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RESEARCH ARTICLE

Automated seizure detection with noninvasive wearable devices: A systematic review and meta-analysis

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Abstract

Objective: This study was undertaken to review the reported performance of noninvasive wearable devices in detecting epileptic seizures and psychogenic nonepileptic seizures (PNES).

Methods: We conducted a systematic review and meta-analysis of studies reported up to November 15, 2021. We included studies that used video-electroencephalographic (EEG) monitoring as the gold standard to determine the sensitivity and false alarm rate (FAR) of noninvasive wearables for automated seizure detection.

Results: Twenty-eight studies met the criteria for the systematic review, of which 23 were eligible for meta-analysis. These studies (1269 patients in total, median recording time = 52.9 h per patient) investigated devices for tonic-clonic seizures using wrist-worn and/or ankle-worn devices to measure three-dimensional accelerometry (15 studies), and/or wearable surface devices to measure electromyography (eight studies). The mean sensitivity for detecting tonic-clonic seizures was .91 (95% confidence interval [CI] = .85–.96, $I^2 = 83.8%$); sensitivity was similar between the wrist-worn (.93) and surface devices (.90). The overall FAR was 2.1/24 h (95% CI = 1.7–2.6, $I^2 = 99.7%$); FAR was higher in wrist-worn (2.5/24 h) than in wearable surface devices (.96/24 h). Three of the 23 studies also detected PNES; the mean sensitivity and FAR from these studies were 62.9% and .79/24 h, respectively. Four studies detected both focal and tonic-clonic seizures, and one study detected focal seizures only; the sensitivities ranged from 31.1% to 93.1% in these studies.

Significance: Reported noninvasive wearable devices had high sensitivity but relatively high FARs in detecting tonic-clonic seizures during limited recording time in a video-EEG setting. Future studies should focus on reducing FAR, detection of other seizure types and PNES, and longer recording in the community.

KEYWORDS

ambulatory/noninvasive device, automated seizure detection, epilepsy/seizures, video/EEG use in epilepsy

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1 | INTRODUCTION

Accurate seizure detection is paramount for optimizing care in patients with epilepsy. The current gold standard practice for evaluation of epilepsy is inpatient video-electroencephalographic (EEG) monitoring (VEM), which is limited due to the high level of expertise and resources required and is impractical to be undertaken over long periods of time.¹ In routine practice, reporting of seizures usually relies on patients or caregivers completing seizure diaries. However, seizure diaries are often unreliable, as patients or caregivers commonly do not recognize their seizures and many conditions can mimic epileptic seizures, such as psychogenic nonepileptic seizures (PNES).^{2,3}

The diagnostic delay in patients with epileptic seizures and PNES carries a significant burden on patients, caregivers, and health services.⁴ Inaccurate knowledge of the seizure type and frequency can lead to inappropriate management and suboptimal seizure control.⁵ The consequences of this include a decreased quality of life, with negative impacts on mental health and increased health care utilization.⁴ In addition, delayed epilepsy diagnosis and treatment may increase the risk of status epilepticus, myocardial infarction, and sudden unexpected death in epilepsy.⁴

Noninvasive wearable devices are expanding rapidly into the health care sector. Devices capable of automated seizure detection are a rapidly growing area of research. These devices typically measure motor and autonomic features of seizures, including three-dimensional (3D) accelerometry, surface electromyographic (EMG) signals, electrodermal activity (EDA), heart rate, and heart rate variability, using either wrist-worn or wearable surface devices. Data collected by the device is analyzed by trained algorithms for automated seizure detection and classification. In addition to providing more accurate seizure recording for review during consultation, wearable devices with real-time detection may alert care providers to help prevent injuries or falls associated with seizures, particularly tonic-clonic seizures (TCS).^{6–9} Automated seizure detection with the use of noninvasive wearable devices therefore has the potential to assist clinicians in the diagnosis and management of patients with both epileptic and nonepileptic seizures in a timely manner.^{7,10,11}

Recently, the International League Against Epilepsy (ILAE) and International Federation of Clinical Neurophysiology (IFCN) established a joint working group to formulate a guideline on the use of wearable devices for automated seizure detection in patients with epilepsy.¹² The working group systematically reviewed the published evidence up to October 2019. However, a meta-analysis of studies in terms of sensitivities and false alarm

Key Points

- Wrist-worn and wearable surface devices measuring 3D accelerometry and/or surface EMG have high sensitivities but relatively high FARs in the automated detection of TCS
- Parameters that are not motion-based such as heart rate and/or heart rate variability need to be explored further through noninvasive and wearable devices to determine their potential in detecting both TCS and focal seizures
- Few studies have assessed wearable devices for detecting PNES
- Future revision of the ILAE-IFCN guideline may consider referring to the overall sensitivity and FAR for TCS as benchmarks for the evaluation of future devices, and greater emphasis on developing devices with lower FAR and ability to detect other seizure types and PNES

rates (FARs) for different seizure types was not undertaken. Furthermore, the guideline did not include studies of devices for detection of PNES.

