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Use of screening tools to assess comorbidities and adverse events in patients with epilepsy. A European Reference Network for Rare and Complex Epilepsies (EpiCARE) survey

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ABSTRACT

Purpose: As comorbidities can affect treatment decisions, quality of life, and prognosis in epilepsy, it is important that they are detected and addressed as soon as possible. Screening tools can help by rapidly assessing various additional challenges in epilepsy.

Methods: To map the use and perceived benefit of different screening instruments for quality of life, psychiatric comorbidity, and cognition, along with side effects from anti-seizure medication in Europe, we sent an online questionnaire to dedicated epilepsy centres departments within the European Reference Network for Rare and Complex Epilepsies (EpiCARE).

Results: Among the 40 hospitals in the EpiCARE network, we received responses from 25 (63%), with 28 individual respondents. Most respondents reported using screening for quality of life (86%) and psychiatric comorbidity (82%), but relatively few (14%) screen for sexual problems. Many (47) different tools were used for evaluation of cognitive dysfunction, but just a few (5) different tools were used to screen for adverse events. The optimization of individual patient care was one main reason given for using screening tools (58%–100% - depending on purpose of tool), another was research (50% - 88% - depending on purpose of tool). A major benefit of using screening tools perceived by the respondents is the detection of “hidden” comorbidity (67% - 90% - depending on purpose of tool).

Conclusion: In the absence of a broad consensus regarding use of screening tools, practices vary considerably among epilepsy centres. Greater emphasis should be directed towards harmonizing use of screening tools. Future research should address how screening results influence treatment choices, and how these might affect clinical care.

1. Introduction

Epilepsy is a common neurological disorder with a lifetime prevalence of 7.60 per 1000 persons [1]. In addition to seizures, epilepsy is characterized by the cognitive, psychological, and social consequences of the disease [2]. It has been estimated that about 50% of adults with epilepsy have at least one comorbid somatic or psychiatric condition [3,

4]. Comorbidities can affect treatment decisions, as anti-seizure medications (ASM) can positively or negatively affect the comorbidities [5, 6]. Comorbidities can also negatively affect quality of life (QoL) and prognosis of epilepsy [7,8]. For many people with epilepsy this can have a greater negative impact on QoL than the seizures themselves [9]. It can also result in an increased use of, and thereby increased costs for, the healthcare system [10].

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In order to provide the best-possible, comprehensive care for people with epilepsy, comorbid conditions should be detected and addressed or treated as soon as possible. Regular screening with adequate tools can contribute to solving this task [3] and has been broadly recommended, especially for psychiatric comorbidities [11–15]. The advantages are that screening tools can provide a quick assessment, although subsequent clinical assessments for interpretation and evaluation of results are needed. A recent study from Australia found a lack of concordance between the results from screening and a clinical psychiatric assessment for depression and anxiety in about 30% of patients [16]. From clinical experience, we know that screening tools and single cognitive tests may be sensitive to cognitive dysfunction, but do not provide a sufficient basis for overall decisions regarding treatment, cognitive rehabilitation, or psycho-educative interventions. Nevertheless, results from screening tools may provide a good indication of which patients may require more thorough investigation. These tools can be a useful supplement in the busy clinical everyday practice.

The use of screening instruments for epilepsy patients varies widely [13], as do reasons for implementing them in the clinic. We wanted to map the use of screening tools in epilepsy treatment centres in Europe, and also investigate the perceived benefit from clinicians from the different instruments for screening for several factors, including ASM side effects, QoL, psychiatric comorbidity, and cognitive problems. In a wider perspective, use of harmonized screening tools between centres might be an additional benefit, as this would enable better communication and improve data analysis among centres.

2. Material and methods

All members, both full and associate, of the European Reference Network for Rare and Complex Epilepsies (EpiCARE) ($n = 40$) were sent a link to an online questionnaire (suppl. 1) in December 2020. We sent reminders to non-responding recipients up to three times. The respondents were asked to report about their type of workplace (epilepsy center or neurological ward in an academic hospital), their position (psychologist or physician), and their patient age group (pediatric or adult patients). Questions were then asked about screening tools, with the same set of questions used for screening instruments for QoL in epilepsy, psychiatric comorbidity, cognitive functioning, adverse events, and sexual dysfunction. We asked whether screening tools were used, if so, why they were being used, which specific screening tools were being used, and how frequently they were used (“For all/nearly all patients (>90%)”, “For the majority of patients (>50%)”, “For a minority of patients (50–10%)”, or “For few patients (<10%)”).

