Automated seizure detection using wearable devices: a guideline of the International League Against Epilepsy and International Federation of Clinical Neurophysiology

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Keywords: algorithms; automated detection; epilepsy; seizure detection, wearable devices

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Summary

The objective of this clinical practice guideline (CPG) is to provide recommendations for healthcare personnel working with patients with epilepsy, on the use of wearable devices for automated seizure detection in patients with epilepsy, in outpatient, ambulatory settings. The Working Group of the International League Against Epilepsy and the International federation of Clinical Neurophysiology developed the CPG according to the methodology proposed by the ILAE Epilepsy Guidelines Working Group. We reviewed the published evidence using The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement and evaluated the evidence and formulated the recommendations following the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. We found high level of evidence for the accuracy of automated detection of generalized tonic-clonic seizures (GTCS) and focal-to-bilateral tonic-clonic seizures (FBTCS), and moderate level of evidence for seizure types without GTCs or FBTCs. However, it was uncertain whether the detected alarms resulted in meaningful clinical outcomes for the patients. We recommend using clinically validated devices for automated detection of GTCS and FBTCS, especially in unsupervised patients, where alarms can result in rapid intervention (weak / conditional recommendation). We do not recommend clinical use of the currently available devices for other seizure types (weak / conditional recommendation). Further research and development are needed to improve the performance of automated seizure detection and to document their accuracy and clinical utility.

Keywords: algorithms; automated detection; epilepsy; seizure detection, wearable devices

Key point box:

- This clinical practice guideline addresses automated seizure detection using wearable devices.
- The guideline was developed by a working group of the ILAE and IFCN using the GRADE system.
- Wearable devices are recommended for automated detection of generalized tonic-clonic seizures and focal-to-bilateral tonic-clonic seizures.

Introduction

The International League Against Epilepsy (ILAE) and The International Federation of Clinical Neurophysiology (IFCN) have joined forces to develop clinical practice guidelines (CPGs) for application of neurophysiological methods in epilepsy. The objective of this CPG is to provide recommendations on the use of wearable devices for automated seizure detection in outpatients with epilepsy in ambulatory setting, to reduce the morbidity and mortality associated with seizures and to improve the objective documentation of seizure frequency.

We developed the CPG according to the methodology proposed by the ILAE Epilepsy Guidelines Working Group[1]. The development was evidence-based and consensus-driven. It followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system[2,3]. The target audience of this CPG is healthcare personnel working with patients with epilepsy. The CPG was endorsed by both international societies.

Identifying the topic and developing the clinical questions

There is a need for automated seizure detection using wearable devices, to decrease morbidity and mortality associated with seizures and for objective seizure identification and quantification. Approximately one third of patients with epilepsy are not seizure-free, in spite of adequate treatment[4]. The unpredictability of seizure-occurrence is distressing for patients and for caregivers. It contributes to social isolation and decreased quality of life. Patients with generalized seizures and those with focal impaired awareness seizures are not able to call for help during seizures. Therapeutic decisions in clinical practice, as well as drug trials use self-reporting of seizures[5] which are largely unreliable. Studies in video-EEG monitoring units demonstrated that 47-63% of seizures remain unrecognized by patients[6] and this is even higher (86%) for nocturnal seizures[7].

Generalized tonic-clonic seizures (GTCS), including focal-to-bilateral tonic-clonic seizures (FBTCS), may lead to injuries, and constitute the main risk factor for sudden unexpected death in epilepsy

(SUDEP), especially in unattended patients, during nighttime hours[8]. Each year, 25% of the patients with GTCS experience at least one serious injury related to the GTCS, causing disability or requiring hospitalization or surgical intervention, and patients with five or more GTCS per year have a 3.5 times higher odds ratio for injuries, compared with patients who only have one seizure per year[9]. The majority of SUDEP cases that were video-EEG documented, occurred after a GTCS[10]. The risk of SUDEP was 27 times higher in patients experiencing GTCS during the preceding year, whereas no excess risk was seen in patients with non-GTCS seizures[11]. The combination of not sharing a bedroom and having at least one GTCS per year had a 67-fold increased risk of SUDEP[11]. The risk of SUDEP increases in association with increasing frequency of GTC occurrence[12]. Therefore, GTCS (including FBTCS) is the most important seizure-type that needs to be detected automatically, to decrease morbidity and mortality associated with seizures.