To fill the knowledge gap, we conducted an updated systematic review of studies investigating the sensitivity and FAR of noninvasive wearable devices for the detection of both epileptic seizures and PNES while subjects underwent inpatient VEM. In addition, we performed a meta-analysis of the sensitivity and FAR of these devices for the detection of TCS.

2 | MATERIALS AND METHODS

We performed the review in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Figure 1). Our systematic review was prospectively registered on PROSPERO (International Prospective Register of Systematic Reviews; registration ID: CRD42019126849).

2.1 | Systematic review

A systemic literature search was conducted up to April 30, 2021. A second search was conducted on November 10, 2021. We searched the databases PubMed and Embase using the terms “automated detection” OR “algorithm” AND “detection” OR “wearable” AND “detection” AND “epilepsy” OR “seizure”. The National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool for

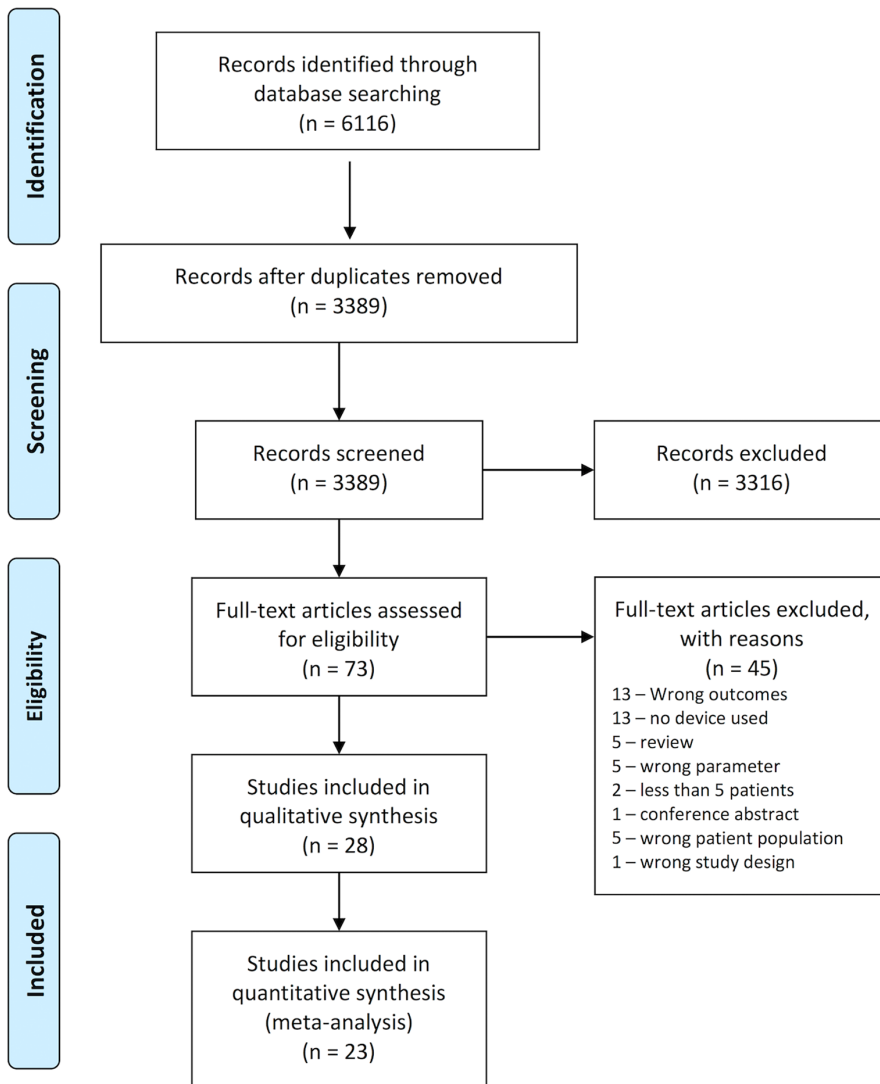


FIGURE 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram showing identification, screening, eligibility, and included studies. Reasons for excluding studies included the use of invasive rather than noninvasive devices, results not being compared to video-electroencephalographic monitoring diagnoses, only pediatric patients being included, and studies involving fewer than five patients.

cross-sectional studies was used for the systematic assessment of risk of bias. The inclusion criteria included (1) evaluation of a wearable and noninvasive device in patients with epilepsy or PNES, with a minimum of five participants; (2) primary measurement of interest for seizure detection was not EEG (EEG can be included as an auxiliary measurement); (3) studies reported the sensitivity for the detection of seizures and FAR (as a measure over time); and (4) devices and algorithms must have been trained and evaluated using noninvasive video-EEG monitoring as the gold standard comparator for the detection of epileptic seizures and PNES. We excluded studies that evaluated nonwearable or invasive devices, or wearable devices that measured EEG only.

