# Multimodal nocturnal seizure detection in children with epilepsy

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RESEARCH ARTICLE

# Multimodal nocturnal seizure detection in children with epilepsy: A prospective, multicenter, long-term, in-home trial

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## Abstract

**Objective:** There is a pressing need for reliable automated seizure detection in epilepsy care. Performance evidence on ambulatory non-electroencephalography-based seizure detection devices is low, and evidence on their effect on caregiver's stress, sleep, and quality of life (QoL) is still lacking. We aimed to determine the performance of NightWatch, a wearable nocturnal seizure detection device, in children with epilepsy in the family home setting and to assess its impact on caregiver burden.

**Methods:** We conducted a phase 4, multicenter, prospective, video-controlled, in-home NightWatch implementation study (NCT03909984). We included children aged 4–16 years, with ≥1 weekly nocturnal major motor seizure, living at home. We compared a 2-month baseline period with a 2-month NightWatch intervention. The primary outcome was the detection performance of NightWatch for major motor seizures (focal to bilateral or generalized tonic–clonic [TC] seizures, focal to bilateral or generalized tonic seizures lasting >30 s, hyperkinetic seizures, and a remainder category of focal to bilateral or generalized clonic seizures and "TC-like" seizures). Secondary outcomes included caregivers' stress (Caregiver Strain Index [CSI]), sleep (Pittsburgh Quality of Sleep Index), and QoL (EuroQol five-dimension five-level scale).

**Results:** We included 53 children (55% male, mean age = 9.7 ± 3.6 years, 68% learning disability) and analyzed 2310 nights (28 173 h), including 552 major motor seizures. Nineteen participants did not experience any episode of interest during the trial. The median detection sensitivity per participant was 100% (range = 46%–100%), and the median individual false alarm rate was .04 per hour (range = 0–.53). Caregiver's stress decreased significantly (mean total CSI

*Contribution of authors and coinvestigators of the Dutch TeleEpilepsy Consortium are listed in Appendix 1 and 2.

score = 8.0 vs. 7.1, $p = .032$), whereas caregiver's sleep and QoL did not change significantly during the trial.

**Significance:** The NightWatch system demonstrated high sensitivity for detecting nocturnal major motor seizures in children in a family home setting and reduced caregiver stress.

**KEYWORDS**

caregiver, NightWatch, seizure detection device, SUDEP, wearable

## 1 | INTRODUCTION

There is a pressing need for reliable automated seizure detection in epilepsy care.[1,2] Seizures are unpredictable and may cause life-threatening situations through injury, status epilepticus, and sudden unexpected death in epilepsy.[3] Convulsive seizures (i.e., focal to bilateral or generalized tonic–clonic seizures) have the highest mortality risk, particularly among those with nocturnal convulsions sleeping alone.[4–6] This suggests that having someone providing essential support following a convulsion can be lifesaving. Seizure detection devices (SDDs) are developed to alert caregivers in case of potentially dangerous seizures. This enables timely intervention, which may help reduce seizure-related risks.[3,5,7] Accurate detection may also empower people with epilepsy, by allowing them to sleep alone and relieving the burden of seizure vigilance for their caregivers.[4,8,9] Evidence on the effect of an SDD on caregiver's stress, sleep, and quality of life (QoL), however, is still lacking.[8] SDDs also have the potential to improve seizure documentation, as seizure diaries are known to be unreliable.[10]

Various ambulatory non-electroencephalography (EEG)-based SDDs are available, but their performance evidence is low.[1,11] Many devices lack external validation. Almost all SDD studies were performed in a clinical setting with short follow-ups and lacking essential user feedback.[11–13] Long-term, home-based trials addressing aspects related to usability (classified as phase 4 by recent guidelines) are therefore mandatory to guide SDD implementation.[12]

In a prospective phase 4 study, we demonstrated the good performance of a wearable multimodal device (NightWatch) for the detection of nocturnal major motor seizures (median sensitivity of 86% per person and median false alarm rate [FAR] of .25 per night).[14] Subsequent validation of NightWatch in a pediatric cohort revealed higher FARs, with rates amounting to .2 per hour.[15] To improve performance, we adapted the algorithm and found that it could reduce FAR to levels close to that of adults while maintaining high sensitivity.[15]

**Key points**

- Performance evidence on wearable seizure detection devices is low, and evidence on its impact on caregiver burden is still lacking
- We conducted a phase 4, multicenter, prospective, video-controlled, in-home NightWatch implementation study on 53 children with frequent nocturnal seizures
- This trial provides class II evidence that NightWatch accurately detects nocturnal major motor seizures in children with frequent nocturnal seizures
- Median sensitivity per participant for the detection of major motor seizures was 100%, with a median individual false alarm rate of .04/h
- Caregivers reported significantly lower stress scores during NightWatch use, whereas caregiver's sleep and quality of life did not change

We, therefore, set up a long-term, home-based phase 4 study to prospectively validate the performance of the adjusted NightWatch algorithm in children with severe epilepsy while monitoring the effect on caregiver's stress, sleep, and QoL.

