 years, n (%)	212 (7.3)	148 (7.1)	69 (6.2)	27 (4.3)
21–50 years, n (%)	2219 (76.3)	1608 (76.8)	869 (77.6)	491 (77.6)
>50 years, n (%)	478 (16.4)	339 (16.2)	182 (16.3)	115 (18.2)
Geographic location, n	2803	2070	1120	630
USA, n (%)	2757 (98.4)	2038 (98.5)	1120 (98.7)	620 (98.4)
Time since diagnosis, n	3044	2130	1121	637
Mean (SD), years	17.7 (14.1)	17.4 (13.8)	17.8 (13.7)	16.7 (13.3)
Age at first seizure, n	2906	2095	1121	633
Mean (SD), years	17.2 (13.5)	17.1 (13.3)	16.5 (13.0)	17.8 (13.4)
Seizure type, n	3073	2135	1121	639
Generalized, n (%)	727 (23.7)	604 (28.3)	344 (30.7)	178 (27.9)
Partial, n (%)	729 (23.7)	621 (29.1)	376 (33.5)	202(31.6)
Mixed, n (%)	859 (28.0)	713 (33.4)	394 (35.1)	232 (36.3)
Unknown, n (%)	758 (24.7)	197 (9.2)	7 (0.6)	27 (4.2)
AED treatment[b,c], n	1773	1593	1121	594
Monotherapy, n (%)	912 (51.4)	802 (50.3)	484 (47.6)	288 (48.5)
Polytherapy, n (%)	861 (48.6)	791 (49.7)	533 (52.4)	306 (51.5)
Newer AEDs only[d], n (%)	1000 (56.4)	899 (56.4)	570 (56.0)	333 (56.1)
Older AEDs only[d], n (%)	351 (19.8)	309 (19.4)	183 (18.0)	158 (26.6)
Combination of newer and older AEDs, n (%)	422 (23.8)	385 (24.2)	264 (26.0)	103 (17.3)
Comorbidities[e], n	2271	1769	986	538
Patients with ≥1 comorbid condition, n (%)	1224 (53.9)	970 (54.8)	549 (55.7)	301 (55.9)
Migraine, n (%)	638 (28.1)	506 (28.6)	280 (28.4)	145 (27.0)
Anxiety disorder, n (%)	400 (17.6)	316 (17.9)	178 (18.1)	107 (19.9)
Major depressive disorder, n (%)	316 (13.9)	259 (14.6)	152 (15.4)	87 (16.2)
Hypertension, n (%)	239 (10.5)	190 (10.7)	112 (11.4)	59 (11.0)

AED, antiepileptic drug; PRO, patient-reported outcome; SD, standard deviation.
[a] Not all parameters were completed by all patients.
[b] Patients recorded ≥1 AED treatment.
[c] Members of the PatientsLikeMe Epilepsy Community who do not self-report AED treatment may take no AED(s) or may have not reported their treatment.
[d] Older AEDs include the following: acetazolamide, benzodiazepines, carbamazepine, ethosuximide, methsuximide, phenobarbital, phenytoin, sulthiame, and valproic acid. Newer AEDs include the following: felbamate, gabapentin, lacosamide, levetiracetam, lamotrigine, oxcarbazepine, pregabalin, rufinamide, retigabine, tiagabine, topiramate, vigabatrin, and zonisamide.
[e] Comorbidities recorded by ≥10% of the patients from a preset comorbidity checklist are reported.

seizure occurrence was seen in the social functioning and seizure worry domains.

In the PRO population, the mean (SD) total EQ-5D-3L utility score was 0.75 (0.20), which reflects a moderately impaired HRQoL. Slightly lower mean EQ-5D-3L utility scores were seen in patients experiencing ≥1 non-GTC seizure (0.73 [0.20]; $p < 0.001$; n = 429) or ≥1 GTC seizure (0.70 [0.21]; $p < 0.001$; n = 124) than in those not reporting seizures (0.78 [0.19]; n = 568) during the 4 weeks preceding the assessment.