The titles and abstracts were independently screened by two reviewers (V.N. and S.S.) using Covidence (Veritas Health Innovation). The full-text records identified during the screening were extracted and reviewed for inclusion. Conflicts were resolved by a third reviewer (P.K.). Assessment of bias were performed by two reviewers (V.N.

and S.S.), where disagreements were resolved by consensus. V.N. extracted the data. The extracted data included (1) device type, (2) parameters measured, (3) seizure type detected, (4) total number of patients, (5) number of patients who experienced a seizure, (6) number of seizures recorded by VEM, (7) number of seizures detected by the device, (8) total recording time (hours), (9) sensitivity, (10) FAR, and (11) method of analysis utilized for the automated detection of seizures. To assess the risk of bias, two reviewers (V.N. and S.S.) graded each paper independently according to the NHLBI quality assessment tool.

2.2 | Meta-analysis

A meta-analysis was performed on the studies detecting TCS. A meta-analysis could not be done on the studies detecting PNES or focal seizures owing to insufficient number of studies. We used random-effects meta-analysis with DerSimonian and Laird method to estimate pooled

sensitivity and FAR for epileptic seizures with motor activity. FAR was presented as the average FAR within 24 h in each study. We subsequently stratified the studies by device type (wrist-worn or wearable surface device) and parameter used (3D accelerometry, surface EMG signals, or EDA).

We performed meta-regression to further explore the sources of heterogeneity. Heterogeneity was assessed using I^2 . We calculated the change in I^2 values to assess the proportion of the observed variability in the observed effect size for a group of experiments explained by device type (wrist-worn vs. surface), number of parameters (unimodal vs. multimodal), and study duration (total and per patient).

We performed Egger test on publication bias for both sensitivity and FAR. Freeman–Tukey double arcsine transformation was used on sensitivity data.

All statistical analyses were performed by using STATA version 16 (StataCorp), with user-written packages "metaprop" for meta-analysis of proportions.

3 | RESULTS

We screened 3389 publications, of which 3316 were excluded as they were not relevant. A further 45 studies were excluded due to the use of invasive devices, no devices used, measuring the wrong or insufficient outcomes, reviews, conference abstract, using only EEG as a parameter, enrolling less than five patients, wrong patient population, and wrong study design. A total of 28 studies met eligibility criteria for inclusion into the systematic review. Eleven of these were published after the publication of the ILAE-IFCN guideline.^{6–8,13–20} Twenty-three of these were eligible for meta-analysis, focusing on the detection of TCS including focal to bilateral TCS (FBTCS) and/or generalized TCS (GTCS). Three of the 28 studies also detected PNES and were included in the descriptive analyses. Four studies detected TCS, focal aware seizures (FAS), and focal impaired awareness seizures (FIAS). One study detected only FAS and FIAS. All studies were included in the descriptive analyses. We performed a quality assessment using the NHLBI tool and rated eight studies as good and 20 studies as fair, as seen in Table S1.

3.1 | Meta-analysis of TCS and clonic seizures

The characteristics of the 23 studies included are summarized in Table 1. Of these, 14 studies utilized a wrist-worn device, measuring 3D accelerometry, with three studies measuring both 3D accelerometry and EDA. One study

utilized a wrist- and ankle-worn device, measuring 3D accelerometry, heart rate, and surface EMG. Eight studies utilized a wearable surface device, measuring surface EMG signals. Two studies used both a wearable and a wrist-worn device, measuring 3D accelerometry and EDA. A total of 1269 patients were enrolled into these 23 studies (median = 58, interquartile range [IQR] = 16–76). The total recording time was 66109.7 h. This corresponded to a median recording time of 52.9 h (IQR = 34.8–73.6) per patient during the period of assessment under VEM.

Of the 1269 patients, 388 (30.6%) experienced seizures during the recording period. The median number of patients who had seizures during VEM was 11. A total of 1248 motor seizures were recorded during VEM (median = 22, IQR = 17–31). Of the 1248 motor seizures, 54 (4.3%) were specified to be FBTCS, 86 (6.9%) were defined as clonic seizures, and the remaining 1108 (88.8%) were GTCS. Of the 1248 motor seizures, 1061 (85%) were detected by the wearable device through automated seizure detection. Breaking this down, 53 (98.1%) FBTCS, 86 (100%) clonic seizures, and 922 (83.2%) GTCS were detected by the wearable and noninvasive device.

The results of the meta-analysis are summarized in Figures 2 and 3, categorized by device type. Figure 2 shows the results of the sensitivities. The mean sensitivity for the detection of FBTCS, TCS, and clonic seizures was .91 (95% confidence interval [CI] = .85–.96, I^2 = 83.8%). The subtotal sensitivity for studies utilizing wrist-worn devices was .93 (95% CI = .85–.99, I^2 = 84%). The subtotal sensitivity for studies utilizing wearable surface devices was .9 (95% CI = .71–1.00, I^2 = 85.3%).

Figure 3 shows the results for the FARs. The total number of false alarms in the 23 studies was 8569. The overall FAR of the 23 studies was 2.1/24 h (95% CI = 1.7–2.6, I^2 = 99.7%). The subtotal FAR of the studies that utilized wrist and ankle worn devices was 2.5/24 h (95% CI = 1.95–3.1, I^2 = 99.8%), and the subtotal FAR of the studies that utilized a wearable surface device was .96/24 h (95% CI = .25–1.66, I^2 = 99.1%).