## 2 | MATERIALS AND METHODS

### 2.1 | Standard protocol approvals, registrations, and patient consents

We conducted a multicenter, prospective, long-term, in-home implementation study (the PROMISE trial, short for Promoting the Implementation of SDDs in Epilepsy Care). We collected data between August 2018 and August 2020. The trial was registered at Clinicaltrials.gov (identifier: NCT03909984) and approved by the research ethics committee of University Medical Center Utrecht

in the Netherlands (NL62995.041.17). The child's legal representatives provided written informed consent (in most cases, both biological parents) as did participants ≥12 years old when capable.

## 2.2 | Participants

We recruited children with epilepsy aged 4–16 years from three tertiary epilepsy centers in the Netherlands, namely, Stichting Epilepsie Instellingen Nederland (SEIN), University Medical Center Utrecht (UMCU), and Academic Center for Epileptology Kempenhaeghe (KH), with at least one weekly nocturnal major motor seizure event, and living at home. Seizure frequency was based on clinical history and checked with the caregivers before signing informed consent and again before the start of the intervention. We excluded children with comorbid conditions that could lead to high false alarm rates, such as movement disorders, cardiac arrhythmias, or wearing a pacemaker. We originally defined skin pigmentation as an exclusion criterion, as we assumed that the light-based plethysmography (PPG) signal would be less reliable through pigmented skin. After validating NightWatch on pigmented skin, we discovered that the PPG method worked reliably on all types of skin pigmentation, so we abandoned this criterion after 42 inclusions.

## 2.3 | Seizure detection algorithm

The multimodal algorithm of NightWatch, based on photoplethysmography and accelerometry (ACC) data, is described in more detail in previous publications.[14,15] Heart rate (HR) values are determined and updated every second based on a 5-min average of past individual peak-to-peak intervals. The accelerometry sensor measures motion and position, where position represents the angle of the sensor with respect to the gravity vector. Rhythmic movements are identified by counting the number of zero crossings for each axis per second. The plethysmographic waveform is evaluated to estimate the signal quality, and the multimodal algorithm is applied if the signal quality is adequate (>80%). If HR is unreliable, then only the ACC algorithm is used for detection. When both modalities are active, they work in parallel. Several situations may trigger an alarm: increasing HR slope when it exceeds an absolute or relative threshold (compared to baseline), and sustained rhythmic movements. We applied the adjusted algorithm developed in the previous pediatric trial.[15]

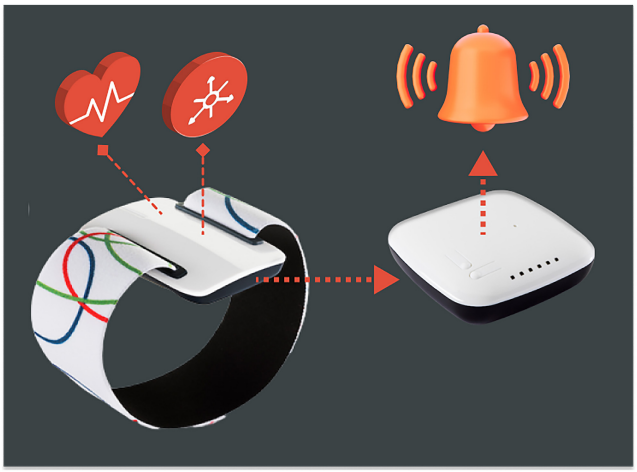

**FIGURE 1** NightWatch. The NightWatch bracelet contains a photoplethysmographic heart rate module and a three-dimensional accelerometer. When a specific heart rate or movement threshold or pattern is detected, the algorithm triggers an alarm so caregivers can intervene. The signals or alarms are transmitted by Digital Enhanced Cordless Telecommunications Ultra Low Energy (DECT ULE) directly to the base, which may be connected to a local area network for further transmission of the data and alarms. DECT ULE is a wireless communication standard with greater range, reliability, and safety than Bluetooth or Wifi. Figure published with permission from Livassured.