3.4. Anxiety and depression

Overall mean (SD) HADS scores were 9.5 (4.2) for anxiety and 6.9 (4.3) for depression, with 36.5% (409/1121) of patients reporting a moderate or severe level of anxiety and 20.2% (226/1121) reporting a moderate or severe level of depression. Overall, 157 of the 266 (59.0%)

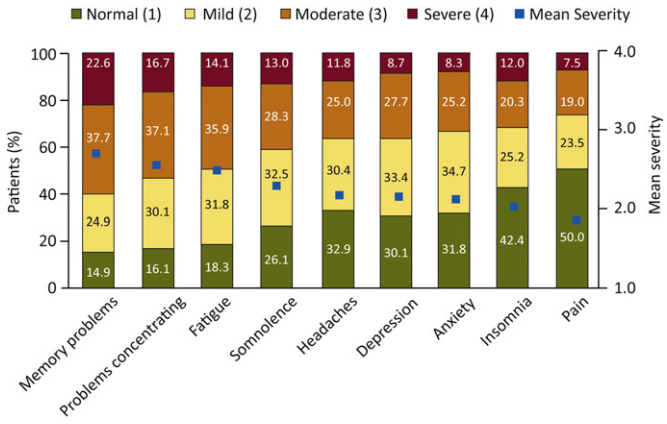

Fig. 1. Distribution and mean symptom severity ratings at first evaluation for patients who completed the predefined symptom checklist (population with symptoms; n = 2135).

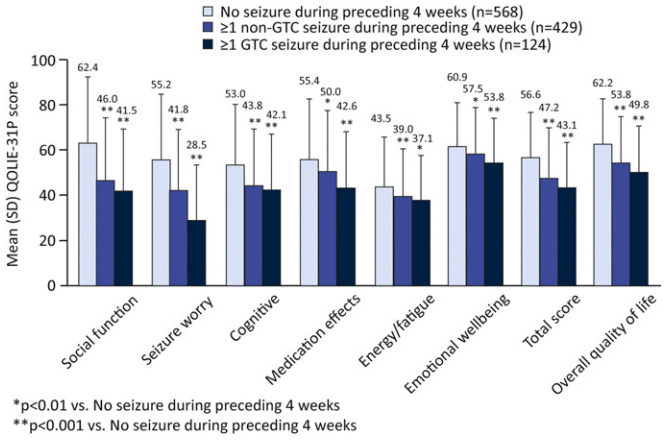

Fig. 2. Mean (SD) QOLIE-31/P scores by seizure status during the 4 weeks preceding the assessment (PRO population, n = 1121).

patients with moderate or severe depression also reported having moderate or severe anxiety, while 157 of the 409 (38.4%) patients with moderate or severe anxiety also had moderate or severe depression.

3.5. Correlation between HADS and QOLIE-31/P

Linear regression analyses, evaluating the association between anxiety or depression (HADS) scores and HRQoL (QOLIE-31/P total score), showed clear negative correlations (anxiety: $r = -0.62$; depression: $r = -0.69$) (Fig. 3), suggesting that the presence of anxiety and depression in this population, and their severity, negatively influenced HRQoL.

3.6. Predictors of poor HRQoL

In patients from the PRO population who had also completed the symptom checklist (n = 1113), 25.1% (279/1113) were classified as having poor HRQoL, based on a QOLIE-31/P total score inferior to the quartile 1 (Q1) score of 37.3. Based on an EQ-5D-3L utility score inferior to the Q1 score of 0.71, 23.6% (263/1113) were classified as having poor HRQoL.

Factors most predictive of poor HRQoL (odds ratio >2 or <0.5; $p < 0.05$) differed according to the PRO instrument evaluated (Fig. 4A and B). For epilepsy-specific HRQoL (measured by QOLIE-31/P), the most predictive factors of poor HRQoL were as follows: moderate/severe problems concentrating, occurrence of ≥1 GTC seizure during the 4 weeks preceding the PRO assessment, moderate/severe depression, epilepsy duration ≤1 year, moderate/severe memory problems, and moderate/severe side effects during the 4 weeks preceding PRO assessment (Fig. 4A). Additionally, patients not recording any AED treatment or those on newer AEDs (monotherapy or polytherapy) were similarly less likely to report poor HRQoL, compared with patients receiving polytherapy with older AEDs exclusively. For the generic HRQoL assessment measured using the EQ-5D-3L, the most predictive factors (odds ratio >2) of poor health status were as follows: moderate/severe pain, moderate/severe depression, ≥1 comorbidity, and comorbidity data missing (Fig. 4B).