For the 23 studies detecting TCS, a regression-based Egger test for the sensitivities and FARs yielded p = .58 and p < .001, respectively. A meta-regression was performed to determine whether device type (wrist-worn vs. surface), number of parameters (unimodal vs. multimodal), and recording duration were possible sources of heterogeneity of the reported sensitivities and FARs. For sensitivities, I^2 changes were .005 increase for both device type and number of parameters, .016 reduction for total recording duration, and .021 reduction for recording time per patient. For FAR, I^2 changes were .0001 increase for device type, <.0001 increase for number of parameters, .0004 reduction for total recording duration, and .012 reduction for recording time per patient.

TABLE 1 Characteristics of studies included that assessed noninvasive wearable devices to detect tonic-clonic seizures in video-EEG monitoring units

First author, year published	Device type	Parameters measured	Patients who had seizures	Total patients recruited	VEM: seizures	Device:seizures	False alarm rate, per 24 h	Sensitivity
Beniczky, 2013 ⁶	Wrist-worn	3D accelerometry	20	73	39	35	.2	89.70%
Beniczky, 2018 ¹³	Wearable surface device	sEMG signals	20	71	32	30	.67	93.80%
Conradsen, 2012 ³⁰	Wearable surface device	sEMG signals	2	5	7	4	.07	57.10%
Conradsen, 2012 ³¹	Wearable surface device	One sEMG signal	11	60	22	22	1	100%
De Cooman, 2018 ³²	Wrist-worn and wearable surface device	3D accelerometry, heart rate, sEMG	7	7	22	21	16.8	95.5%
Halford, 2017 ¹⁴	Wearable surface device	sEMG signals	24	149	29	29	1.44	100%
Johansson, 2019 ³³	Wrist-worn	3D accelerometry	856	75	10	10	1.2	100%
Kramer, 2011 ¹⁵	Wrist-worn	3D accelerometry	15	31	22	20	.11	90.90%
Kusmakar, 2017 ¹⁶	Wrist-worn	3D accelerometry	12	12	21	20	.72	95.20%
Kusmakar, 2018 ³⁴	Wrist-worn	3D accelerometry	11	16	8	6	.59 ^a	75%
Kusmakar, 2018 ³⁵	Wrist-worn	3D accelerometry	8	8	9	9	1.1	100%
Kusmakar, 2019 ⁷	Wrist-worn	3D accelerometry	14	79	26	25	.64 ^b	96.20%
Kusmakar, 2016 ³⁶	Wrist-worn	3D accelerometry	11	16	21	21	.73 ^c	100%
Larsen, 2014 ²⁷	Wearable surface device	sEMG signals	6	6	26	14	53.2 ^d	55.80%
Milosevic, 2014 ³⁷	Wrist- and ankle-worn	3D accelerometry, heart rate, sEMG	14	56	117	117	9.36	100%
Milosevic, 2016 ³⁸	Wrist-worn	3D accelerometry, sEMG	7	56	22	20	1	91%
Naganur, 2019 ¹¹	Wrist-worn	3D accelerometry	5	26	23	11	2.43	47.80%
Onorati, 2017 ⁸	Wrist-worn	EDA, 3D accelerometry	22	69	55	52	.19	94.50%
Onorati, 2021 ^{29e}	Wrist-worn and wearable surface device	EDA, 3D accelerometry	18	85	35	32	1.26	92%
Onorati, 2021 ^{29f}	Wrist-worn and wearable surface device	EDA, 3D accelerometry	18	67	31	29	.57	94%
Poh, 2012 ³⁹	Wrist-worn	EDA, 3D accelerometry	7	80	16	15	.74	93.80%
Szabo, 2015 ¹⁷	Wearable surface device	sEMG signals	11	33	21	20	.02	95.20%
Tang, 2021 ⁴⁰	Wrist-worn	EDA, 3D accelerometry	94	94	548	438	13.6	80%

TABLE 1 (Continued)

First author, year published	Device type	Parameters measured	Patients who had seizures	Total patients recruited	VEM: seizures	Device:seizures	False alarm rate, per 24 h	Sensitivity
Van Andel, 2017 ¹⁸	Wrist-worn	3D accelerometry, heart rate	23	95	86	61	6.9	71%

Note: The data used in the studies^{7,11,16,34–36} were collected under the same study protocol over a span of 4 years. Each study focused on a different aspect of convulsive seizure manifestation and used a subset of patients who were eligible for the study. As the data were incrementally collected, some subjects have been used in multiple studies; however, this does not confound the results of our meta-analysis, as each study represents a unique automated convulsive seizure assessment system based on a different approach.

Abbreviations: 3D, three-dimensional; EDA, electrodermal activity; sEMG, surface electromyography; VEM, video-electroencephalographic monitoring.

^a Twenty false alarms over 813 h of recording.

^b One hundred forty-nine false alarms over 5576 h of recording.