## 2.4 | Intervention

The intervention consisted of a 2-month baseline period without any SDD (usual care) followed by 2 months of NightWatch usage at home (intervention; Figure 1). The NightWatch base station (generating alarms) was installed in the participant's home, with a video camera and audio sensor attached to a pole and directed to the child's bed. Data were generated only during the time NightWatch was worn. We asked participants to wear the NightWatch every night during the intervention period. All data were transmitted to a laptop in the child's room and stored for analysis. We asked the caregivers to keep a seizure diary during the intervention. After the intervention, caregivers, if they wanted to continue using the device, could purchase NightWatch for €750 (half of the regular price).

## 2.5 | Study outcomes

The primary outcome measure was the individual performance of NightWatch to detect major motor seizures, including sensitivity, positive predictive value (PPV), F1 performance score, and FAR per hour. Secondary outcomes included the quality of the signal data, the impact of NightWatch on caregivers' stress, sleep, and QoL, and their expectations and experiences with NightWatch.

## 2.6 | Questionnaires

We used validated questionnaires to examine caregivers' stress (Caregiver Strain Index [CSI]), sleep (Pittsburgh Quality of Sleep Index [PQSI]), and QoL (EuroQol five-dimension five-level scale [EQ-5D-5L]) during the baseline period and following the intervention (Supplementary Material). We asked one caregiver per participant to complete the online questionnaires at the start of the study (T0), after the baseline period (T1), and after NightWatch usage (T2; Figure 2). The CSI includes 13 items assessing the burden of care/stress, each carrying 1 point, with a score of 7 indicating a high-stress level. The PQSI consists of seven components, each with a range of 0–3 points, to assess sleep quality, with a global PSQI score varying from 0 (no difficulty sleeping) to 21 (severe difficulties sleeping). The first part of the EQ-5D-5L combines five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension can be scored on five levels ranging from "no problems" to "extreme problems." In the second part, respondents must indicate how good or bad their health is at the given moment on a scale from 0 (the worst health you can imagine) to 100 (the best health you can imagine). Additionally, we developed a questionnaire with eight items assessing caregiver's expectations and 11 items on experiences with NightWatch using a 5-point Likert scale.

## 2.7 | Sample size

We estimated a sample size of 384 major motor seizures to obtain acceptable confidence limits (precision = 4%) assuming a conservative sensitivity of 80%.[15] We aimed to include 60 participants with ≥1 major nocturnal motor seizure per week. We expected a 2-month intervention period (9 weeks) with a dropout rate < 25% to yield at least 405 significant seizures.

## 2.8 | Data analysis

### 2.8.1 | Data selection

Only full night recordings with complete and sufficient video data were included to analyze the sensor performance. Records were excluded when >75% of data transmission from NightWatch to the base station was lost, when computer storage issues had appeared, or when the nightly average signal quality of the HR measurements was <75%. The first two situations impeded the analysis of trial data but did not impact NightWatch performance at home. Poor quality of the HR data (e.g., if the sensor is not worn correctly) could potentially affect performance. The device itself constantly monitors the quality of the HR signal. If the HR data quality is insufficient for seizure detection, the NightWatch generates a distinct "technical" alarm to alert the caregiver to reposition the sensor.

### 2.8.2 | Annotation process

Although video-EEG monitoring is considered the gold standard for diagnosing epileptic seizures, implementing continuous EEG was not feasible in this long-term home-based trial. We therefore made a pragmatic choice to apply video recordings without EEG as our reference standard, focusing on motor signs for epilepsy classification. Video images were annotated with a specifically developed computer program. Trained trial nurses screened the video of 5% of all nights for missed seizures; every video was screened by one nurse. We also retrospectively analyzed video tracings with a previously validated automated video-based seizure detection algorithm.[16–18] Trial nurses annotated all events (generated NightWatch alarms, video alarms, and caregivers' seizure diary) using the video recordings while blinded for alarm type and NightWatch sensor data (HR and movement). We considered the following seizure types as clinically urgent and classified them as "major motor seizures":

