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Recalling the COVID-19 lockdown: Insights from patients with epilepsy

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ABSTRACT

Purpose: The purpose of our study was to explore health changes among people with epilepsy (PWE) during a national COVID-19 lockdown in the context of patients' clinical characteristics and their experience of receiving epilepsy-related medical services.

Methods: A questionnaire was distributed for adult PWE both online and at a tertiary epilepsy center after the end of a national lockdown in Lithuania. PWE were asked to evaluate their health status during the lockdown and estimate changes in their seizure patterns. Additional questions concerned the accessibility and quality of epilepsy-related consultations.

Results: The study sample consisted of 143 PWE (59 [41.3%] male, mean age 35.1 ± 13.4 years), 94 (65.7%) completed the survey in person, 49 (34.3%) – online. A deterioration in reported physical and mental health during lockdown was observed ($Z = -4.604$, $p < 0.0001$ and $Z = -4.253$, $p < 0.0001$, respectively) and 22 (15.4%) PWE reported seizure exacerbation. In an ordinal logistic regression model (analysis of data from all participants), baseline seizure frequency ($b = 0.413$, $p = 0.031$), reported physical health before lockdown ($b = -0.462$, $p = 0.031$) and the ease of proper antiepileptic drug (AED) use during the imposed restrictions ($b = -0.535$, $p = 0.006$) were statistically significant variables associated with changes in seizure frequency. The latter were not affected by modifications in AED use (Mann–Whitney $U = 1127.0$, $p = 0.307$) irrespective of the data collection method.

With teleconsultations being predominant during the lockdown, an overall decline in the quality of epilepsy-related consultations was observed ($Z = -2.895$, $p = 0.004$). Among all participants, 46 (32.2%) lost an epilepsy-related consultation or medical service because of the lockdown. This loss was found to be associated with seizure exacerbation (Mann–Whitney $U = 1622.5$, $p = 0.046$).

Conclusion: Our study indicates that a national COVID-19 lockdown may have led to worse seizure control and health status in some PWE. Easy access to AEDs and their appropriate use may be especially useful to prevent seizure exacerbation during strict COVID-19 restrictions. The quality and accessibility of remote epilepsy-related consultations was suboptimal and may require further improvement during disruption of in-person services.

1. Introduction

In late 2019, SARS-CoV-2 emerged as a rapidly spreading infectious agent and soon became a serious health threat around the globe [1]. Various countries and communities chose to manage the transmission of the novel coronavirus by enforcing strict national or state lockdowns, which fundamentally disrupted everyday life. Alongside changes in societal and professional activities came transformations of medical services (e.g., remote consultations often replaced visits in person) and their accessibility. The risk of falling ill with COVID-19 and the difficulties of obtaining routine medical care presented a double challenge for people with epilepsy (PWE) [2,3]. Emerging recommendations for specialists emphasized the need to ensure the availability of antiepileptic medication (e.g., access to repeated prescriptions), minimize changes in epilepsy treatment plans and provide both reassurance and basic information to reduce the risk of seizure exacerbation [4–6]. Nonetheless, reports from different countries pointed to distress among PWE, issues when seeking antiepileptic drugs (AEDs), reaching epilepsy specialists and preventing an increase in seizure frequency [7–13]. Many surveys regarding the situation of PWE amidst a global pandemic were initiated during national lockdowns and an unstable epidemiological context. Our intention was to provide PWE a defined period of reference for a

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retrospective evaluation of their personal condition during a countrywide COVID-19 lockdown. Therefore, we questioned PWE about their health and experience with healthcare providers after a national three-month-long lockdown ended in Lithuania. Our aims were (1) to determine changes in seizure frequency and physical and mental health during the lockdown, (2) to identify factors that could be essential in influencing the change in seizure frequency and worsening in the reported health status and (3) to explore experiences of PWE regarding medical care for epilepsy.