^c Twenty-five false alarms over 813 h of recording.

^d One hundred forty-four false alarms over 65 h of recording.

^e Onorati, 2021 results for the pediatric population.

^f Onorati 2021 results for the adult population.

3.2 | TCS and focal seizures: Descriptive analysis

Four studies included the detection of both TCS and focal seizures, using a wearable surface device to measure heart rate and heart rate variability. A total of 189 patients were included in these four studies (median = 35, IQR = 27.25–55). The total recording time was 6187 h. This corresponded to a median recording time of 28.5 h (IQR = 24–42.7) per patient during the period of assessment under VEM. A total of 224 focal seizures and TCS were recorded during VEM (median = 38, IQR = 24–70). Of the 224 seizures, 166 seizures were detected by the wearable and noninvasive device, with an overall sensitivity of 74.1%. The total number of false alarms in the four studies was 259 (median = 46, 95% CI = 37.3–73.6). The overall FAR of the four studies was .04/24 h.

3.3 | Focal seizures: Descriptive analysis

One study included the detection of focal seizures only. A wearable surface device was used, measuring heart rate and heart rate variability. Eleven patients were recruited, and each patient had a seizure during their admission. Forty-seven focal seizures were recorded during VEM, and 33 (70.2%) of these were detected by the device. FAR was reported to be 50.6/24 h. The characteristics of this study detecting focal seizures as well as the four studies detecting TCS and focal seizures can be seen in [Table 2](#).

3.4 | PNES: Descriptive analysis

All three studies that investigated PNES utilized a wrist-worn device, measuring 3D accelerometry. A total of 58 patient participated in these three studies (median = 16, IQR = 16–21). The total recording time was 3394.6 h. This corresponded to a median recording time of 25.4 h (IQR = 22.7–72.7) per patient during the period of assessment under VEM.

Of the 58 patients, 17 (29.3%) patients had seizures during the recording period. The median number of patients who had seizures during their VEM admission was six. A total of 62 seizures were recorded during VEM (median = 21, IQR = 14.5–27). The overall sensitivity of the three studies was 62.9%, as 39 of the 62 seizures were detected by the wearable and noninvasive device through automated seizure detection. The total number of false alarms in the three studies was 112, with an overall FAR of .79/24 h. The characteristics of the studies detecting psychogenic nonepileptic seizures can be seen in [Table 3](#).

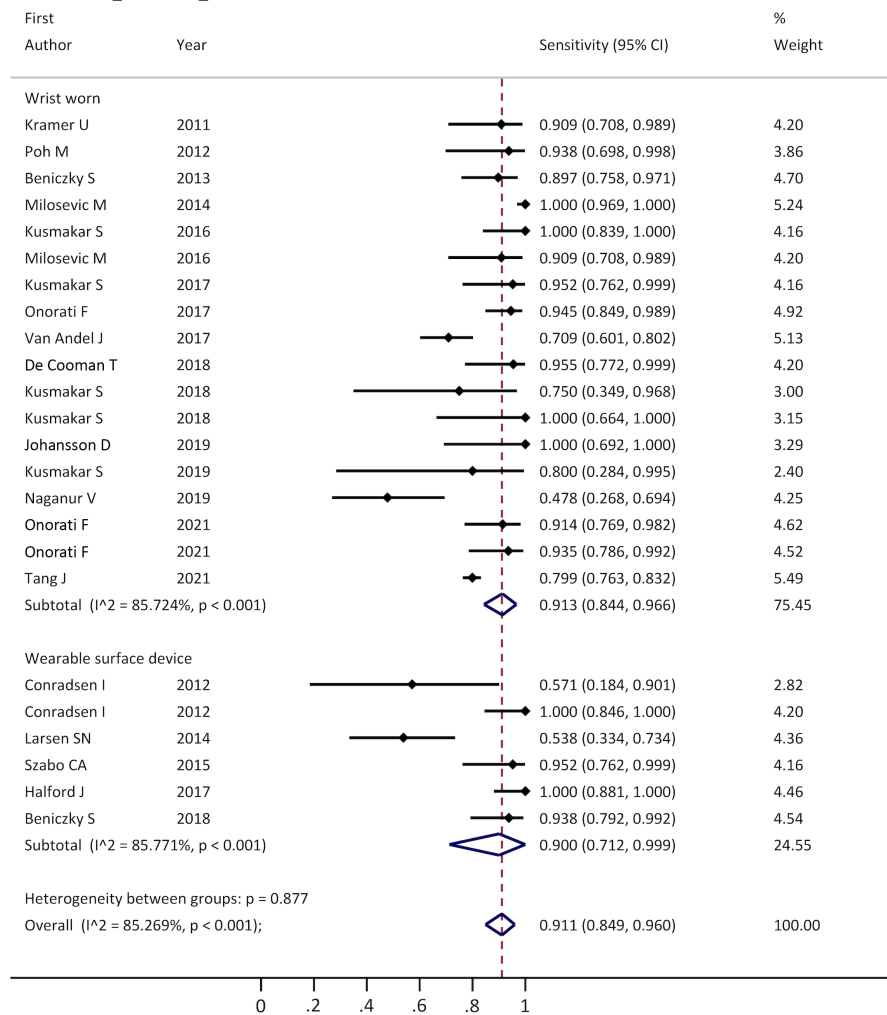


FIGURE 2 Forest plot of sensitivities of noninvasive wearables for detecting tonic-clonic seizures, overall and stratified by device type. The red dotted line indicates the estimated overall sensitivity at .911. The hollow blue diamonds are centered at the estimates of the overall or subgroup sensitivity, and the widths of the diamonds represent the corresponding 95% confidence intervals (CIs).