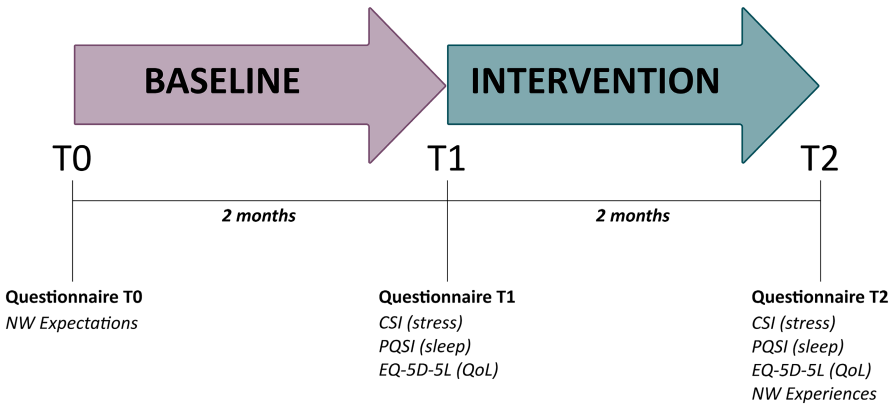


**FIGURE 2** Study flow including a 2-month baseline period with usual care followed by a 2-month intervention period with NightWatch at home, and the different questionnaires at study points T0, T1, and T2. CSI, Caregiver Strain Index; EQ-5D-5L, EuroQol five-dimension five-level scale; NW, NightWatch; PQSI, Pittsburgh Quality of Sleep Index; QoL, quality of life.

(1) generalized or focal to bilateral onset tonic–clonic seizures (TCs); (2) focal to bilateral or generalized onset tonic seizures lasting >30 s (T > 30); (3) focal onset hyperkinetic (HK) seizures; and (4) a remainder category of other major (OM) motor seizures. Category 4 includes focal onset clonic, generalized onset, and "TC-like" seizures, the latter defined as bilateral movements without classical TC pattern (i.e., no tonic phase, pronounced asymmetry, short duration, or quick recovery). All other seizures that did not meet these criteria were classified as "non-major motor seizures" and, if detected, as false positives. In case of discrepancies (when the recorded night was annotated by one nurse, but screened by another) or doubt, the trial nurses consulted one of the principal investigators (R.D.T., R.H.C.L.) for a final decision. The principal investigators double-checked a random sample of 5% of the annotations.

An event was considered true positive when an alarm was generated within 3 min before or 3 min after the annotated start of a seizure of interest. Other detections within a 3-min interval were scored as one event; this rule was applied for true and false positives.

## 2.9 | Performance

We estimated performance (sensitivity, PPV, FAR, F1) per subject and the median individual performance on the population level. We excluded participants who did not have seizures of interest during the intervention period from the sensitivity, F1, and PPV analysis, but included these cases in the FAR analysis. The following formula estimated the F1 score for detection performance accuracy: $F_1$ score = 2 * (PPV × sensitivity)/(PPV + sensitivity). We performed post hoc analyses to identify clinical determinants of NightWatch performance, including age, sex, presence of learning disability, and distribution of seizure types (% TCs of the total amount of major motor seizures).

## 2.10 | Statistics

Data are presented as mean ± SD or median and range where appropriate. We used paired *t*-tests to analyze differences between secondary study outcomes at T1 and T2, and Mann–Whitney *U*-tests (sex, presence of learning disability), and Spearman rank correlation (age, % TCs) to identify clinical determinants of NightWatch performance.

# 3 | RESULTS

We identified 85 eligible children, and 60 caregivers consented to participate in the trial. Seven withdrew before the intervention started due to personal situations ($n = 4$) or seizure freedom ($n = 3$). Of the remaining 53 participants (38 from SEIN, 10 from UMCU, and five from KH) who completed the intervention, two were excluded from the performance analysis due to lack of video recordings or recordings of insufficient video quality (e.g., wrong position of the camera; Figure 3).

Table 1 presents the demographics of the 53 children (55% male, mean age = 9.7 ± 3.6 years, 68% learning disability). The questionnaires were completed by 51 biological parents and two legal representatives. We analyzed 2310 nights (28 173 h of data, median = 611 h per participant [range = 26–1298 h]), including 552 major motor seizures (median number of seizures per participant = 2 [range = 0–147]). In total, 1402 h (5%) of all recorded nights were screened, ranging from half a night to four full nights per participant. All participants had a history of at least one nocturnal major motor seizure per week upon inclusion, but 19 did not have such a seizure during the intervention period. We noted medication adjustments in 18 children, resulting in higher doses of antiseizure medication in 15 children and lower doses in three.