2. Methods

2.1. Survey design and data collection

A questionnaire in Lithuanian was designed to gather information about the clinical characteristics of PWE, their health changes and altered use of healthcare services during a national lockdown. Because of low infection rates countrywide, questions regarding infections with SARS-CoV-2 were not included. A translated version of the questionnaire is provided as a Supplementary file. Following a cover letter that informed about the purpose of the survey and included a statement for anonymous data collection, the questionnaire consisted of several parts:

- Questions about gender, age, years with diagnosed epilepsy, epilepsy type, baseline seizure frequency, use of AEDs, change in AED dose and/or rate of use a month before or during lockdown
- Inquiry about health changes around the time of lockdown: reported physical and mental health before and during lockdown, estimate of the change in seizure frequency (all measures were based on a Likert scale from one to seven, four being neutral) [14]
- Indication whether fatigue, apathy, sadness, disturbed sleep and disturbed appetite were felt more often than usual during lockdown
- Evaluation of reported stress during lockdown (Likert scale from one to seven, where 1 – no stress, 7 – very high stress) and selection of causes for increased stress [14]
- The Lithuanian version of the Generalized Anxiety Disorder scale-7, GAD-7 (respondents were asked to recall a period of two weeks during lockdown and imagine their situation at that time) [15]. The severity of anxiety is measured by increase in GAD-7 scores. While different cut-off values can be used to determine clinically significant stress levels, we chose to interpret the GAD-7 score as a continuous variable (rather than a binary presence or absence of anxiety).
- Questions about the use of healthcare services for reasons regarding epilepsy, the quality and availability of medical consultations

The period defined as "COVID-19 quarantine" in the questionnaire referred to the official national lockdown comprised of strict restrictions on all non-essential societal and professional activities, which lasted three months from March 16, 2020, to June 16, 2020 [16]. The survey was published online in two closed social networking groups that provide a community platform for PWE across Lithuania. An identical questionnaire form was distributed for all willing patients at a tertiary epilepsy center during routine outpatient consultations. In the latter case, a nurse administered the questionnaire without collecting any personal patient data. To mitigate situational influences, patients provided answers in the waiting area before the medical visit and did not discuss the survey with the treating epileptologist. One of the authors (K.P.) collected all forms at once at the end of the study and entered the anonymous data to a dedicated electronic file. Exclusion criteria were unwillingness to participate, inability to complete the questionnaire (e.g., because of cognitive, vision deficits) and age of less than 18 years. Data for this study were collected from July 3, 2020, to August 21, 2020. No approval from the Regional Bioethics Committee was required according to local regulations because of the survey's anonymous design.

2.2. Statistical analysis

IBM SPSS v23.0 was used for all statistical tests. We employed Mann–Whitney U and χ^2 tests for between-group comparisons and the Wilcoxon Signed Ranks test for estimates of change in reported health and consultation quality. To quantify the relationship between variables, we calculated Spearman's correlation coefficients and created ordinal logistic regression models to determine the best predictor variables for reported changes in seizure frequency. The variables selected for inclusion in the regression models were based on statistically significant correlation results. Missing values were replaced by running five rounds of multiple imputation (only pooled estimates are reported, whenever possible).

3. Results

3.1. Reported health changes in PWE during lockdown

Patient characteristics and survey data concerning health changes are presented in Table 1. The study sample comprised 143 patients of relatively young age (mean = 35.1 ± 13.4), 94 (65.7%) of who had completed the questionnaire in person, while 49 (34.3%) provided answers online. Except for differences in gender distribution ($p = 0.003$), no statistically significant dissimilarities in age, years with epilepsy, baseline seizure frequency and number of AEDs use have been identified between the two groups. On the other hand, PWE who responded online had higher stress and anxiety levels ($p < 0.0001$) and reported worse mental health status ($p = 0.015$) during lockdown.

The overall median of reported physical health (Md = 5 both before and during lockdown) indicated no substantial impact of the lockdown. However, if regarded as a simulation of paired measurement in time, both the reported physical and mental health status were found to be lower during the lockdown: the Wilcoxon Signed Ranks test revealed asymmetrical distributions in spite of a matching median value ($Z = -4.604$, $p < 0.0001$ and $Z = -4.253$, $p < 0.0001$ for physical and mental health status, respectively). A similar decrease was present in both subgroups: PWE who completed the questionnaire in person and those who filled-out the survey online.

