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BRIEF COMMUNICATION

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Nonadherence to treatment regimens in epilepsy from the patient's perspective and predisposing factors: Differences between intentional and unintentional lack of adherence

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Summary

Nonadherence to recommended antiepileptic drug (AED) treatment regimens can result in seizure relapse with increased health risks. Nonadherence can be unintentional (eg, patients forget to take a dose), or intentional, when patients consciously decide not to follow the agreed AED treatment regimen. We aimed to determine the extent to which Norwegian patients with epilepsy (PWEs) report taking their AED differently from prescribed, either intentionally or unintentionally, and to identify risk factors for either form of nonadherence. Of 1182 PWEs who completed an online survey presented on the website of the Norwegian Epilepsy Association, 40% reported that they sometimes or often forget to take their AED as scheduled, and about 30% reported that they consciously chose not to follow the AED treatment plan agreed upon with their physician. Independent variables significantly associated with unintentional nonadherence include the following: feeling depressed, being younger than the mean age, and having memory problems. Independent factors significantly associated with intentional nonadherence include the following: feeling depressed, male gender, and perceptions of stigmatization. To improve the treatment of PWEs, it is important to distinguish between intentional and unintentional nonadherence to AED treatment regimens, as different risk factors and reasons associated with nonadherence to AED treatment regimens might require different interventions.

KEYWORDS

adherence, challenges, compliance, drug treatment, epilepsy

1 | INTRODUCTION

Epilepsy is one of the most common neurologic disorders. It has a global prevalence of 0.6%-1.2%.[1,2] Appropriate treatment with antiepileptic drugs (AEDs) can result in 60%-70% of epilepsy patients becoming seizure-free.[3]

Adherence is defined as "the extent to which a person's behavior taking medication corresponds with agreed recommendations from a health care provider."[4] Nonadherence is defined as any deviation from the recommendations, both regarding timing and dosage of a prescribed regimen.[5] Nonadherence to AED treatment plans among patients with epilepsy (PWEs) can result in seizure relapse,[6] status epilepticus,[7] hospital admission,[8] and increased health care costs.[9,10] Nonadherence may also even be related to sudden unexplained death in epilepsy (SUDEP).[11] Nonadherence may be unintentional—for example, the patient forgets to take a dose or accidently takes an incorrect dosage. Moreover, there may be misunderstandings

between the physician and patient regarding the agreed dosage or medication.[12] Nonadherence may also be intentional; in such cases, for various reasons the patient makes a conscious decision not to follow the agreed AED treatment plan.

The primary aim of this study was to determine the extent of both unintentional and intentional nonadherence among Norwegian PWEs. The secondary aim was to identify and compare risk factors for unintentional and intentional nonadherence.

2 | MATERIAL AND METHODS

2.1 | Study population

The study was a collaboration between the National Center for Epilepsy and the Norwegian Epilepsy Association (NEA). An online questionnaire (Data S1) was developed and made available on NEA's homepage, as a pop-up for all those who visited the page, between April 1, 2017 until September 5, 2017. Each participant could complete the questionnaire only once.

Visitors to the page were asked to complete the questionnaire regarding epilepsy and epilepsy-related challenges. Questions included background information and also covered the patient's epilepsy, treatment, and follow-up. Information on whether the respondents unintentionally or intentionally used AEDs differently than recommended by, and agreed upon with, their physician was determined from responses to the two questions: "Does it happen that you accidentally take your antiepileptic medication differently than agreed with you physician?" and "Does it happen that you intentionally (on purpose) take your antiepileptic medication differently than agreed with your physician?" The respondents could choose between the following alternative answers for each of these questions: "never," "rarely," "sometimes," or "often."

During analysis, we dichotomized the answers into two groups: "never or rarely" vs "sometimes or often" for unintentional nonadherence, and "never" vs "rarely, sometimes, or often" for intentional nonadherence.

Respondents were asked to report the reasons for taking antiepileptic medication differently than agreed with their physician. Alternative answers were: "I have adverse events," "I am afraid of having side effects," "I think the medication has no effect," "I am afraid of experiencing adverse events," and "I am afraid that the medication might harm me." In addition, the respondents could provide comments and explanations for nonadherence in a free text part of the questionnaire.

The study was evaluated by the regional ethics committee (ref. no. 2017/563) prior to implementation.