## 3.1 | Primary outcome: NightWatch performance

Four hundred ninety-two of 552 major motor seizures were correctly detected by NightWatch (overall seizure sensitivity = 89%). Median sensitivity per participant for the detection of major motor seizures was 100% (range = 46%–100%, mean = 90% [95% confidence interval (CI) = 84%–95%]; Table 2). We found 204 TC (37%), 30 T > 30 (5%), 48 HK (9%), and 270 OM (49%) seizures during the intervention. NightWatch performance for these different major motor seizure types was (median sensitivity per participant [range], overall seizure sensitivity): TC (100% [71%–100%], 94%), T > 30 (100% [0%–100%], 53%), HK (75% [0%–100%], 83%), OM (100% [0%–100%], 91%; Figure 4).

The median false negative alarm rate for NightWatch per participant per hour, representing the seizures missed, was 0 (range = .00–.04, mean = .002 [95% CI = .0001–.005]). NightWatch missed 60 episodes (25 OM, 14 T > 30, 13 TC, eight HK). These seizures were identified by the video algorithm ($n = 40$, 67%), screening ($n = 13$, 22%), or the caregiver ($n = 10$, 17%). The video algorithm and the caregivers detected three missed seizures together.

We identified 1642 false alarms, including 469 non-major motor seizures (29%). Median FAR per subject per hour amounted to .04 (range = .00–.53, mean = .07 [95% CI = .04–.10]). Median PPV per participant was 24% (range = 3%–94%, mean = 31% [95% CI = 23%–40%]). The

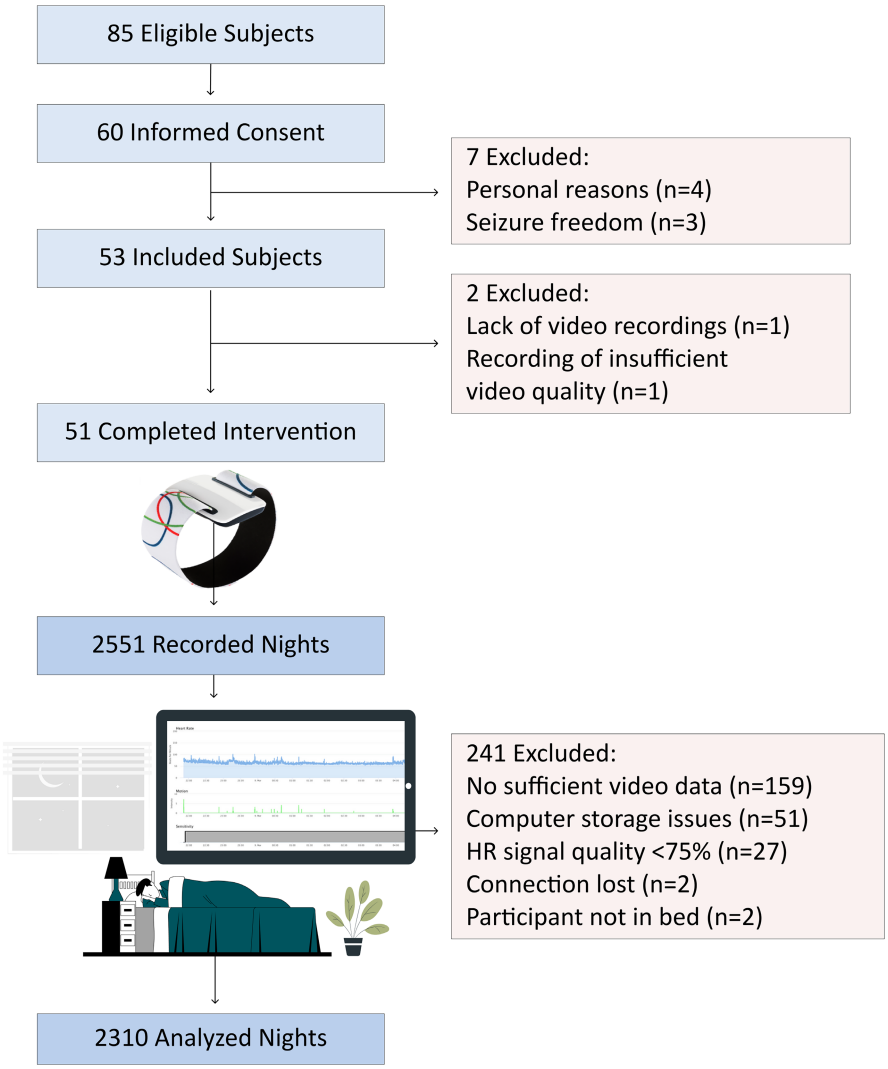


**FIGURE 3** Study and data flow diagram, presenting overview of eligible subjects, included and excluded participants, and selected data with reasons for exclusion. HR, heart rate.

overall F1 score amounted to .47, with a median score of .38 per participant (range = .05–.97).