Among those who reported changes in seizure frequency, an increase was noted by 22 (15.4%) and a decrease by 17 (11.9%) respondents (overall Md = 4, indicating no change). Overall, this change did not depend on the data collection method (Mann–Whitney $U = 1760.0$, $p = 0.083$), patient gender (Mann–Whitney $U = 2049.5$, $p = 0.746$) or epilepsy type ($p = 0.270$). Correlations between altered seizure frequency and variables from the survey are presented in Table 2. An ordinal regression model that comprised data from all PWE in our study indicated baseline seizure frequency, reported physical health before lockdown and the level of ease to use AEDs appropriately during lockdown as statistically significant explanatory variables that are associated with variation in seizure frequency (Table 3). Finally, PWE who experienced disturbed sleep (Mann–Whitney $U = 15410$, $p = 0.013$), felt apathy (Mann–Whitney $U = 1602.0$, $p = 0.034$) or sadness (Mann–Whitney $U = 1572.000$, $p = 0.030$) more often reported seizure exacerbation.

Table 1
Patient characteristics and survey results concerning reported health changes, stress and anxiety. AED – antiepileptic drug, GAD-7 – Generalized Anxiety Disorder scale-7, Md – median, SD – standard deviation, * – $p < 0.05$, ** – $p < 0.0001$.

Questionnaire item	Results (n, % if not indicated otherwise)	Results online, $n = 49$ (n, % if not indicated otherwise)	Results from the tertiary center, $n = 94$ (n, % if not indicated otherwise)	p value
Gender (M/F)	59 (41.3)/ 84 (58.7)	12 (24.5)/ 37(75.5)	47 (50.0) /47 (50.0)	**0.003***
Age (mean, SD)	35.1 (13.4)	32.3 (8.3)	36.5 (15.2)	0.392
Years with epilepsy (Md, range)	14 (0–59)	17 (1–59)	12 (0–44)	0.114
Epilepsy type				0.185
Focal	52 (36.4)	16 (32.7)	36 (38.3)	
Generalized ("whole-body" seizures)	51 (35.7)	18 (36.7)	33 (35.1)	
Generalized (absence or myoclonic seizures)	8 (5.6)	5 (10.2)	3 (3.2)	
Other	12 (8.4)	6 (12.2)	6 (6.4)	
Unknown to the respondent	20 (14.0)	4 (8.2)	16 (17.0)	
Number of different AEDs				0.372
0	4 (2.8)	0 (0.0)	4 (4.3)	
1	56 (39.2)	21 (42.9)	35 (37.2)	
2	50 (35.0)	20 (40.8)	30 (31.9)	
3	19 (13.3)	4 (8.2)	15 (16.0)	
4 or more	14 (9.8)	4 (8.2)	10 (10.6)	
Change in patterns of AED use one month before or during lockdown	24 (16.8)	13 (26.5)	11 (11.7)	**0.024***
Frequency of seizures				0.137
Several a day	7 (4.9)	3 (6.1)	4 (4.3)	
Several a week	17 (11.9)	4 (8.2)	13 (13.8)	
Several a month	44 (30.8)	22 (44.9)	22 (23.4))	
Several a year	18 (12.6)	6 (12.2)	12 (12.8)	
Less than one a year	52 (36.4)	14 (28.6)	38 (40.4)	
Missing	5 (3.5)	0 (0.0)	5 (5.3)	
Change in seizure frequency during lockdown: 1 – significant reduction, 7 – significant increase (Md, range)	4 (1–7)	4 (1–6)	4 (1–7)	0.083
Reported physical health (Likert scale 1 to 7)				
Before lockdown (Md, range)	5 (1–7)	5 (1–7)	5 (1–7)	0.972
During lockdown (Md, range)	5 (1–7)	4 (1–7)	5 (1–7)	0.199
Change (Z statistic, significance)	−4.604, $p < 0.0001$	−3.122, $p = 0.002$	−3.501, $p < 0.0001$	
Reported mental health (Likert scale 1 to 7)				
Before lockdown (Md, range)	6 (1–7)	5 (1–7)	6 (1–7)	0.164
During lockdown (Md, range)	5 (1–7)	4 (1–7)	5 (1–7)	**0.015***
Change (Z statistic, significance)	−4.253, $p < 0.0001$	−2.940, $p = 0.003$	−3.158, $p = 0.002$	
Symptoms more present during lockdown than usually				
Fatigue	63 (44.1)	28 (57.1)	35 (37.2)	**0.023***
Apathy	47 (32.9)	21 (42.9)	26 (27.7)	0.066
Sadness	48 (33.6)	18 (36.7)	30 (31.9)	0.562
Disturbed sleep	47 (32.9)	20 (40.8)	27 (28.7)	0.144
Disturbed appetite	31 (21.7)	17 (34.7)	14 (14.9)	**0.006***
Reported stress during lockdown (Likert scale 1 to 7)	3 (1–7)	4 (1–7)	2 (1–7)	**<0.0001****
Major causes of stress during lockdown				
The risk of becoming ill with COVID-19	46 (32.2)	14 (28.6)	32 (34.0)	0.506
The risk of not receiving appropriate healthcare for COVID-19	39 (27.3)	17 (34.7)	22 (23.4)	0.150
The risk of not receiving appropriate healthcare for epilepsy	63 (44.1)	30 (61.2)	33 (35.1)	**0.003***
Social consequences of the pandemic (e.g., loss of communication, socializing)	55 (38.5)	27 (55.1)	28 (29.8)	**0.003***
Economic impact of the pandemic (e.g., lost job, decrease in income, worse outlook for future employment)	58 (40.6)	23 (46.9)	35 (37.2)	0.262
Informational and societal issues (e.g., information overload, frequent news updates)	39 (27.3)	19 (38.8)	20 (21.3)	**0.026***
Inability to work from home	17 (11.9)	9 (18.4)	8 (8.5)	0.084
Inability to keep social distancing measures, lack of PPE	8 (5.6)	6 (12.2)	2 (2.1)	**0.020***
GAD-7 score (Md, range)	5 (0–21)	7 (0–21)	3 (0–21)	**<0.0001****