Several large surveys of patients with epilepsy, their caregivers and healthcare professionals demonstrated that there was a need for reliable seizure detection using wearable devices (WDs) in the home environment of the patients[13–17]. WDs are becoming widely used, and this trend has reached healthcare applications, including epilepsy: there are hundreds of Wearable Devices (WD) on the market that measure health parameters and biosignals[18] and many of them make unsubstantiated claims to detect epileptic seizures. There is a considerable gap between the rapidly developing field of digital technology and the arguably conservative clinical practice. This is largely due to lack of evidence-based guidelines for clinical implementation of automated seizure detection using wearable devices. The scope of this ILAE-IFCN CPG is to bridge this gap, by reviewing the evidence behind the performance of these devices and recommending its application in patients with epilepsy.

We used the PICO approach (Population, Intervention, Comparator and Outcome) to construct the clinical questions (Table 1). We aimed at answering the following questions: (1) Can automated devices accurately detect GTCS, including FBTCS? (2). Can automated devices accurately detect impaired awareness seizures without tonic-clonic component?

Evaluation of the efficacy of closed loop systems, where automated seizure detection triggers a therapeutic intervention to stop the seizure, was beyond the scope of this CPG.

Establishing the CPG Working Group

The ILAE Commission on Diagnostic Methods and the Executive Committee of the IFCN each appointed four members of the CPG Working Group, to achieve a multidisciplinary composition and a broad geographic representation[19]. The Working Group and the CPG development protocol was approved by the Guidelines Task Force before starting the literature search.

Reviewing the evidence

We conducted the systematic review of the published evidence, and the results of the systematic review of the published evidence were reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement[20].

We searched in PubMed and EMBASE using the following string: ((automated detection) OR (algorithm AND detection) OR (wearable AND detection)) AND (epilepsy OR seizure). The date last searched was October 16th, 2019. Additionally, experts were asked to contribute relevant references. We selected studies published as papers in peer-reviewed journals, without language limitations, corresponding to phase 2, 3 or 4 clinical validation trials, according to the previously published standards for testing and clinical validation of seizure detection devices[21]. Briefly, these were based on the key features for validation of seizure detection devices: subjects, recordings, data analysis and alarms, and reference standard. Depending on how the studies addressed these features, they were classified into phases 0 to 4, similar to therapeutic trials, where phase 3 studies provide compelling evidence and phase 4 studies are in-field, follow-up studies on the feasibility and utility of the devices in the home environment of the patients[21]. To qualify as phase 3, studies had to fulfill the following criteria: prospective, multicenter study analyzing continuous recordings from a dedicated seizure

detection device, including at least 30 seizures recorded from at least 20 patients (for a sensitivity over 90%), with real-time detection of seizures (signal analysis running during the recording) using a pre-defined algorithm with a pre-defined detection cut-off value and reference standard from video or video-EEG recordings interpreted by experts. The studies had to specify the key outcome measures (sensitivity and false alarm rate) reported according to the STARD (Standards for Reporting Diagnostic Accuracy Studies) criteria[22]. For systematic assessment of risk of bias, we have adapted the items from the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) to the specific application for this health technology assessment[3,23]. Bias introduced by patient selection, patient flow, execution of the automated data analysis (seizure detection), and the reference standard, were present in phase-2 studies, and non-significant in phase-3 studies.

The following data were extracted from the studies: 1) signal used for seizure detection; 2) prospective versus retrospective study; 3) real-time versus off-line analysis and seizure detection; 4) seizure-types that were analyzed; 5) number of patients with seizures; 6) number of recorded seizures; 7) sensitivity (proportion of true seizures detected); 8) device deficiency time (percentage of time when the device was not functional); 9) latency of seizure detection from seizure onset; 10) false alarm rate (per 24 hrs.) and number of false alarms per night - as surrogate for specificity (Table 2).