4 | DISCUSSION

This systematic review and meta-analysis has several important findings that may be considered in future revision of the ILAE-IFCN guideline. First, our meta-analysis quantified the overall reported sensitivity and FAR of wearable devices for detecting TCS. These may be used as benchmarks for evaluation of future devices. Second, the limited evidence suggests that wearable devices may have the potential to detect not only TCS but also PNES. Discussion of the use of these devices for detecting PNES may be considered in a future guideline. Third, given the high sensitivity but also relatively high FAR for detecting TCS, future effort should focus on reducing FAR as a priority. Fourth, our systematic review found only one report that specifically studied focal (non-TCS) seizures, with low sensitivity and high FAR, concurring with the ILAE-IFCN recommendation on the need to improve device performance especially for seizures without generalized convulsions.

For the detection of TCS, 3D accelerometry was the most commonly utilized parameter to identify ictal motor manifestations. The high sensitivity obtained from 3D

accelerometry reflects the utility of this measure for detection of TCS. Although there are multiple methods to analyze 3D accelerometry tracings produced by TCS, we found that the threshold applied to differentiate accelerometry tracings between seizures and normal activity was similar across the 21 studies included in the meta-analysis. All studies empirically used .2 g as the lower threshold to classify seizure activity based on the lower bound (a value that is less than or equal to every element of a set of data) of the collected 3D accelerometry data, where g represents the gravitational force. This leaves very little space for false negatives, as most if not all seizure activity is recorded, and may account for the large proportion of studies reporting high sensitivities. Surface EMG also yielded high sensitivities of up to 100% for TCS. However, more studies are needed to establish whether surface EMG alone, or the combination of surface EMG and 3D accelerometry, is more sensitive and specific for the automated detection of TCS.

3D accelerometry was the only parameter used for the automated detection of PNES in the three studies included in the meta-analysis. This is in line with the previous finding that time frequency analysis of 3D accelerometry data