PWE who affirmed changes in their use of AEDs one month before or during lockdown had greater stress and GAD-7 scores (Mann–Whitney $U = 940.0$, $p = 0.008$ and Mann–Whitney $U = 822.5$, $p = 0.013$, accordingly). Besides, they more often reported disordered sleep ($p = 0.004$). Such findings were not evident in the subgroup of online respondents (Mann–Whitney $U = 192.500$, $p = 0.341$ Mann–Whitney $U = 203.500$, $p = 0.489$ for stress and GAD-7 scores, respectively, $p = 0.265$ for sleep disturbances). However, changes in seizure frequency did not depend on modified AED use (Mann–Whitney $U = 1127.0$, $p = 0.307$ for all respondents) irrespective of the respondent subgroup (Mann–Whitney $U = 344.5$, $p = 0.607$ for in-person respondents, Mann–Whitney $U = 181.5$, $p = 0.194$ for online respondents).

3.2. Access to healthcare and its relationship with reported health variables

Survey results about healthcare use during lockdown are presented in Table 4. A third of participants in our survey ($n = 46$, 32.2%) indicated that some form of planned epilepsy-related medical consultation or service had not been provided because of the lockdown. Worse availability of medical services was reported by

Table 2
Correlation coefficients between variables in the survey and reported changes in seizure frequency. AEDs – antiepileptic drugs, * – $p < 0.05$, ** – $p < 0.0001$.