Two independent reviewers screened titles, abstracts and full text articles for eligibility criteria. A third reviewer resolved disagreements at the full text screening phase and the data abstraction phase. The PRISMA flow diagram (Figure 1) shows that of the 1750 relevant citations found, 170 abstracts were screened for eligibility, 47 articles were reviewed in full text, and 28 fulfilled criteria for inclusion in the evidence synthesis. Due to the large heterogeneity in study design and the use of different devices and algorithms, quantitative synthesis (meta-analysis) was not possible. We thus conducted a qualitative synthesis of the included studies (Table 2). Only three studies fulfilled the criteria for phase 3 and two studies for phase 4 (one study reported both phase 3 and 4)[24]. The remaining studies were phase 2. We identified several limitations and potential sources of bias,

especially for phase 2 studies (Table 2). In particular, offline analysis of the biosignals and the use of several post-hoc cut-off values raise the possibility of overfitting to the recorded dataset and questions the generalizability of the results. Important aspects, such as detection latency and device deficiency were often omitted from the reports and only a few studies were reported according to the STARD guidelines.

Evidence from phase 3 studies for detection of seizures with sensitivity of at least 90% was available only for GTCS, including FBTCS. One study used accelerometer, one study used surface electromyography and one study used a multimodal device (accelerometry and heart rate) (Table 2). The sensitivity of these devices was between 90% and 96%, with a false alarm rate of 0.2-0.67/24-hrs. (0-0.03/night). All three devices validated in phase 3 studies have approval for use as medical device (CE-mark) in the European Union. Two phase 4 studies demonstrated the feasibility of WDs and their usability for detecting GTCS in the home environment of the patients[24,25]. However, it is important to note that most patients included into the phase 4 studies had severe epilepsy and intellectual disability, living in a residential care setting.

For other seizure-types only phase 2 studies were available. Best performance (sensitivity of 99%) was achieved by automated analysis of EEG recorded with intracranial electrodes[26,27] (Table 2). Of the non-invasive devices, sensitivity over 90% has been achieved using heart rate and heart rate variability (Table 2).

Evaluating the evidence and formulating the recommendations

We evaluated the quality of the evidence, using the GRADE approach, with specific consideration for the aspects related to diagnostic tests and strategies[2,3]. We assessed the factors that decreased the quality of evidence for diagnostic tests, specifically adapted to the topic of this CPG. We considered phase 3 validation studies to provide high level of evidence, phase 2 studies to provide moderate level of evidence and phase 1 studies to provide low level of evidence. For each clinical question and each

seizure-type, we considered the studies with the highest available evidence (Table 3). In addition to the evidence, we evaluated the determinants of the strength of recommendations, adapted to the topic of the CPG (Table 4). We used a Delphi process to develop consensus-driven conclusions[28].

The Working Group found high quality evidence for detection of GTCS and FBTCS, and moderate for seizures without a tonic-clonic component. Although there was broad consensus concerning the need for automated detection of both seizure categories, the Working Group considered that for the currently available devices it was uncertain whether the desirable effects (seizure detection) outweigh undesirable effects (e.g., false alarms, burden of usage and cost) for seizures other than GTCS and FBTCS. There is evidence from a single study (phase 4) suggesting that the use of automated seizure detection devices helped prevent injuries related to GTCS[25]. Although there is compelling evidence that SUDEP mainly occurs in unsupervised patients with GTCS, it was uncertain whether detection of such seizures could lead to sufficiently rapid and effective intervention[29].

Recommendations for automated seizure detection using wearable devices

The ILAE-IFCN Working Group recommends using clinically validated wearable devices for automated detection of GTCS and FBTCS, especially in unsupervised patients who do not share a bedroom but where alarms can result in rapid intervention, within 5-10 minutes (weak / conditional recommendation).