4. Discussion

This retrospective analysis of data from the PatientsLikeMe Epilepsy Community provides valuable real-world data on epilepsy, its treatment, and overall impact on patients' lives for a large population of online community users. The demographic characteristics suggested that the PatientsLikeMe Epilepsy Community was not representative of the general population with epilepsy [5,19–21]. The PatientsLikeMe Epilepsy Community had a greater proportion of female patients (71.5%) compared with data from the U.S. 2005 National Health Interview Survey in adults with epilepsy (55.9%; [19]) and with PharMetrics (53.6%; a claims database representative of the U.S. commercially insured population, November–December 2008 [22]). In addition, comparison with data from PharMetrics showed that the PatientsLikeMe Epilepsy Community had a greater proportion of patients aged between 21 and 50 years (76.3% vs. 44.2%) and patients receiving AED polytherapy (48.6% vs. 28.7%) [22]. These differences are indicative of biases compared with the general population with epilepsy as a whole. Gender and age differences can have implications on patients' perception of their disease, the comorbidities they suffer, the AEDs they use, and their general well-being. For example, in the population with epilepsy, depression is more commonly associated with females than males [23], and a significant age-by-gender interaction for major depressive disorder has been reported [24]. These differences could result in gender-specific preponderance on certain assessments and further indicate that members from the PatientsLikeMe Epilepsy Community may not be fully representative of the population with epilepsy as a whole. The age and gender characteristics of the PatientsLikeMe Epilepsy Community population are generally reflecting the characteristics of online users of health forums willing to share personal data [25,26]. However, it is interesting to mention that the most frequently recorded comorbidities, moderate or severe symptoms, and medication-related side effects patients perceived to be related to their treatment in this PatientsLikeMe community were similar to those reported in other studies in patients with epilepsy [5,27].

Patients with epilepsy are at an increased risk of medical comorbidities. In total, 53.9% of patients recorded at least one comorbid condition, similar to recent findings based on multiple health plans across the United States, in which 58% of patients with epilepsy had one or more of 29 prespecified comorbidities [28]. The proportions of patients recording migraine (28.1%), anxiety disorder (17.6%), and major depressive disorder (13.9%) as a comorbidity were within estimated prevalence ranges reported for patients with epilepsy: migraine, 1.7–33.6% [29]; anxiety, 15–20% [30]; depression, 4.1–32.5% [31]; and overall, 13.0% [31]. Comorbidities complicate treatment in general and, in particular, treatment adherence in epilepsy. Pharmacological treatments for other conditions and AEDs can result in drug–drug interactions which in turn may affect the treatment efficacy/tolerability profile. Additionally, common psychological comorbidities such as depression and anxiety can have considerable effects on a patient's quality of life [32].

Of the large proportion of patients who completed the predefined symptom checklist (69.5%), the vast majority (87.5%) recorded at least one moderate or severe symptom. Moreover, 20.8% of patients recorded medication-related side effects that they associated with their treatment. The predefined symptom checklist and the side effects screen record different yet complementary information. The symptom checklist

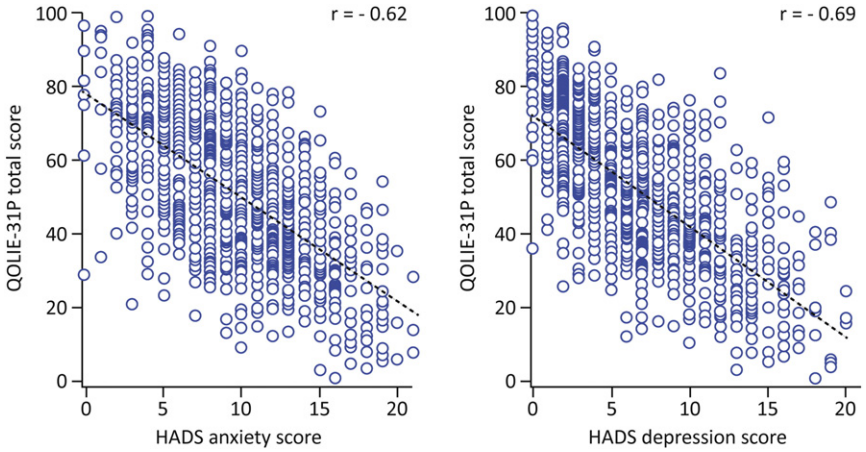

Fig. 3. Correlation between QOLIE-31/P total score and HADS anxiety and depression scores (n = 1113; PRO population who had also completed the symptom checklist).