	Results from all respondents, $n = 143$		Results from online data, $n = 49$		Results from tertiary center data, $n = 94$	
	Spearman's ρ	p value	Spearman's ρ	p value	Spearman's ρ	p value
Age	0.036	0.688	−0.122	0.407	0.115	0.280
Years with epilepsy	0.126	0.151	0.225	0.121	0.021	0.850
Number of AEDs used	0.136	0.125	0.151	0.302	0.106	0.340
Baseline seizure frequency	**0.265**	**0.002***	**0.350**	**0.013***	0.188	0.091
Reported physical health (before lockdown)	**−0.347**	**<0.0001****	**−0.299**	**0.036***	**−0.427**	**<0.0001****
Reported physical health (during lockdown)	**−0.337**	**<0.0001****	−0.246	0.089	**−0.440**	**<0.0001****
Reported mental health (before lockdown)	**−0.264**	**0.002***	−0.175	0.230	**−0.313**	**0.011***
Reported mental health (during lockdown)	**−0.285**	**0.001***	−0.196	0.178	**−0.326**	**0.004***
Ease of appropriate AED use	**−0.219**	**0.020***	**−0.385**	**0.009***	−0.185	0.136
Generalized Anxiety Disorder scale-7 score	**0.215**	**0.013***	0.106	0.472	**0.262**	**0.014***
Reported stress during lockdown	**0.228**	**0.013***	0.250	0.083	0.190	0.079

Table 3
Ordinal logistic regression models with pooled estimates after multiple imputation for missing values (the dependent variable is the reported change in seizure frequency). AED – antiepileptic drug, * – $p < 0.05$, a – Nagelkerke Pseudo$\overline{R}^2 = 0.274$, model fit $p < 0.0001$ (all imputed datasets), b – Nagelkerke Pseudo$\overline{R}^2 = 0.341$, model fit $p < 0.05$ (all imputed datasets), c – Nagelkerke Pseudo$\overline{R}^2 = 0.357$, model fit $p < 0.0001$ (all imputed datasets).

	[a] Model for results from all PWE, $n = 143$			[b] Model for results from data online, $n = 49$			[c] Model for results from tertiary center data, $n = 94$		
	Estimate b	p value	95% Confidence Interval	Estimate b	p value	95% Confidence Interval	Estimate b	p value	95% Confidence Interval
Baseline seizure frequency	**0.413**	**0.031***	**0.039 to 0.787**	**0.659**	**0.027***	**0.077 to 1.241**	0.074	0.787	−0.466 to 0.615
Reported physical health (before lockdown)	**−0.462**	**0.031***	**−0.882 to −0.042**	−0.362	0.255	−0.985 to 0.262	−0.482	0.222	−1.256 to 0.292
Reported physical health (during lockdown)	−0.022	0.909	−0.407 to 0.362	0.127	0.609	−0.360 to 0.614	−0.577	0.159	−1.379 to 0.226
Reported mental health (before lockdown)	0.105	0.598	−0.289 to 0.499	0.135	0.624	−0.404 to 0.673	0.262	0.470	−0.459 to 0.983
Reported mental health (during lockdown)	−0.077	0.671	−0.436 to 0.282	−0.104	0.672	−0.586 to 0.378	−0.111	0.711	−0.697 to 0.476
Reported stress during lockdown	0.169	0.249	−0.119 to 0.456	0.270	0.275	−0.215 to 0.755	0.127	0.520	−0.262 to 0.515
Ease of appropriate AED use	**−0.535**	**0.006***	**−0.915 to −0.156**	**−0.727**	**0.009***	**−1.275 to −0.180**	−0.477	0.074	−1.001 to 0.047
Generalized Anxiety Disorder scale-7 score	0.014	0.769	−0.081 to 0.109	−0.05	0.480	−0.188 to 0.089	0.025	0.773	−0.145 to 0.195

29 PWE (44.6% of those who provided a score). While the need for greater efforts to obtain a prescription for AEDs was noted by 21 PWE (18.6% of those who provided a score), 22 (19.5%) indicated that this task was easier than before the lockdown. When evaluated by survey participants, a decrease in consultation quality during lockdown was observable (Md = 6 before lockdown, Md = 4 during lockdown, $Z = -2.895$, $p = 0.004$). The latter phenomenon as well as issues pertaining to access to healthcare, ease of acquiring a prescription or appropriately using AEDs did not depend on the data collection method (i.e., online or in person).