We analyzed the determinants for true positive and false positive alarms. Because multiple causes can trigger one alarm, the sum of the individual numbers and percentages is more than the total amount. Of the 492 true positive alarms, 424 (86%) were triggered by accelerometry, 114 (23%) by rapid HR increase, and 90 (18%) by tachycardia. The false positive alarms were also mainly triggered by accelerometry ($n = 1086$, 66%), followed by rapid HR increase ($n = 592$, 36%) and tachycardia ($n = 103$, 6%). A minority of alarms (27% of true positive and 8% of false positive alarms) were triggered by more than one signal.

### 3.1.1 | Post hoc analyses

Our post hoc analyses revealed that children with learning disabilities were more like to exhibit higher FAR (.05/h) than those without (.02/h, $p = .001$), whereas we found no contrasts in sensitivity between both groups. The other factors (age, sex, proportion of TCs) did not impact NightWatch performance.

## 3.2 | Secondary outcomes

### 3.2.1 | Quality of signal data

Two hundred forty-one of 2551 recorded nights were excluded from analysis due to insufficient video data ($n = 159$), computer storage issues ($n = 51$), inadequate HR signal quality ($n = 27$), lost connection with the base station ($n = 2$), or because the child was no longer in bed ($n = 2$; Figure 3). In the 27 excluded nights because of poor HR data, caregivers did not respond to the technical alarm to reposition the sensor. No data loss due to insufficient HR data was seen in cases in which NightWatch was used correctly. The accelerometry sensor provided sufficient quality signal throughout the entire study.

**TABLE 1** Summary of participants' demographics.

| Demographic data, $n = 53$ | $n$ (%) | Mean | Range |
|---|---|---|---|
| Sex | | | |
| Male | 29 (55%) | | |
| Female | 24 (45%) | | |
| Age, years | | 9.7 ± 3.6 | 4–16 |
| Learning disability | | | |
| Yes | 36 (68%) | | |
| No | 17 (32%) | | |
| Epilepsy etiology | | | |
| Structural | 13 (25%) | | |
| Genetic | 20 (38%) | | |
| Infectious | 1 (1%) | | |
| Metabolic | 0 (0%) | | |
| Immune | 0 (0%) | | |
| Unknown | 19 (36%) | | |
| Epilepsy treatment | | | |
| ASMs, $n$ | | 2.5 ± 1.2 | 0–6 |
| Ketogenic diet | 6 | | |
| VNS | 2 | | |

Abbreviations: ASM, antiseizure medication; VNS, vagal nerve stimulation.

### 3.2.2 | Adverse effects

Eight children developed mild, reversible skin irritation during the first trial period from the NightWatch device. We advised alternating recording sites (e.g., left and right arm), and in three cases we advised wearing the NightWatch around the lower leg because of skin irritation on both arms. The manufacturer developed a laser-cut kinesiology tape to stick on the inner side of NightWatch to soften skin contact. With the use of the tape, no further skin irritation was reported.

### 3.2.3 | Video detection algorithm

The video detection algorithm was initially designed to detect convulsive seizures and showed a median sensitivity of 44% (range = 0%–100%, mean = 42% [95% CI = 25%–59%]) for this type of seizure. For the detection of all major motor seizures, the median sensitivity per participant was 30% (range = 0%–100%, mean = 29% [95% CI = 19%–39%]), with a median FAR per hour of .05 (range = .00–1.44, mean = .13 [95% CI = .06–.20]). We performed a post hoc investigation to understand why scores were lower than previously reported[16,17] and noticed that the video recordings had an unstable frame rate, which may hinder the performance of the detection algorithm. In a prospective setting this problem would never emerge, but during retrospective analysis we discovered that it is very important that the video recordings are stored with a fixed frame rate, because the algorithm has to detect specific frequencies in movement. An unstable frame rate disrupts these frequencies and thereby influences the algorithm's performance.

### 3.2.4 | Questionnaires

The online questionnaires on caregiver's stress, sleep quality, and QoL were fully completed by 25 (47%) and partly completed by 17 (32%) caregivers, and the questionnaires on caregiver's expectations and experiences were fully completed by respectively 25 (47%) and 22 (42%) caregivers.