The ILAE-IFCN Working Group does not recommend clinical use of the currently available wearable devices for seizure types other than GTCS and FBTCS (weak / conditional recommendation).

There is need for further research and development in the following areas:

1) To increase the performance of wearable devices and detection algorithms (higher sensitivity and lower false detection rate), especially for seizures without generalized convulsions.
2) To conduct properly designed clinical validation studies.
3) To demonstrate whether automated seizure detection leads to meaningful clinical outcomes, such as decreased morbidity and mortality associated with seizures, objective seizure quantification, improved quality of life. Similarly, patient preferences and costs should be considered in the evaluation of impact of this technology.

Acknowledgments

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Disclosure of Conflicts of Interest

Author SB served as a scientific consultant for Brain Sentinel and Epihunter. WOT was principal investigator for the clinical trial using Brain Sentinel device. The remaining authors do not have any conflict of interest to disclose, related to this paper.

Ethical Publication Statement

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.

Table 1

Population	Children and adults with epilepsy, who are not seizure-free and who have either (1) GTCS, including FBTCS or (2) focal impaired awareness seizures, without tonic-clonic component.
Intervention	Automated seizure detection using a wearable device and room or bed-placed sensors.
Comparator	Electroclinical seizures identified by trained experts, based on video-EEG or video recordings.
Outcome	Sensitivity, false alarm rate, adverse events, usability.

Table 2

Study	Phase	Modality	Study design	Patient age range	Types of seizures	Number of patients with seizures.	Number of seizures	Sensitivity	False alarm rate	Device deficiency time	Detection latency
Kramer U. et al. 2011[30]	2	Wrist 3D-accelerometer	Prospective / Real-time	Not reported	Motor seizures.	15	22	20 out of 22 (90.9%)	0.11/24 h (0 at night).	Not reported	17 s of onset of motor component (range, 12–35 s).
Beniczky S. et al. 2013[31]	3	Wrist 3D-accelerometer (Epi-care)	Prospective / Real-time	13-63 years (mean 37 years)	Generalized tonic-clonic seizures.	20	39	35 out of 39 (89.7%)	0.2/24 h (0 at night).	Time not reported. However, device deficiency was reported 15 times in total.	Mean 33 s from onset of GTCS and 55 s from onset of focal seizure (95% [CI] 38–73 s).
Patterson A. et. al 2015[32]	2	Wristwatch accelerometer (SmartWatch)	Prospective / Real-time	5-41 years	Generalized tonic-clonic, myoclonic/myoclonic-tonic, partial onset with minimal motor component, partial-onset hypermotor, and tonic seizures.	41	191	GTCs: 16/51 (31%). Myoclonic, tonic, myoclonic-tonic seizures: 3/32 (6%). Partial-onset seizures with motor component: 11/45 (24%). Partial onset with minimal motor	Not reported	Not specified. However, two seizures were excluded because it is unknown if the SmartWatch was activated, two because the watch was	Not reported

								component: 1/63 (2%). Total 16%.		disconnected, and two because the video was not available.	
Velez M. et al. 2016[33]	2	Wristwatch accelerometer	Prospective / Real-time	19-66 years	Generalized tonic-clonic seizures.	12 (all seizure types) 10 (GTC)	13 GTCS and 49 non-GTCS	12 of 13 GTCs (92.3%). No focal seizures were detected.	Not specified, but there was a total of 81 FPs.	Not specified, but three patients were excluded.	Not reported
Kusmakar S. et al. 2017[34]	2	Wrist accelerometer	Prospective / Offline	Not reported	Generalized tonic-clonic seizures.	12	21	20 out of 21 (95.23%)	Mean: 0.72/24 h.	Not reported	Not reported
Meritam P. et al. 2018[25]	4	Wrist 3D-accelerometer (Epi-Care).	Retrospective survey with long-term follow-up. / Real-time	7-72 years (median 27 years)	Generalized tonic-clonic seizures.	71	Seizure number not applicable (in-field study)	Median: 90%.	Median: 0.1/24 hr. (mean = 1.4/24 hr.) – increased in a subgroup with > 5 seizures/ day.	7 cases (10%) stopped using device.	Not applicable (in-field study)
Kusmakar S. et al. 2019[35]	2	Wrist 3D-accelerometer	Retrospective / Offline	19-59 years	GTCs (21), PNES (20), CPS (5).	20	46	40 of 46 (20/21 GTC)	1.16/24 h, (GTC only - 0,64/24 h).	Not reported	Not reported