PWE who reported a loss of healthcare services had higher anxiety levels (as scored by the GAD-7, Mann–Whitney $U = 1473.0$, $p = 0.016$), but not stress scores (Mann–Whitney $U = 1894.5$, $p = 0.165$). These individuals also rated their physical and mental health as being worse during lockdown (Mann–Whitney $U = 1573.5$, $p = 0.005$, Mann–Whitney $U = 1555.0$, $p = 0.004$, respectively) in contrast to PWE who had received healthcare services or did not need them. Such a difference between the groups was absent for reported health scores before lockdown (Mann–Whitney $U = 1972.5$, $p = 0.294$ for physical health, Mann–Whitney $U = 1830.5$, $p = 0.109$ for mental health). Respondents with unfulfilled healthcare needs were more likely to present with exacerbated seizures (Mann–Whitney $U = 1622.5$, $p = 0.046$), fatigue ($p = 0.039$) and disturbed sleep ($p = 0.007$). They also expressed a greater need for remote consultations after the pandemic (Mann–Whitney $U = 1471.5$, $p = 0.005$). Subgroup analysis revealed that online respondents who had lost medical services were also more likely to indicate need for telehealth (Mann–Whitney $U = 199.5$, $p = 0.046$). PWE who filled the questionnaire in person and could not access healthcare during lockdown indicated worse physical health (Mann–Whitney $U = 597.0$, $p = 0.039$) and sleep disturbances ($p = 0.008$) during this period. However, other findings related to inaccessible services were not reproducible on the subgroup level.

4. Discussion

4.1. General findings

It is of note that the design of our survey was different from investigations during other national lockdowns as it relied on retrospective information provided by the respondents. In this way, (1) all respondents had an identical period of reference for any changes in health status to occur, (2) the survey was administered in person as well as online as routine outpatient healthcare services had already been restored and (3) situational influences (e.g., on-going stress, recent bad experience with access to healthcare) of the lockdown itself were partly evaded.

Our study reports a statistically significant reduction in reported physical and mental health during a national COVID-19 lockdown. Increased fatigue was the most frequently selected symptom in our survey, while one in three respondents felt apathy, sadness more often than usually or experienced sleep disturbances. Physical symptoms have been found to be more expressed during COVID-19 lockdown in other studies as well [17,18]. Among

Table 4
Survey results regarding healthcare use during lockdown. § – answers provided by respondents only if applicable, † – variable that had a missing value rate of more than 10%, AED – antiepileptic drug, GP – general practitioner, Md – median, * – $p < 0.05$.