The most commonly used screening tools were listed in the questionnaire, but respondents could also add additional tools. Finally, we asked about the perceived benefits achieved from using the different screening tools.

3. Results

We received responses from 28 recipients from 25 (63%) of the 40 EpiCARE member institutions. Most respondents (75–80%) reported using screening tools for evaluation of QoL, detection of psychiatric comorbidity, or cognitive dysfunction. Only 40% reported used screening tools for treatment-related adverse events and only 15% for

Table 1
Extent of the use of screening tools for various different challenges.

Do you use tools to screen for:	N	Yes: n (%)	No: n (%)
Quality of life in epilepsy?	28	24 (86)	4 (14)
Psychiatric comorbidity?	28	23 (82)	5 (18)
Cognitive dysfunction?	27	20 (74)	7 (26)
Adverse events?	27	11 (41)	16 (59)
Sexual dysfunction?	28	4 (14)	24 (86)

sexual dysfunction (Table 1).

The main reasons for using screening tools were reported to be for optimizing individual patient care (60–100%), for research (50–90%), or as part of standard clinical care (20–60%) (Table 2). A wide variety of different screening tools were reported for screening for QoL (21 different tools), detection of psychiatric comorbidity (42 different tools), and cognitive function (47 different tools). However, for other factors, fewer tools were reported, with seven different tools reported for adverse events and just three different tools for sexual dysfunction. Eleven respondents used at least one tool for evaluating QoL in most (>50%) of their patients, eight did so for psychiatric comorbidity, five for cognitive dysfunction, nine for adverse events, and three for sexual dysfunction. One respondent used at least one screening tool for the majority of patients in all five categories (QoL, psychiatric comorbidity, cognitive dysfunction, adverse events, and sexual dysfunction), three respondents in four categories, three respondents in three categories, nine respondents in two categories, and 15 respondents in one category.

3.1. Respondents

Among the 28 respondents participating in the survey, four were psychologists and 24 were physicians. Of these, 18 worked at specialized epilepsy centres and ten worked at a section for epilepsy within a department of neurology. Regarding patient groups, 11 worked with children, nine with adults, and eight with both children and adults.

3.2. Quality of life in epilepsy

Those instruments most used for evaluating QoL were: Quality of life in epilepsy 10 (QOLIE-10) ($n = 9$), QOLIE 31 ($n = 9$), and QOLIE 89 ($n = 5$). Details on the extent of use of these tools at the various centres are provided in Table 3.

The perceived benefits of screening for QoL in epilepsy included: detection of “hidden” comorbidity, assistance in deciding which ASM to choose, and facilitation of research (Table 4).

3.3. Psychiatric comorbidity

The most frequently used instruments to screen for psychiatric comorbidity were: Beck Depression Inventory ($n = 15$), Beck Anxiety Inventory ($n = 10$), Hospital Anxiety and Depression Scale (HADS) ($n = 9$), Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) ($n = 5$), General Anxiety Disorder-7 (GAD-7) ($n = 5$), and Aberrant Behaviour Checklist (ABC) ($n = 5$). Details on the extent scope of these tools at the various centres are provided in Table 3.

The perceived benefits of screening for psychiatric comorbidity in epilepsy included: detection of “hidden” comorbidity, improved patient care, facilitation of research, use as a basis for referral to specialist, assistance in deciding which ASM to choose, to reduce taboo around the subject easier/ and thus facilitating discussion, and for use as a basis for referral to multidisciplinary team (Table 4).

Table 2
Reasons for using different screening tools.