Johansson D. et al. 2019[36]	2	Wrist 3D-accelerometer	Prospective / Offline	18-77 years (median 35 years	Tonic-clonic seizures	11	37	I*: 10 of 10 II*: 9/10 III*: 9/10	I*: 1.2 FP/24 h. II*: 0.24 FP/24 h. III*: 0.48 FP/24 h.	22% (total of 1952 hours) in 29 patients (average 65 hr/pt) missing data.	Not reported
Szabo C. et al. 2015[37]	2	Surface EMG	Prospective / Offline	14-64 years (mean 40 years)	Generalized tonic-clonic seizures.	11	21	20 out of 21	0.017/24 h (0 during sleep).	Not reported	Mean 15.2 s of onset of GTCS (range 4 to 56s).
Halford J.J. et al. 2017[38]	2	Surface EMG	Prospective / Offline	3-72 years	Generalized tonic-clonic seizures. "Intent to monitor cohort" (IMC), and "properly placed cohort" (PPC).	61	46 GTCSs in the IMC, 29 GTCSs in the (PPC).	In the IMC, 35 of 46 GTCSs. In the PPC 29 of 29 GTCSs.	In the IMC, mean FAR: 2.5/ 24 h. In the PPC, mean FAR: 1.4/ 24 h.	Not reported	Average: In the IMC: 7.45 s In the PPC: 7.75 s.
Beniczky S. et. al 2018[39]	3	Surface EMG	Prospective / Real-time	10-62 years (mean 34)	Generalized tonic-clonic seizures.	20	32	30 out of 32 (93,8%)	0.67/24 hours.	<5%	9 sec
Boon P. et al. 2015[40]	2	Cardiac-based seizure detection algorithm (Aspire)	Prospective / Offline post-hoc analysis of various thresholds	Not reported	Focal seizures (unspecified), Simple partial seizure, Complex partial seizure, Secondarily generalized, Other seizures.	16	Focal seizures: (unspecified) 8, Simple partial 26, CPS 31, sGTC 17, Other seizures 5	I*: 11/11 II*: 16/27 (59.3%). III*: 7/15 (46.7%). IV*: 8/23 (34.8%) V*: 3/11 (27.3%). VI*: 3/16 (18.8%).	False positive rate per hour: I*: 7.15 (5.31, 9.94). II*: 2.72 (1.70, 3.91). III*: 0.49 (0.20, 0.96).	Not reported	Median: I*: 6.0s II*: 27.5s III*: 35.0s.