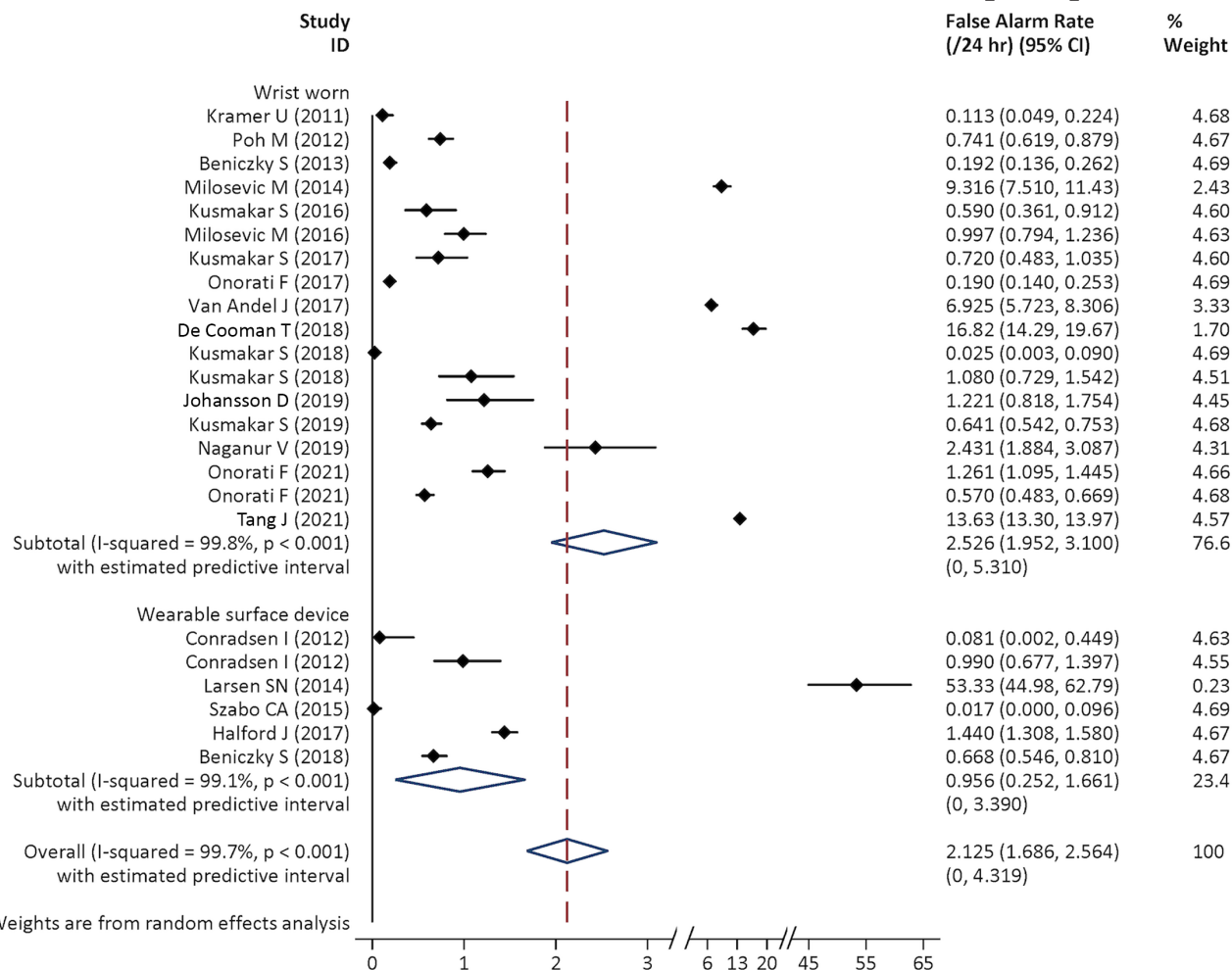


FIGURE 3 Forest plot of false alarm rate of noninvasive wearables for detecting tonic-clonic seizures, overall and stratified by device type. The red dotted line indicates the estimated overall false alarm rate at 2.125/24 h. The hollow blue diamonds are centered at the estimates of the overall or subgroup false alarm rates, and the widths of the diamonds represent the corresponding 95% confidence intervals (CIs).

from a wrist-worn device was effective in differentiating between TCS and PNES.^{10,11} However, due to the wide range of sensitivities these studies demonstrated, the utility of other parameters such as surface EMG, heart rate, and heart rate variability needs to be explored. This will assist in establishing which parameters and thus which algorithms will achieve consistently high sensitivities and low FARs.

There were four studies identified that detected both focal seizures and TCS and one separate study that focused on reporting only focal seizures, all using heart rate and heart rate variability. Although the first four studies demonstrated FARs of <2/24 h, the sensitivities ranged from 39% to 93%.^{20–23} The one study detecting only focal seizures measured the same parameters and demonstrated a much higher FAR that would be impractical for long-term use.¹⁹ The results from these five studies present a mixed picture about the potential of heart rate and heart rate variability in the automated

detection of focal seizures as well as of both focal seizures and TCS.

The ability of noninvasive and wearable devices to detect TCS has shown great promise. However, it is important to note that most of these studies have not reported whether and how many focal seizures the same set of patients were experiencing alongside TCS. It will be helpful if future studies collect and report these data. This will help to emphasize the high number of patients who experience both focal seizures and TCS and therefore the need for a noninvasive and wearable device that has a high sensitivity and low FAR for detecting both focal seizures and TCS separately. We hope to see a change in the significant gap between the evidence we have for wearable devices in detecting TCS and in focal seizures.

Patients with epilepsy generally preferred higher sensitivities over lower FARs.²⁴ The reported sensitivity of >90% from our meta-analysis is in line with the needs

TABLE 2 Characteristics of two studies detecting tonic-clonic and focal seizures and one study detecting focal seizures

First author, year published	Device type	Parameters measured	Type of seizure	Patients who had seizures	Total patients recruited	VEM: seizures	Device: seizures	False alarm rate, per 24 h	Sensitivity
Jeppesen, 2019 ²⁰	Wearable surface device	Heart rate and heart rate variability	TCS and focal seizures	23	100	18 TCS, 108 focal	17 TCS, 97 focal	1	Overall: 93.10% Focal: 89.8% TCS: 94.4%
Jeppesen, 2020 ²¹	Wearable surface device	Heart rate and heart rate variability	TCS and focal seizures	11	19	10 TCS, 12 focal	9 TCS, 10 focal	.9	Overall: 87% Focal: 83.3% TCS: 90%
Hegarty-Craver, 2021 ²²	Wearable surface device	Heart rate and heart rate variability	TCS and focal seizures	25	40	12 TCS, 13 focal	11 TCS, 7 focal	1.03	Overall: 72% Focal: 53.8% TCS: 91.7%
Jahanbekam, 2021 ²³	Wearable surface device	Heart rate and heart rate variability	TCS and focal seizures	30	30	51 ^a	16 ^a	1.2	31.1%
Vandecasteele, 2017 ¹⁹	Wearable surface device	Heart rate and heart rate variability	Focal seizures	11	11	47	33	50.6	70%

^aNumber of TCS and focal seizures not specified.

Abbreviations: TCS, tonic-clonic seizures; VEM, video-electroencephalographic monitoring.