Why do you use tools to screen for:	N	For researchn (%)	It is standard clinical care in my hospitaln (%)	To optimize individualpatient caren (%)
Quality of life in epilepsy?	24	21 (88)	5 (21)	14 (58)
Psychiatric comorbidity?	22	17 (77)	12 (55)	18 (82)
Cognitive dysfunction?	19	15 (79)	11 (58)	15 (79)
Adverse events?	10	6 (60)	3 (30)	7 (70)
Sexual dysfunction?	2	1 (50)	1 (50)	2 (100)

Table 3
Frequency of use of different screening tools by patient proportion.

How often do you use these tools to screen for:	N	For all/nearly all patients (>90%)	For the majority of patients >50%	For a minority of patients 50–10%	For few patients <10%
Quality of life in epilepsy					
QOLIE-10	9	1	1	3	4
QOLIE-31	12	2	4	1	5
QOLIE-89	5	1	1	1	2
PEDsQoL	2		1	1	
SF36	2		2	1	
Personal impact of Epilepsy scale, IPES	2			2	
All the following tools reported by one respondent: QOLIE-AD-48, Subjective Handicap in Epilepsy, Danish WHO-5 Well-being Index,	1		1 each		
All the following tools reported by one respondent: ELDoL, FALKE, CBCL, CGI-I, CHEQOL-25	1			1 each	
All the following tools reported by one respondent: WHOQOL-BREF, ESSQ-19, QOLCE, ICC, CHQ, DISABKIDS, KIDSCREEN	1				1 each
Psychiatric comorbidity					
Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)	5	2	1		2
Neurological Disorders Depression Inventory for Epilepsy-youth (NDDI-E-Y)	2				2
Beck Depression Inventory	15		6	6	3
Beck Anxiety Inventory	10		1	7	2
General Anxiety Disorder-7 (GAD-7)	5		2	1	2
Self-rating anxiety scale (SAS)	2		1		1
Hospital Anxiety and Depression Scale (HADS)	9	1		3	5
Liverpool Adverse Events Profile	4		1	2	1
Aberrant Behavior Checklist (ABC)	5	1		1	3
All the following tools reported by one respondent: Extended AEP, CBCL – YRS	1	1 each			
All the following tools reported by one respondent: FPZ personality questionnaire, MINI, SNAP-IV, Spence Childrens Anxiety Scale, Beck Ungdom,	1		1 each		

Table 3 (continued)

How often do you use these tools to screen for:	N	For all/nearly all patients (>90%)	For the majority of patients >50%	For a minority of patients 50–10%	For few patients <10%
Strengths and Difficulties Questionnaire, SCID-II, CONNERS, SAFA, questions (e.g., suicide)					
All the following tools reported by one respondent: STAI A/B, HDRS, HARS, NPI, PSS, DIKJ, AFS, KD-SADS, ADIE/ADOS, M.I.N.I.KID, JTCI 12–18R, Major Depression Inventory, TAND, Bayley, ADOS	1			1 each	
All the following tools reported by one respondent: Child behavior checklist, Toronto ALexithymia Scale, Social and physical Anhedonia Scale, Coping Inventory for Stressfull Situations, Lille Apathy Rating Scale Short, State Trait Anxiety Inventory, MMT, Liverpool seizure severity scale	1				1 each
Cognitive function					
EpiTrack	7	1		1	5
EpiTrack Jr.	5	1		2	2
Boston Naming Test	6		3	2	1
Brief Visuospatial Memory Test-BVMT-R	4	1	1	2	
California Verbal Learning Test- CVLT II	2		1		1
Behavior Rating Inventory of Executive Function Adult version –BRIEF A	3			1	2
Behavior Rating Inventory of Executive Function –BRIEF	5			2	3
Strengths and Difficulties Questionnaire	1			1	
Montreal Cognitive Assessment –MoCA	6			3	3
Mini-Mental Status Examination –MMSE (n = 8)	8			4	4
Cambridge Neuropsychological Test Automated Battery (CANTAB)	2			1	1
FePsy	2				2
NeuroCog FX	1			1	
Wechsler scale of intelligence (WPPSI IV, WISC IV, WAIS IV)	9	2	3	4	
REY Complex Figure	2	1		1	
WMS III	2	1		1	

(continued on next page)

Table 3 (continued)