### 3.2.5 | Caregiver's stress, sleep, and QoL

The mean CSI score was >7 points throughout the study, indicating high levels of caregiver stress. During the intervention period there was a small but significant decrease in caregiver stress (mean total CSI score = 8.0 vs. 7.1, $p = .032$). The median difference in stress score was −1, and nine caregivers indicated that ≥2 items (of 13) on the CSI were no longer difficult for them to handle. Caregiver sleep quality and QoL did not significantly change following NightWatch usage (mean total PSQI score = 7.9 vs. 6.7, $p = .117$; mean total EQ-5D-5L score = .9 vs. .9).

### 3.2.6 | Caregiver's expectations and experiences

Table S1 summarizes the results of the online questionnaires on caregivers' expectations and experiences with NightWatch. Trial participants had high expectations of the NightWatch before the start of the trial. Nearly all users reported that NightWatch was easy to use. Postintervention, caregivers were asked if they decided to keep using NightWatch (which meant they needed to buy it); 32% of caregivers ($n = 7$) (strongly) agreed, 18% ($n = 4$) were neutral, and 50% ($n = 11$) disagreed. Reasons to differ included a decrease in seizure frequency during the trial ($n = 5$); high FAR ($n = 3$), too expensive to purchase ($n = 2$), and skin irritation ($n = 1$).

## 4 | DISCUSSION

This phase 4 SDD trial provides class II evidence that NightWatch accurately detects nocturnal major motor

**TABLE 2** Characteristics of included subjects and individual results.

| | Characteristics, child | | | | | Recorded data | | |
|---|---|---|---|---|---|---|---|---|
| Subject | Sex | Age, years | Epilepsy etiology | Learning disabilities, yes/no) | ASMs, *n* | Recorded nights, *n* | Major motor seizures, *n* | Type of seizures |
| 1 | F | 8 | Genetic | No | 3 | 63 | 9 | HK |
| 2 | M | 7 | Structural | No | 3 | 43 | 0 | — |
| 3 | F | 14 | Unknown | No | 2 | 62 | 0 | — |
| 4 | M | 15 | Unknown | Yes | 3 | 38 | 4 | TC |
| 5 | F | 8 | Structural | Yes | 3 | 61 | 4 | TC, T > 30 |
| 6 | F | 6 | Unknown | No | 2 | 65 | 0 | — |
| 7 | M | 16 | Genetic | Yes | 2 | 51 | 2 | HK, OM |
| 8 | M | 9 | Structural | Yes | 3 | 30 | 0 | — |
| 9 | M | 14 | Unknown | Yes | 5 | 14 | 13 | TC, T > 30, OM |
| 10 | M | 14 | Genetic | Yes | 2 | 56 | 147 | TC, T > 30, HK, OM |
| 11 | F | 15 | Genetic | Yes | 2 | 14 | 5 | HK, OM |
| 12 | M | 6 | Genetic | Yes | 4 | 60 | 22 | TC, T > 30, OM |
| 13 | F | 13 | Structural | Yes | 3 | 70 | 0 | — |
| 14 | F | 10 | Structural | Yes | 1 | 56 | 24 | TC, T > 30, OM |
| 15 | M | 5 | Unknown | Yes | 1 | Excl[b] | — | — |
| 16 | F | 12 | Genetic | Yes | 3 | 25 | 0 | — |
| 17 | M | 11 | Structural | No | 2 | 32 | 7 | OM |
| 18 | F | 16 | Genetic | Yes | 1 | 18 | 0 | — |
| 19 | M | 10 | Genetic | No | 3 | 59 | 0 | — |
| 20 | F | 5 | Genetic | Yes | 2 | 81 | 3 | OM |
| 21 | F | 12 | Unknown | Yes | 2 | 20 | 0 | — |
| 22 | F | 15 | Genetic | Yes | 4 | 56 | 6 | TC, T > 30, OM |
| 23 | F | 13 | Unknown | Yes | 3 | 45 | 17 | TC, HK, OM |
| 24 | F | 15 | Unknown | No | 2 | 31 | 17 | HK |
| 25 | F | 10 | Genetic | Yes | 2 | 41 | 10 | TC, OM |
| 26 | M | 4 | Genetic | No | 2 | 30 | 1 | OM |
| 27 | M | 8 | Genetic | Yes | 6 | 16 | 0 | — |
| 28 | M | 9 | Genetic | Yes | 4 | 57 | 86 | OM |
| 29 | M | 12 | Structural | Yes | 3 | 54 | 70 | TC, T > 30, HK, OM |
| 30 | M | 4 | Genetic | Yes | 3 | 80 | 0 | — |
| 31 | F | 7 | Genetic | Yes | 1 | 54 | 1 | TC |
| 32 | M | 14 | Unknown | Yes | 0 | 16 | 6 | TC, T > 30 |
| 33 | M | 10 | Unknown | No | 2 | 30 | 4 | TC, OM |
| 34 | F | 8 | Genetic | Yes | 2 | 27 | 12 | TC, T > 30, OM |
| 35 | M | 13 | Unknown | No | 2 | 18 | 0 | — |
| 36 | M | 8 | Structural | No | 2 | 2 | 2 | TC |
| 37 | M | 14 | Unknown | Yes | 3 | 59 | 35 | TC, OM |
| 38 | M | 5 | Infectious | Yes | 2 | Excl[b] | — | — |
| 39 | F | 5 | Structural | Yes | 5 | 59 | 0 | — |
| 40 | F | 12 | Unknown | No | 3 | 57 | 2 | T > 30, OM |