TABLE 3 Characteristics of studies detecting psychogenic nonepileptic seizures

First author, year published	Device type	Parameters measured	Patients who had seizures	Total patients recruited	VEM: seizures	Device: seizures	False alarm rate, per 24 h	Sensitivity
Kusmakar, 2018 ³⁴	Wrist-worn	3D accelerometry	6	16	8	8	.59 ^a	100%
Kusmakar, 2016 ³⁶	Wrist-worn	3D accelerometry	6	16	8	7	.73 ^b	87.50%
Naganur, 2019 ¹¹	Wrist-worn	3D accelerometry	5	26	33	13	2.43	39.30%

^aTwenty false alarms over 813 hours of recording.

^bTwenty five false alarms over 813 hours of recording.

Abbreviations: 3D, three-dimensional; VEM, video-EEG monitoring.

and experiences of patients with epilepsy.^{24–26} However, the FAR of $>2/24$ h did not meet user expectations. A study found that patients with epilepsy desired FARs that ranged 1–2 per month for patients with a lower seizure frequency and 1–2 per week for those with a higher seizure frequency.²⁶ Future studies should focus on reducing the FAR.

A few major caveats need to be acknowledged in the some of the studies included in this systematic review. Some studies restricted analyses of the algorithms developed for automated seizure detection to only patients who had seizures or who displayed ictal tachycardia or bradycardia during their period of recording under VEM.^{20,21} Preselecting these patients introduces bias into these studies and could result in grossly underestimating the true FARs and overestimating the sensitivities of these algorithms and devices. Another major source of bias is the overlap between the testing and training sets of patients to develop and then test the algorithm during retrospective data analyses. Both introduce bias, as these algorithms were not predefined or run real-time and instead were specifically catered to the patients included in these studies, in a VEM setting. Therefore, the results of the algorithm and respective device would not accurately reflect the sensitivity and FAR in a non-VEM setting, such as the patients' home environments, and with an entirely new group of patients.

The regression-based Egger test results found no significant small-study effect or publication bias for the sensitivities of the 23 studies detecting TCS. The results for the FARs of these studies indicate significant small-study effects. This suggests that the results of the smaller studies differ systematically from the results of the remaining larger studies. This may be due to the two studies that had very high FARs (53.2/24 h and 6.9/24 h, respectively) but relatively short total recording person-time (64.8 and 402 h, respectively) compared to the rest of the studies.^{18,27} It may also suggest potential publication bias toward larger studies reporting lower FARs.

There were limitations encountered in this systematic review and meta-analysis. Most studies detecting motor epileptic seizures did not specify whether the TCS were purely tonic-clonic or encompassed focal to bilateral TCS, tonic seizures, or clonic seizures. For this reason, we could not analyze the ability of the parameters or the algorithms to detect specific motor seizure types. There was a high level of heterogeneity in sensitivity and FAR within studies detecting TCS. However, our findings demonstrate that device type, number of parameters, total recording duration, and recording duration per patient did not contribute toward study heterogeneity. The variability in the algorithms used to analyze the data collected by the devices may underlie study heterogeneity. To avoid increasing

heterogeneity further, we did not include studies that utilized invasive EEG measurements in the training dataset.²² As intracranial recordings may detect seizures that occur in deeper structures but are missed on scalp EEG, these studies may be incorporated in future systematic reviews and meta-analyses.²⁸

Wrist-worn or wearable surface devices could continue to be utilized to measure 3D accelerometry and/or surface EMG signals for detecting TCS. 3D accelerometry for PNES detection and heart rate/heart rate variability for focal seizures also showed promising results. However, more well-designed studies that explore parameters that do not rely on motion for detecting focal seizures and PNES are required to confirm these preliminary findings. Using promising, predefined algorithms in studies with larger groups of patients who have not been preselected will decrease heterogeneity and increase the quality of the study. This will further justify the use of the same algorithms in multicenter clinical settings, as demonstrated in recent studies.^{6,8,29} Studies should clearly report the total recording time by the device used, device deficiency time, recording time per patient, total number of false alarms, and FAR, as it will allow for accurate analyses of the device, parameter, and algorithm used. Standardized reporting will facilitate the assessment and establishment of clinical guidelines for the use of noninvasive and wearable devices for the automated detection of both epileptic seizures and PNES.

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AUTHOR CONTRIBUTIONS

Vaidehi Naganur: Served as principal investigator, drafted and revised the manuscript for intellectual content, reviewed clinical data, analyzed data, contributed to the statistical analysis, contributed to the interpretation of data, and prepared the tables. Shobi Sivathamboo: Contributed to the acquisition and interpretation of data, reviewed clinical data, and revised the manuscript for intellectual content. Zhibin Chen: Contributed to the statistical analysis and interpretation of data, prepared the figures, and critically revised the manuscript for intellectual content. Shitanshu Kusmakar: Contributed to the acquisition of data and revised the manuscript for intellectual content. Ana Antonic-Baker: Critically revised the manuscript for intellectual content. Terence J. O'Brien: Provided scientific direction and critical revision of the manuscript for intellectual content. Patrick Kwan: Served as principal investigator, provided scientific direction, reviewed clinical data, contributed to the interpretation of data, and critically revised the manuscript for intellectual content.

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