How often do you use these tools to screen for:	N	For all/nearly all patients (>90%)	For the majority of patients >50%	For a minority of patients 50–10%	For few patients <10%
Developmental Test of Visual-Motor Integration. VMI (n = 2)	2	1		1	
All the following tools reported by one respondent: NEPSY –II, RAVLT, Raven	1	1 each			
All the following tools reported by one respondent: TEMA, Cognitive Neurophysiological Test (CNT)	1		1 each		
All the following tools reported by one respondent: STROOP, FCSRT, LONDON TOWER, FCRO, EDINBURG, BENTON, VOSP, CUBS, BNT, TOKEN, CORSI, DIGITS, TMT, SDMT, Bayley, D- KEFS, K-ABC, Claeson-Dahl auditivt verbalt inlärningsprov, Leiter-3, Mental fatiguescale, 50 Faces Forced Choise	1			1 each	
All the following tools reported by one respondent: Global Screening BLTT (Dementia), Denver, Griffiths, Psychecattell.	1				1 each
Adverse events (Liverpool) Adverse events profile (AEP)	7	2		1	4
Complaints-Assessment-Scale (CAS)	1				1
Extended AEP	1	1			
All the following tools reported by one respondent: PsyTrack (psychiatric), Specific questions (e. g., headache)	1		1 each		
Own application				1	
Sexual dysfunction Arizona Sexual Experiences Scale (ASEX)	1			1	
Extended AE	1	1			
Specific questions	1		1		

3.4. Cognitive dysfunction

The most commonly used instruments to screen for cognitive dysfunction were: Wechsler scale of intelligence (WPPSI IV, WISC IV, WAIS IV) (n = 9), Mini-Mental Status Examination –MMSE (n = 8), EpiTrack (n = 7), Boston Naming Test (n = 6), Montreal Cognitive Assessment –MoCA (n = 6), EpiTrack Jr. (n = 5), and Behavior Rating Inventory of Executive Function –BRIEF (n = 5). Details on the extent of use of these tools at the various centres are provided in Table 3.

The perceived benefits of screening for changes in cognitive

functioning in epilepsy included: detection of “hidden” comorbidity, facilitation of research, assistance in deciding which ASM to choose, and for use as a basis for referral to multidisciplinary team (Table 4).

3.5. Adverse events

The most commonly used instrument to screen for adverse events was Liverpool Adverse Events Profile (LAEP) (n = 5). Further details on the extent of use of this and other instruments at the various centres are provided in Table 3.

The perceived benefits of screening for adverse events included: assistance in deciding which ASM to choose, facilitation of research, and for use as a basis for referral to multidisciplinary team (Table 4).

3.6. Sexual dysfunction

The only instrument explicitly addressing this issue was the Arizona Sexual Experiences Scale (ASEX) (n = 1). Further details on the extent of use of this tool at the various centres are provided in Table 3.

The perceived benefits of screening for sexual dysfunction in epilepsy were: detection of an often “hidden” comorbidity, assistance in deciding which ASM to choose, for use as a basis for referral to multidisciplinary team or a specialist, and to facilitate talking about the subject by reducing taboo (Table 4).

4. Discussion

4.1. General considerations

Our survey shows there is extensive use of different instruments among the European epilepsy population for screening for a range of factors, such as: ASM side effects, QoL in epilepsy, psychiatric comorbidity, and cognition.

The most frequently reported perceived benefits of screening were: detection of “hidden” comorbidities, choice of ASM, facilitation of research, and basis for referral to multidisciplinary teams. A relevant limitation to be considered is whether the tests used are appropriate for reliable detection of the targeted issue [17].

4.2. Quality of life in epilepsy

In our survey, most respondents reported using “QoL in epilepsy” questionnaires on a regular basis for some patients, with QOLIE-10, –30, and –89 the most frequently used. It has long been known that the physical, psychological, and social consequences of epilepsy have a considerable impact on QoL [18–20]. The Epilepsy-specific QoL measures are particularly relevant to specific aspects of epilepsy and its treatments, and therefore are very sensitive and responsive patient-reported outcomes [21,22]. QOLIE-10 consists of 10 questions and is easy to use, whereas QOLIE-89 is more comprehensive, with 17 multi-item scales and a generic core (short form 36 (SF 36)). It covers most aspects of life and the generic core (SF 36) provides the opportunity for comparing QoL scores between different chronic diseases.