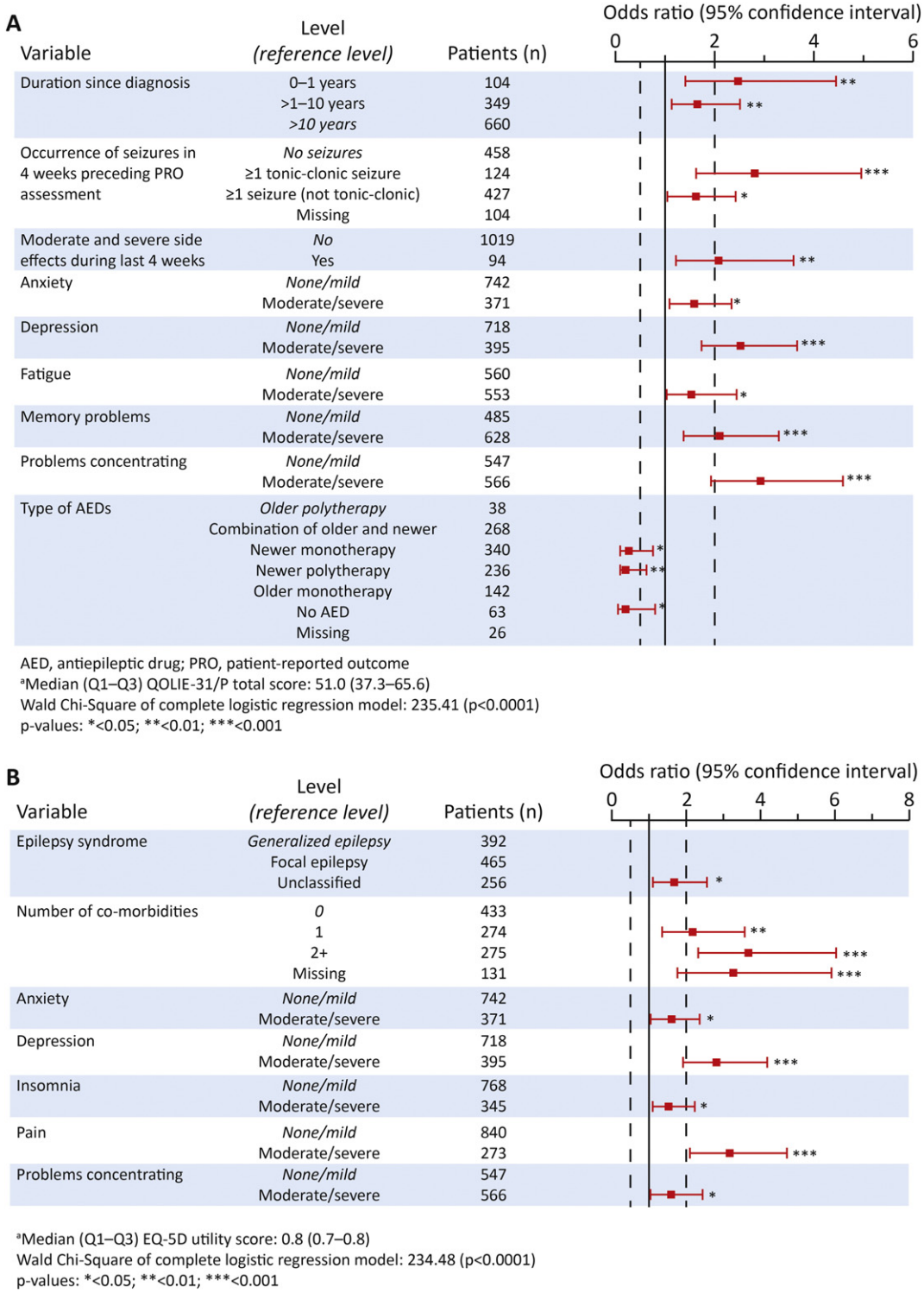

Fig. 4. Factors associated with poor health-related quality of life ($p < 0.05$) by multivariate logistic regression analysis. Predictors (odds ratio >2 or <0.5; $p < 0.05$, as indicated by dotted lines) of low QOLIE-31/P total score (<Q1)[a] (A) and low EQ-5D-3L utility score (<Q1)[b] (B) in the PRO population who had also completed the symptom checklist (n = 1113).