2.2 | Statistical methods

To test possible group differences, Pearson's chi-square tests were performed. Tested variables with a P value < 0.05

TABLE 1 Demographic and clinical characteristics of the PWE participants in the survey

Characteristics	Response to specific question n (N = 1182); %	n; %	Mean; range
Age in years	1156; 97.8		41.80; 11-93
Male gender	1150; 97.3	372; 31.5	
Being in a relationship	1157; 97.9	697; 59.0	
Age at first seizure	1152; 97.5		21.01; 1-80
Number of years with epilepsy	1129; 95.5		20.42; 0-72
Seizure types	1180; 99.8		
Focal, aware		346; 29.3	
Focal, impaired awareness		425; 36.0	
Tonic–clonic		719; 60.9	
Absences		263; 22.3	
PNES		55; 4.7	
Other		86; 7.3	
Don't know		108; 9.1	
Seizure-free last year	1179; 99.7	479; 40.6	
Epilepsy etiology	1174; 99.3		
Known		543; 46.3	
Unknown		631; 53.7	

PNES, psychogenic nonepileptic seizures.

were included in a multivariate logistic regression analysis. Independent variables tested for unintentional and intentional nonadherence were the following: gender, polytherapy (two or more AEDs), above or below mean age of group, seizure freedom for the previous 12 months, seizure frequency (daily or weekly vs less frequently), perception of own health (very poor/poor or good/very good), feeling depressed, had obtained information about the need for regular AED treatment, had been informed about possible adverse effects, memory problems, had been involved in treatment decisions, and had perceived themselves as being stigmatized.

3 | RESULTS

During the study period, the website received 48 249 hits, and 1182 PWEs participated in the survey by completing the questionnaire, either partly or fully. Demographic and clinical characteristics of the participants are summarized in Table 1.

Of the 1176 PWEs who answered the question on unintentional nonadherence, 16% reported that they never forget to take their AEDs, whereas 40% reported that they sometimes or often forgot to take the drugs as scheduled. Of the 1169 PWEs who answered the question on intentional nonadherence, about 30% reported that they intentionally did not follow the AED treatment plan agreed upon with their physician (Figure 1).

Independent variables significantly associated with unintentional nonadherence included reporting feeling depressed (odds ratio [OR] 1.410; confidence interval [CI] 1.077-1.848; $P = 0.012$), being younger than the mean age of 41.8 years (OR 1.448; CI 1.111-1.886; $P = 0.006$), and having memory problems (OR 1.529; CI 1.137-2.053; $P = 0.005$).

Independent factors significantly associated with intentional nonadherence included reporting feeling depressed (OR 1.579; CI 1.194-2.087; $P = 0.001$), male gender (OR 1.751; CI 1.263-2.427; $P = 0.001$), and perceptions of stigmatization (OR 1.599; CI 1221-2.094; $P = 0.001$).

No association between unintentional and intentional nonadherence and the following factors was found: polytherapy (two or more AEDs), seizure freedom for the previous 12 months, seizure frequency (daily or weekly vs less frequently), perception of own health (very poor/poor or good/very good), had obtained information about the need for regular AED treatment, had been informed about possible adverse effects and whether PWE had been involved in treatment decisions (Table S1).

The most common explanations by PWEs reporting intentional nonadherence were that they had previously experienced adverse effects from AEDs (n = 79); they were afraid of being harmed by AEDs (n = 41); they had not experienced seizure-reducing effects from AED treatment (n = 43); they were afraid of adverse effects (n = 28); they were afraid of becoming addicted to the AEDs (n = 12).