Fisher RS. et al. 2016[41]	2	Heart rate (ECG)	Prospective / Offline	21-69 years	Simple partial seizure, Complex partial seizure, Secondary generalized seizures.	16	89	28 of 38 seizures with impaired awareness and GTC (74%). 7 of 37 (19%) SPS.	216/24h (with setting: 20% increase in HR).	Not reported	8 sec (with 20% HR increase).
Vandecasteele K. et al. 2017[42]	2	Heart rate (ECG and photoplethysmography (PPG))	Prospective / Offline	19-67 years	Complex partial seizures.	11	47	The wearable ECG 70%. The PPG 32%.	ECG: 50.64/24 h, PPG: 43,2/24 h.	Not reported	Not reported
Jeppesen J. et al. 2019[43]	2	Heart rate (ECG)	Prospective / Offline	4-79 years (median 34 years)	Focal seizures and Convulsive seizures (FBTCS & GTC)	43	126	Best algorithm: 93.1% of all seizures from responders. (90.5% of focal seizures, 100% of convulsive seizures).	1.0/24 h. (0.11 during sleep at night)	Not reported. However, data from 1 of 100 patients was excluded due to bad connection.	30 s. (median latency from first clinical or EEG sign of seizure).
Karayiannis NB. et al. 2006[44–46]	2	Video	Retrospective / Offline	Not reported	Myoclonic seizures (80 segments), focal clonic seizures (80 segments).	54	160	>95% scheme 1. <95% scheme 2.	Not applied but specificity was: >90% scheme 1 and <95% scheme 2.	Not reported	Not reported
Geertsema E. et al 2018[47]	2	Video-based algorithm in a residential care setting.	Retrospective / Offline	Not reported	Convulsive seizures (generalized clonic and generalized tonic-clonic seizures) and tonic > 30 s, hyperkinetic, major motor seizures.	Training set: 50 patients, Test set: 12 patients.	Training set: 72 convulsive seizures, Test set: 50 convulsive seizures.	100% for convulsive seizures. 3/5 (60%) “hyperkinetic” seizures. 6/9 (67%) other “major” seizures.	Median false detection rate: 0.78 per night (8 h).	Not reported	CS: ≤10 s in 78% of detections from the start of the oscillatory period. Hyperkinetic and other

											major: 7-35 s.
Arends JB. et al. 2016[48]	2	Sound detection	Prospective / Offline	18-42 years (mean 34 years)	GTCs, clonic seizures, tonic generalized seizures.	10	112	81% (range 33%-100%).	Mean FAR 1.29 per night, due to minor seizure.	Not reported	Not reported
Narechania et al. 2013[49]	2	Under-mattress device (ElectroMechanical Film Emfit®)	Prospective / Real-time	18-81 years (mean 38 years)	Generalized tonic-clonic seizures.	13	18	16 out of 18	0.13/24h (0 at night).	Not reported	9 s of onset of bilateral clonic motor movement (range: −37 to +39 s).
Fulton S. et al. 2013[50]	2	Two under-mattress devices. (ST-2 model and Medpage Model MP5 devices)	Prospective / Real-time	1-22 years	9 GTCs; 8 sGTC; 10 complex partial; 2 simple partial-motor; and 40 generalized myoclonic, tonic, or myoclonic-tonic.	15	69	MP5 bed monitor: 4.3% (1/23) (a generalized detected). The ST-2: 2.2% (1/46) (a complex partial detected).	Not reported	Not reported, however four patients found the MP5 device too uncomfortable and asked that it be removed.	Not reported
Baldassano S. et al. 2017[27]	2	Intracranial EEG	Retrospective / Offline	Not reported	Focal seizures	8 patients and 4 dogs in competition test set, 18 patient validation data set	95 in competition test set, 393 in validation set.	Performance was measured with AUC. Best algorithm had 0.975 test set, and 0.963 in validation dataset	Threshold of 1 FP/24 h of interictal data was preset to test the seizure detection sensitivities computed at a	Not reported	Not reported

									specificity .		
Gu Y. et al. 2018[51]	2	Behind-the-Ear-EEG	Prospective / Offline	19-64 years (mean 36 years)	Focal onset impaired awareness seizures.	12	47	Median 94.5%, Mean 82.17%	12.48/24 hours.	Not reported	Not reported
Baldassano S. et al. 2019[26]	2	Closed-loop implantable neural stimulators	Retrospective / Offline	Not reported	Electrographic focal-onset seizures	11	982	99%	0.72/24 h	Not reported	Not reported
Jeppesen J. et al. 2015[52]	2	Near Infrared Spectroscopy (NIRS)	Prospective / Offline	20-58 years (median 39 years)	Focal seizures. 20 temporal-, 11 frontal-, 2 parietal- lobe, one unspecific.	15	34	12 parameters analyzed. Detection sensitivity was 6-24%.	Not reported	Not reported	Not reported
Onorati F. et al. 2017[53]	2	Wristband electrodermal activity (EDA) and accelerometer	Prospective / Offline	4-60 years	Focal tonic-clonic seizures and focal to bilateral tonic-clonic seizures.	22	55	Best classifier: 94.55%	0.2 pr. day. FAR/seizure: 0.91.	Not reported	Median = 29.3 s (range = 14.8-151 s).
van Andel J. et al. 2017[54]	2	Heart rate (ECG) and accelerometer	Prospective / Offline	2-65 years (median 15 years)	Generalized tonic-clonic seizures, Generalized tonic seizures, Hypermotor seizures, Clusters of short	23	86	Sensitivity 71% for all seizures and 87% for “clinically urgent seizures”	2.3-5.7 per night (8 h).	Due to failures in connection data from 52 of 95 patients could not be used. 8 pts data could	Average delay: 13 s.