allows key symptoms associated with epilepsy to be monitored in a systematic and standardized way (whether related to the disease, to co-morbid conditions, or to medication-related side effects), while the side-effect reporting system allows patients to record side effects they perceive to be associated with a medication. It is important to note that it may be difficult for patients or their caregivers to differentiate symptoms attributable to the disease from side effects resulting from the patient's medication. Furthermore, spontaneous reporting of medication-related side effects is subjective [33], while the use of standardized tools to record symptoms allows for the collection of 'complaints' data from all patients. Although both approaches have their limitations, it is interesting that the two tools provided a similar pattern of reported complaints, with cognitive problems, somnolence, and fatigue being the most frequent. This is consistent with data from the U.S. 2010 National Health Interview

Survey suggesting that individuals with epilepsy are more likely to report cognitive limitations and moderate or severe fatigue compared with those without epilepsy [34] and is also consistent with data reported by other sources [5,33,35–37].

Data from this retrospective analysis provide insight into the different factors impacting patients' HRQoL. The mean QOLIE-31/P total score (51.5) and EQ-5D-3L utility score (0.75) are indicative of a patient population with a moderately impaired HRQoL.

It is well-documented that the occurrence of seizures substantially reduces patient HRQoL [4,38]. This was replicated in our analysis, particularly with the most severe type, GTC seizures. Depression and anxiety have also been found to contribute to poor HRQoL in epilepsy [21]. Previous results [38,39] from linear regression analyses indicate clear negative correlations ($r < -0.6$) between anxiety and depression scores and HRQoL, as measured by QOLIE-31/P, an association that was confirmed in the present multivariate, logistic regression analysis.

The multivariate analysis identified several additional factors associated with poor HRQoL and showed that predictors of poor HRQoL differed between the two measures (QOLIE-31/P and EQ-5D-3L). Generalized tonic–clonic seizures occurring within the preceding 4 weeks, epilepsy duration of ≤1 year, the presence of moderate or severe depression, problems concentrating, and memory problems were all highly predictive of poor HRQoL, as measured by QOLIE-31/P. Whereas, for the EQ-5D-3L, the number of comorbidities (≥1) and moderate/severe pain or depression were highly predictive of low HRQoL. The EQ-5D-3L instrument includes moderate/severe pain/discomfort and moderate/severe anxiety/depression as specific items within the measure; thus, it is unsurprising that these factors appeared as predictive factors for poor HRQoL in this assessment. Previous studies also found that comorbidities, mood problems, the occurrence of seizures, and daily functioning had a greater effect on HRQoL than short-term seizure control [40,41]. The only highly predictive factor common to both PRO measures was moderate/severe depression.

The disparities in predictive factors of poor HRQoL between the two measures are likely the result of differences in the conceptual frameworks of these measures, which cover different dimensions of patients' HRQoL. Interestingly, the occurrence of seizures, the main outcome considered by treating physicians and patients and by clinical trials, was not associated with poor HRQoL measured by the EQ-5D-3L instrument. In part, this could be explained by the different recall periods of these two instruments and also illustrates the limitation of using generic measures in the context of epilepsy. Limitations of the EQ-5D-3L have been described elsewhere [42,43] and have led to the development of the first epilepsy-specific utility measure, the Quality of Life in Newly Diagnosed Epilepsy Instrument—6D (NEWQOL-6D) [44,45], which covers HRQoL dimensions more relevant to epilepsy, such as worry about seizures, depression and social functioning, memory problems, cognitive problems, control of condition, and perceived stigma. Indeed, the dimensions covered by NEWQOL-6D were each identified in this research as being relevant to patients with epilepsy.

Contradictory data have been published on the HRQoL of patients on newer and older AEDs (on monotherapy and polytherapy) [35,46,47]. The results from this multivariate analysis to identify predictive factors of poor HRQoL indicate that a patient not recording AED treatment, or those on newer AEDs (monotherapy or polytherapy), was less likely to report poor HRQoL (QOLIE-31/P), compared with those on polytherapy with older AEDs. However, these data must be interpreted with caution, as different factors relating to individual patient profiles and disease characteristics, and not necessarily to AED treatment itself, could affect both the AED treatment regimen and the HRQoL outcome.