Questionnaire item	Results, $n = 143$ (n, % or Md, range)	Results from online respondents, $n = 49$ (n, % or Md, range)	Results from the tertiary center visitors, $n = 94$ (n, % or Md, range)	p value
Score of medical consultation quality concerning epilepsy (Likert scale 1 to 7)				
Before lockdown	6 (1–7)	5 (1–7)	7 (1–7)	**0.030***
During lockdown §	4.5 (1–7)	4 (1–7)	6 (1–7)	**0.016***
Change (Z statistic, significance) §	−2.895, $p = 0.004$	−2.553, $p = 0.011$	−1.667, $p = 0.095$	
Type of healthcare services used (epilepsy-related) §				
Neurologist/epileptologist consultation (in person)	18 (12.6)	7 (14.3)	11 (11.7)	0.658
GP consultation (in person)	20 (14.0)	9 (18.4)	11 (11.7)	0.275
Neurologist/epileptologist consultation (by phone)	27 (18.9)	12 (24.5)	15 (16.0)	0.216
GP consultation (by phone)	54 (37.8)	24 (49.0)	30 (31.9)	**0.046***
Neurologist/epileptologist consultation (online)	2 (1.4)	1 (2.0)	1 (1.1)	1.000
Emergency services	12 (8.4)	8 (16.3)	4 (4.3)	**0.023***
In-patient services (hospitalization)	5 (3.5)	3 (6.1)	2 (2.1)	0.339
Mental health services (remotely)	5 (3.5)	4 (8.2)	1 (1.1)	**0.047***
During the consultation I was informed: §				
How the AEDs I use can influence my outcome if I was treated for COVID-19	9 (6.3)	0 (0.0)	9 (9.6)	**0.028***
About the need to contact relatives several times a day	9 (6.3)	2 (4.1)	7 (7.4)	0.719
That emergency services should be called in case of a prolonged seizure, regardless of lockdown	19 (13.3)	7 (14.3)	12 (12.8)	0.799
About the need to seek help from a mental health specialist in case of strong negative emotions	7 (4.9)	2 (4.1)	5 (5.3)	1.000
Availability of healthcare services (1 – much worse than before lockdown, 7 – much better than before lockdown) §	4 (1–6)	4 (1–6)	4 (1–6)	0.784
Ease of acquiring a prescription for AEDs during lockdown (1 – much more difficult, 7 – much easier) §	4 (1–7)	4 (2–7)	4 (1–7)	0.691
Ease of appropriate AED use during lockdown: routine dose, frequency, all AEDs used are available (1 – much more difficult, 7 – much easier) §†	4 (1–7)	4 (1–7)	4 (1–7)	0.288
Loss of consultation or service concerning epilepsy because of lockdown	46 (32.2)	22 (44.9)	24 (25.5)	**0.019***
Need for routine remote consultations (in a post-pandemic world)	4 (1–7)	5 (1–7)	4 (1–7)	0.102

PWE, they could be components of emerging depressive or sleep disorders as some are included in psychometric scales [7,12]. The rate of seizure increase was similar to results from Italy (18%), but higher than reported in China (9%) and Spain (10%) [7,8,12]. This increase may be multifactorial and depend on SARS-CoV-2 infections among PWE, their feeling of stress and disrupted access to healthcare [19]. While patients were not questioned about being infected with SARS-CoV-2, it is known from the authors' personal practice that none of the patients treated at the tertiary center had COVID-19 during the lockdown period. Further considering that there was no statistically significant difference in seizure change between online and in-person respondents, it is unlikely that the observable seizure exacerbation was caused by COVID-19 directly.

Overall, stress and anxiety levels in our sample of PWE were relatively low. Major stressors included not receiving care for epilepsy, confronting social and economic consequences of the pandemic. Such results could be determined by relatively well-managed infection rates in Lithuania and a limited risk of becoming infected: the first peak of individuals that were simultaneously positive for SARS-CoV-2 reached 1048 in April 20, 2020 (representing around 0.037% of the country's population) and less than 1800 total cases had been recorded by the end of the lockdown [16]. That is, the lockdown itself rather than the risk of COVID-19 might be more important to determine stress in PWE in regions with relatively handled epidemiological situations [20].

4.2. Seizure worsening

Findings concerning the exacerbation of seizures mostly replicated results of similar survey-based studies [7,8,12,13]. Clinical characteristics that were present before the pandemic (e.g., baseline seizure frequency), difficulties in proper use of AEDs and sleep disturbances during the lockdown are found to be important determinants of whether patients have a risk of increase in seizures. In our study, reported stress, anxiety and mental health status during the pandemic were correlated with seizure exacerbation, but did not reach statistical significance in the regression model. Further, we could not state that a greater number of AEDs used or changes in the AED treatment plan are linked to an increase in seizure episodes during lockdown. These findings could be explained by differences in methodology – while we asked PWE to estimate the change in seizure episodes and the ease of proper AED use on a Likert scale, some studies relied on binary (Yes/No) categories [7,8]. Despite the differences concerning AED use, our study further indicates that patients with clinical profiles of more severe forms of epilepsy (i.e., high baseline seizure frequency, worse reported physical health before the pandemic) may be at greater risk of seizure worsening. Continuous supply of AEDs and timely prescriptions might therefore be the most essential factors in minimizing seizure occurrence during a COVID-19 lockdown [9]. While "change in AED regimen" or "non-compliance" were found to be associated with increase in seizures elsewhere, we had decided to distinguish coordinated changes in AED regimen from difficulties of properly using AEDs [7,12]. This discrimination revealed that modifying the patient's treatment plan might not increase the risk of seizure exacerbation. Nonetheless, altered AED use patterns were associated with worse mental health, increase in anxiety and stress. That might be manifestations of psychiatric side effects of newly prescribed or up-titrated AEDs. For instance, symptoms like anxiety and irritability have been associated with levetiracetam and tiagabine [21]. While changing patterns of AED