4.3. Psychiatric comorbidity

Psychiatric symptoms are common in epilepsy, with one in three people with epilepsy fulfilling the criteria of a psychiatric diagnosis at some stage in their lives [23]. These symptoms affect not only QoL, but are also associated with a poorer medical outcome; early treatment is thus highly recommended [24,25]. Self-reported questionnaires can be a useful tool and a first step in the evaluation of whether a psychiatric disorder is present [12]. Thus, it is unsurprising that psychiatric comorbidity was the factor most frequently screened for in our survey. In addition, over 80% of respondents reported using one or several questionnaires to evaluate anxiety or depressive symptoms in daily clinical

Table 4
Perceived benefits from using screening tools.

What is your perceived benefit of screening for:	N	Detection of “hidden” comorbidityn (%)	Helps to decide which ASM to choose n (%)	Facilitates researchn (%)	Basis for referral to multidisciplinary teamn (%)	Basis for referral to specialistn (%)	Makes talking about the subjecteasier/ reduces taboo n (%)	Psychiatric comorbidity is prevalent and screening improves patient care n (%)	Other (%)
Quality of life (23	17 (74)	5 (22)	20 (87)					4 (17)
Psychiatric comorbidity	22	19 (86)	10 (46)	17 (77)	8 (36)	14 (64)	8 (36)	19 (86)	0
Cognitive function	29	18 (90)	9 (45)	14 (70)	12 (60)				1 (5)
Adverse events?	11		9 (82)	8 (73)	5 (46)				
Sexual dysfunction?	3	2 (67)	1 (33)	0	2 (67)	2 (67)	2 (67)		1 (33)

Choice not available.

care. Some screening tools, such as NDDI-E, have been validated for use in the epilepsy population [26]. Other questionnaires that are used may be non-specific and not validated for the epilepsy population; for these tools it is less clear how well a score above cut off corresponds with a psychiatric diagnosis. Overall, screening for psychiatric comorbidity appears useful and forms a basis for further exploration of a possible underlying undiagnosed psychiatric disorder. More thorough investigation, with a psychiatric interview, could often, depending on access be the next step after screening.

In our experience, both NDDI-E and GAD-7 are very useful tools for the clinician and supplement other information when evaluating psychiatric status in patients. In addition the NDDI-E has the advantage that it was designed to exclude somatic symptoms of depression that are also common adverse medication effects, allowing easier differentiation of adverse ASM effects and comorbid depression [26]. Screening for anxiety and depression simultaneously with adverse events of ASMs can be a valuable approach, as adverse events of ASMs can be even more intense when depression is also present [27].

4.4. Cognitive dysfunction

Cognitive dysfunction occurs frequently among patients with epilepsy [28,29]. It may be a result of the underlying pathology, such as developmental brain abnormalities, traumatic brain injury, or tumours. It may also be related to ongoing epileptic activity and/or may be a result of medical treatment. The majority of our respondents reported frequent use of tools to screen for cognitive dysfunction, but with considerable variation regarding the instruments in use. This finding seems to be in line with those from a similar survey recently conducted in pediatric epilepsy centres [30].

A wide variety of tools are listed, of which some (e.g., EpiTrack/ EpiTrackJr, MMS, MoCa; BRIEF) can be categorized as screening tools, but others are single tests or test batteries that are typically included in broader neuropsychological assessments. Other than the EpiTrack/ EpiTrackJr, very few tools have been validated for use in the epilepsy population and for disease and treatment monitoring [31,32]. Although most healthcare professionals may use cognitive screening tools, other tests of cognitive functions typically require specific training. As our respondents were reporting on their own clinical practices, our findings should be interpreted in light of the fact that there were many more neurologists among our respondents than (neuro)psychologists. The detection of “hidden” comorbidity was reported as the main reason for using cognitive tests/ screening instruments. This probably reflects that professionals at epilepsy centres are well aware that epilepsy-related cognitive impairment may be subtle and difficult to detect if not specifically addressed in the clinic.