The concept of online tools for tracking epilepsy is not new, as evidenced by systems including Epilepsy.com, SeizureTracker.com, and numerous smartphone apps. Increasingly, patients are being encouraged to take an active role in the management of their disease, and online communities have the potential to provide an easily accessible platform and tools for this purpose. Recording symptom and medication-related side-effect information in a standardized way and sharing it with a physician, for instance by printing out information or inviting the physician to view their profile electronically, may help support informed treatment decisions by highlighting issues previously unknown to the physician, who in turn could adjust the healthcare provided in view of improving outcomes, as described in previous observational studies [5,33]. Indeed, one of the perceived benefits of PatientsLikeMe has been identified as better healthcare, as a result of recording symptoms [11]. With the current number of PatientsLikeMe Epilepsy Community users nearing 10,000, the perceived benefits and support network such an online platform could potentially offer to patients with epilepsy are extremely encouraging.

A limitation of this analysis is the different recall periods each of the PRO instruments request respondents to consider when answering the questions. Therefore, conclusions and correlations drawn by comparing data from the QOLIE-31 assessment (4-week recall period), the EQ-5D-3L (day of assessment), and the HADS instrument (1-week recall period) should be undertaken with caution.

Further limitations are related to the cross-sectional nature of this analysis and the reliability and robustness of self-reported data. Such data may be considered subjective, as they are dependent on the patients' own perception of their disease, and of questionable reliability, as they are not validated by a healthcare practitioner. Furthermore, the requirement for internet access and sufficient patient competency to engage with such systems (previously shown to be lower in patients with chronic disease) [48] should be considered. Moreover, participation bias may arise in those patients who are more likely to complete a certain assessment or record their side effects. The '1% rule', which states that, within internet communities, 90% of members observe and do not participate, 9% of members contribute sparingly, and 1% of members create the vast majority of new content, has been observed within four digital health social networks [49]. That being said, analysis of the data from the PatientsLikeMe Epilepsy Community suggested substantial involvement of its members in completing the different assessments at least once (69% completed the symptoms checklist, 36% completed the PRO instruments, and 21% recorded medication-related side effects). Additionally, as it was not mandatory for patients to complete all the information, sample sizes for each parameter were somewhat variable, and thus, the sample size for multivariate analyses was smaller, which may be a limitation of the open nature of the platform itself. Although the PatientsLikeMe Epilepsy Community may not represent the overall population with epilepsy, this is the case for a large number of data sources used for research purposes.

Knowing these limitations, it is interesting to see that these results are consistent with findings from studies in patients with epilepsy using other methods of data collection [5,7,20,27,28,38,50].

4.1. Conclusions

Overall, our findings support the feasibility and usefulness of using anonymized disease-related data recorded by patients on online platforms like PatientsLikeMe for research purposes; for instance, longitudinal tracking of individual patient care or regular cross-sectional assessments of predictors of poor HRQoL to assess changes in treatment standards over time. Indeed, data captured on PatientsLikeMe have been used in a number of research studies relevant to epilepsy [51]. However, it must be noted that, as a new source of information, the validity, generalizability, and relevance to clinical decision-making are yet to be established. The data presented provide a useful insight into real-life patients with epilepsy, allowing for an in-depth understanding of patients' experiences with their disease, and suggest that predictors of poor HRQoL in patients with epilepsy are numerous and not limited to the occurrence of seizures. The variety of factors identified that predicted poor HRQoL confirms that a holistic approach, not focused on seizure control alone, should be considered when treating people with epilepsy.

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Disclosure

K. Mueller and S. Dimova are permanent employees of UCB Pharma and hold stock options in UCB Pharma; S. Borghs is a permanent employee of UCB Pharma; T. Durgin and G. Phillips are former employees of UCB Pharma and were employed by UCB at the time the study was carried out; C. de la Loge is a consultant and former employee of UCB Pharma at the time the study was carried out. P. Wicks is an employee of PatientsLikeMe and holds stock options in PatientsLikeMe. The PatientsLikeMe Research Team has received research funding (including conference support and consulting fees) from Abbvie, Accorda, Actelion, Amgen, AstraZeneca, Avanir, Biogen, Boehringer Ingelheim, Genzyme, Janssen, Johnson & Johnson, Merck, Novartis, Sanofi, and UCB. The PatientsLikeMe R&D team has received research grant funding from Kaiser Permanente, the Robert Wood Johnson Foundation, Sage Bionetworks, The AKU Society, and the University of Maryland. P. Wicks has received speaker fees from Bayer.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.yebeh.2016.07.035.

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