use during COVID-19 lockdowns is not recommended, we believe this topic requires further research [5].

4.3. The impact of disrupted healthcare services

The loss of medical services was significantly related not only to changes in seizure frequency, but also to anxiety and worse mental health evaluation during the lockdown. The reasons for this finding can only be speculated. One explanation could be that the limited capacity of in-person consultations led to specialists prioritizing services for patients at risk of seizure exacerbation or severe AED side-effects [4]. This way, the loss of some services (e.g., case review, AED down-titration, change in AED due to milder side-effects) among other patients could translate into worsening of the reported mental and physical state. Further, consultations for epilepsy are also important for reassurance, lifestyle advice (e.g., information concerning regular sleep patterns) and guidance in cases of existing mental health issues [5]. Loss of such components can lead to the observable anxiety and deterioration of the subjectively perceived health status. Even if provided, the quality of consultations for epilepsy (most were effectuated remotely) was less adequate than before the pandemic. Besides, PWE in our survey rarely received information about the need for daily communication with close relatives, emergency care in case of a prolonged seizure episode or reaching out to mental health specialists when feeling severe emotional symptoms. Such aspects point to a suboptimal quality of epilepsy services during a nationwide lockdown. While the emerging pandemic required rapid implementation of telehealth and novel solutions for safe in-person visits, current actions should be directed towards making medical services for epilepsy at least as accessible as before the spread of SARS-CoV-2 [10,22,23]. Substitutes for in-person visits should be evaluated not only by acknowledging their capabilities of mitigating seizure exacerbation, but also by assessing the potential to provide complex care, which includes reassurance and professional lifestyle advice [5,24].

4.4. Study limitations

Our survey-based study is limited by a lack of narrative opinions from the PWE involved, non-inclusion of objective clinical data from medical records and recall bias because of retrospective questioning. Further, we could not ensure that only PWE (or their caregivers) will complete the survey. However, this risk was judged minimal as the groups are closed from outsiders and are used only for discussions surrounding life with epilepsy. The combination of the online and in-person methods of survey administration was required to gather data from a larger number of respondents during a period of relaxed state restrictions and mitigated spread of SARS-CoV-2. Because of existing differences between the groups, pooled data should be interpreted with caution. Further, our results can be influenced by the fact that the spread of SARS-CoV-2 was relatively well managed in our country and no questions related to being diagnosed with COVID-19 or receiving epilepsy care while being positive for SARS-CoV-2 had been included.

5. Conclusions

Our study presented a retrospective point-of-view when estimating the impact of a COVID-19 lockdown on PWE. Even after a period of nationwide restrictions, we could state that it had significant impact on the physical and mental state of some PWE. The predetermined severity of epilepsy may be important in defining the risk of seizure exacerbations and seeking to improve appropriate AED use might be one of the first priorities to mitigate this risk. While the frequently reported loss of epilepsy-related medical services may also put the patients at risk of seizure exacerbation, it may have additional impact on the patient's overall physical and mental status. It seems essential to restore the pre-pandemic quality of consultations with specialists aiming to both prevent seizure exacerbation (e.g., by ensuring timely AED prescription) and provide professional lifestyle guidance and reassurance for the patients.

Declaration of competing interest

The authors report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2020.107573.

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