4.5. Adverse effects of ASMs

The use of screening for adverse effects of ASMs has been described

in the literature over the past two decades, and the use of such screening tools in epilepsy has evolved; see, e.g., [33,34]. At three centres, Adverse events profile (AEP) and Liverpool adverse events profile (ILAEP) were used, and one center used complaints assessment scale (CAS). The two Adverse events profiles mentioned, although with different names, are the same questionnaire, including 19 items to assess the frequency of different adverse effects by a four-category Likert scale, as in the original adverse events profile in epilepsy, introduced by Gilliam [34]. Other studies, such as Panelli et al. [35], also mention ILAEP, and describe the same questionnaire.

The main reasons why screening tools were reported as being used for adverse effects of AEM included research purposes ($n = 6$) or to optimize individual care ($n = 5$). In three centres they were implemented as part of standard clinical care. The CAS screening tool was also used for a few patients, but only in eight centres, with only one center using it for all patients. The major perceived benefits of screening, from data provided from nine centres, included help in deciding which ASM to choose, facilitating research, and being used as a basis for referral to a multidisciplinary team. A few years ago, we implemented this in the Norwegian epilepsy center as part of increased focus on patients' perspectives on adverse effects and adherence, with focus on patient safety. Our experience, which is supported by the present findings, is that such screening gives very useful additional information for the clinician and that the patients appreciate this approach [36].

4.6. Sexual dysfunction

Very few respondents reported screening for sexual dysfunction in their patients with epilepsy. The Arizona Sexual Experiences Scale (ASEX) was used by one respondent, and others used either specific questions or questions from other screening tools.

The ASEX is a short, easy-to-administer questionnaire that has been validated, although not in a population with epilepsy, fulfilling most of the basic requirements for a screening tool [37]. The main perceived benefits of using a screening tool for sexual dysfunction were to detect “hidden” comorbidity, facilitate referral, reducing taboo, and initiate dialog about sexual dysfunction. Despite most studies reporting an increased rate of sexual dysfunction among patients with epilepsy [37], it is not surprising that only a few respondents reported using screening tools on this area, as many physicians are reluctant to discuss sexual function with their patients [38–40]. According to a systematic review [41], the majority of healthcare providers consider sexuality to be of importance, but still do not discuss this routinely. Possible causes could be lack of knowledge and expertise within this complex area, and the fear of being perceived as intrusive or asking inappropriate questions [41]. However, clinical experience indicates that patients usually welcome questions about their sexuality, and rarely decline discussions on this subject [42,43].

4.7. Limitations

As 38% of the centres contacted did not respond to the questionnaire, this might indicate bias and selection of those respondents who use screening tools more frequently. In addition, we do not have information as to whether each respondent answered for themselves or on behalf of the center. Misunderstandings may also have arisen regarding whether the questionnaire was investigating the use of screening tools specifically for screening or as part of a more extensive evaluation.

5 Conclusions

In the absence of a broad consensus regarding the use of screening tools, practices vary considerably among epilepsy centres. Most respondents in our study use screening tools for screening for QoL information and psychiatric comorbidity, with only a few screening for sexual problems. Many different tools are used for evaluation of cognitive dysfunction, but just a few different tools are used to screen for adverse events. Optimization of individual patient care was the main reason reported for using screening tools, followed by research. The major benefit of screening tools perceived by the respondents is the detection of “hidden” comorbidities. Questions that our study could not answer, but which should be addressed in future research, are whether screening actually influences further treatment and, if so, how does this affect patient care.

Appendix 1

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Sofia Quintas reports a relationship with Eisai Co Ltd, Biomarin, Sanofi that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement.

Declaration of Competing Interests

O.H. reports personal fees from Roche, Eisai, UCB, Novartis, and LivaNova, outside the submitted work. M.I.L. reports personal fees from Eisai, UCB, and Arvelle, outside the submitted work. C.J.L. reports personal fees from Eisai, GW/Jazz, Angelini and UCB Pharma, outside the submitted work. C.H. reports personal fees from UCB, Eisai, Precisis, GW Pharma. A.H.S. reports personal fees from Eisai outside the submitted work. K.Å.A. reports no disclosures.

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Supplementary materials

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