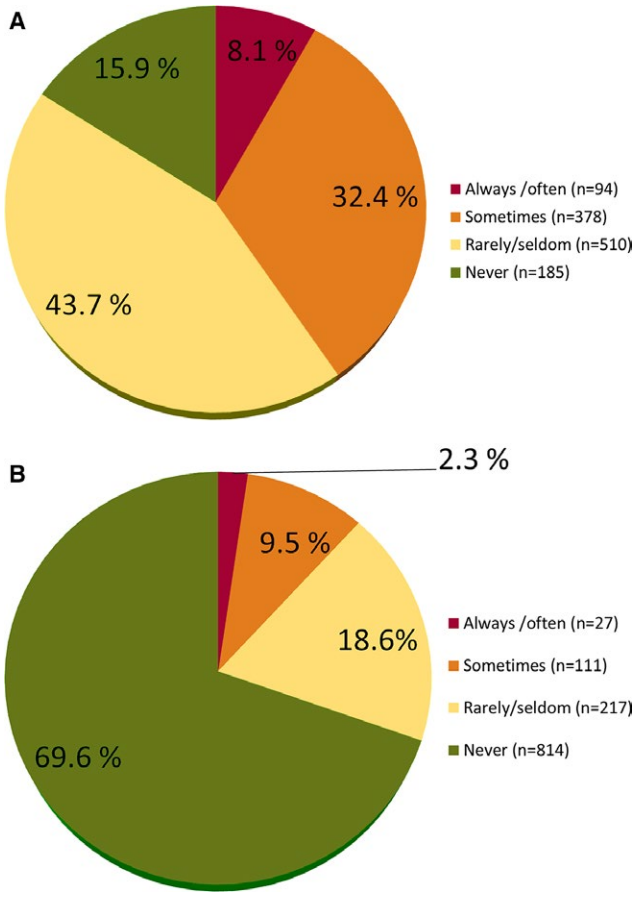

FIGURE 1 Results (%) from reported (A) unintentional (n = 1167) and (B) intentional nonadherence (n = 1169)

Among all participants reporting nonadherence (n = 1003), 210 PWEs (21%) wrote a free comment in the questionnaire to provide reasons for nonadherence. The reasons mentioned most frequently included difficulties remembering the AED treatment schedule (n = 40) and difficulties incorporating a regular AED schedule into busy and complicated life situations (eg, working shifts and traveling) (n = 26).

4 | DISCUSSION

The main finding from this online questionnaire completed by 1189 Norwegian PWEs was that almost one in three chose not to follow their agreed AED treatment plan but had decided to take their AEDs differently than prescribed. In addition, about 40% reported that they sometimes or often forgot to take their AEDs as scheduled. Most studies on adherence to AED treatment of epilepsy do not differentiate between unintentional and intentional nonadherence, but we believe that this distinction is important. With this distinction, the reasons underlying AED nonadherence can be explored, and,

more importantly, the appropriate measures can be implemented to improve the treatment management of this patient group.

The results regarding associations with nonadherence are similar to those from other recently published studies regarding estimates of poor adherence in epilepsy. For example, a French study showed that 79% of 263 participants always followed the prescribed regimen, and those who were nonadherent stated that adverse effects were the main reason.[13] Moreover, a recent German study of 226 PWEs found that 44% had irregular intake of AEDs, and young age and adverse drug effects were the most important predisposing factors for nonadherence.[14] A review reported nonadherence to vary between 26% and 79%, with the wide variability between studies being due mainly to different definitions of adherence and different cutoff values for defining nonadherence.[5]

Different approaches have been used to try to determine adherence. Self-reports, as used in our study, may underestimate the proportion of nonadherence in PWEs. This may be particularly so for unintentional nonadherence, as PWEs who forget to take their AED might not remember that they have forgotten when completing the questionnaire. Patients may also be reluctant to admit intentional nonadherence, although as our data collection was anonymous this may have averted such reluctance. Chapman et al[15] claim that the degree of adherence to a prescribed drug regimen is dependent upon an individual patient's attitude regarding the necessity of treatment and adverse effects of drugs.

It is not clear why male patients are more prone than female patients to intentional AED nonadherence. It could be speculated that men are more willing than women to take risks and less willing to follow recommended treatment schemes. One study has demonstrated that young men with epilepsy are more prone than women to risk-taking behavior.[16] Furthermore, PWEs who experience stigmatization might feel that following a daily drug regimen may reinforce the stigma; such feelings may result in a greater willingness to be nonadherent.

Although the proportion of seizure-free patients in our cohort was lower than expected (41%), we have nevertheless assumed that the participants in our study and completing the questionnaire represent the Norwegian PWE population. The limitations in the validity of close-ended questionnaires are well known, and our study approach, with an online questionnaire, might have resulted in a selection bias. We would expect the bias would be either toward persons who are well-informed about epilepsy and associated risks and thus, perhaps, more likely to be adherent to treatment regimens, or PWEs who know that they are nonadherent and are looking for information on what they should do if they have forgotten to take their medication as prescribed.

In conclusion, our study shows a high rate of nonadherence among PWEs in Norway, both unintentional and intentional, and this may result in elevated seizure frequency and related health problems. Measures to reduce nonadherence in PWEs are important and should be tailored to address both unintentional and intentional lack of adherence.

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CONFLICTS OF INTEREST

Oliver Henning has received speaker's honoraria from Eisai, UCB, and LivaNova. Cecilie Johannessen Landmark has received speaker's honoraria from Eisai and GW Pharma. Morten Ingvar Lossius has been giving talks and participated in expert panels for Eisai and UCB. Karl Otto Nakken has no conflict of interest to disclose. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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