					myoclonic/tonic seizures.					only be partially used.	
Cogan D. et al. 2017[55]	2	Heart rate (ECG), arterial oxygenation, electrodermal activity	Retrospective / Offline	21-64 years	Secondary GTCS, CPS, Bilaternal tonic, primary GTCS.	10	26	I*: 11 of 11 from 7 patients. II*: 10 of 10 from 6 patients.	I*: Potential False positive 0.36/24 h II*: Potential False positive 0	Not reported	Not reported
Arends J. et al. 2018[24]	3 & 4	Heart rate (photoplethysmography) and 3D-accelerometer	Prospective / Real-time	15-67 years (mean 29 years)	Tonic-clonic, generalized tonic >30 seconds, hyperkinetic, clusters (>30 minutes) of short myoclonic/tonic seizures.	28	809	TCS: 81%. Other major motor seizures: 77%. Median detection rate per patient: 96% for GTCS, 86% for all major motor seizures.	0.03 per night (95% CI 0.01-0.05).	Device deficiency time was present, but time-length not specified.	Not specified. Seizures were considered detected if within 3 min before and 5 min after onset.

* Sensitivity/Detection latency/False positive depended on the threshold settings and/or detection method applied.

Abbreviations: GTC(s), Generalized tonic-clonic seizures. sGTC, Secondary generalized tonic-clonic seizures. CPS, Complex partial seizures. SPS, Simple partial seizures. FBTCS, focal to bi- lateral tonic-clonic seizures. FP, False positive. CI, Confidence Interval. ECG, Electrocardiography. EMG, Electromyography. PNES, Psychogenic non-epileptic seizures. PPG, photoplethysmography. IMC, Intent to monitor cohort. PPC, Properly placed cohort. FAR, False alarm rate.

Table 3

Seizures	Quality assessment							№ of		Effect		Quality	Importance
	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Detection modalities	Patients with seizures	Seizures	Sensitivity	FDR		
GTCS & FBTCS	3	Phase 3	Not serious	Not serious	Not serious	Not serious	Accelerometry, sEMG, multimodal	68	880	90-96%	0.2-0.7	HIGH	CRITICAL
Without TC component	8	Phase 2	Serious	Not serious	Not serious	Serious	EEG, PPG, ECG	152	1906	32-90%	0.7-65	MODERATE	IMPORTANT

Abbreviations: FDR, False detection rate. GTCS, Generalized tonic-clonic seizures. FBTCS, focal to bi- lateral tonic-clonic seizures. TC, Tonic-clonic. PPG, photoplethysmography. ECG, Electrocardiography. sEMG, Surface electromyography.

Table 4

Factor	Considerations	GTCS & FBTCS	Seizures without TC component
Balance between desirable and undesirable effects	Do desirable effects (seizure detection) outweigh undesirable effects (i.e., false alarms, burden of usage)?	Yes	Uncertain
Values and preferences	Do patients, caregivers and healthcare personnel need wearable seizure detection devices?	Yes	Yes
Wise use of resources	Does currently available automated seizure detection provide input for meaningful outcome (prevention of injuries, prevention of SUDEP, objective measurement of seizure burden) or increase in the quality of life?	Uncertain	No

Abbreviations: GTCS, Generalized tonic-clonic seizures. FBTCS, focal to bi- lateral tonic-clonic seizures. TC, Tonic-clonic.

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