| Primary outcome: NightWatch performance[a] | | | Secondary outcomes: Parental stress, sleep, and QoL | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sens, % | PPV, % | FAR/h | CSI score T1 | CSI score T2 | PSQI score T1 | PSQI score T2 | QoL score T1 | QoL score T2 |
| 100 | 69 | .01 | 11 | 9 | 9 | 3 | .74 | .80 |
| — | — | .01 | 4 | 2 | 4 | 2 | 1 | 1 |
| — | — | .02 | 4 | 4 | 6 | 6 | 1 | 1 |
| 100 | 21 | .03 | 11 | 10 | 10 | 13 | .86 | .77 |
| 100 | 11 | .04 | 4 | na | 8 | na | .90 | na |
| — | — | .02 | 5 | 2 | 7 | 8 | .82 | .91 |
| 50 | 17 | .01 | 1 | 1 | 2 | 3 | 1 | 1 |
| — | — | .17 | 9 | 7 | 5 | 8 | 1 | 1 |
| 46 | 35 | .06 | 12 | 12 | 11 | 6 | .87 | .87 |
| 80 | 75 | .05 | 10 | 8 | 14 | 12 | .84 | .86 |
| 80 | 29 | .06 | na | na | na | na | na | na |
| 100 | 37 | .05 | 12 | 12 | 8 | 8 | .89 | .89 |
| — | — | 0 | na | na | na | na | na | na |
| 100 | 49 | .03 | 8 | 7 | 8 | 4 | .61 | .92 |
| — | — | — | 12 | 11 | 9 | 10 | 1 | .93 |
| — | — | .19 | 5 | 7 | 10 | 11 | .91 | .93 |
| 86 | 15 | .11 | 7 | 9 | 8 | 7 | na | na |
| — | — | .53 | 4 | 6 | 6 | 4 | 1 | 1 |
| — | — | .05 | na | na | na | na | na | na |
| 100 | 4 | .06 | na | na | na | na | na | na |
| — | — | 0 | na | na | na | na | na | na |
| 100 | 13 | .06 | 5 | 5 | 8 | 9 | .83 | .96 |
| 94 | 17 | .14 | 12 | 9 | 11 | 13 | .75 | .65 |
| 100 | 94 | 0 | na | na | na | na | na | na |
| 100 | 36 | .03 | 10 | na | 4 | na | .85 | na |
| 100 | 9 | .02 | 9 | 8 | 0 | 4 | na | na |
| — | — | .25 | na | na | na | na | na | na |
| 99 | 26 | .34 | 8 | 9 | 8 | 8 | 1 | 1 |
| 87 | 75 | .03 | 9 | 11 | 7 | 6 | .9 | .83 |
| — | — | .18 | 11 | na | 10 | na | 1 | na |
| 100 | 3 | .05 | 9 | 9 | 10 | 7 | .93 | .83 |
| 83 | 10 | .24 | 10 | 9 | 10 | 4 | 1 | 1 |
| 100 | 24 | .02 | na | na | na | na | na | na |
| 100 | 23 | .11 | na | na | 11 | na | na | na |
| — | — | .01 | na | na | na | na | na | na |
| 100 | 67 | .04 | 8 | na | 5 | na | 1 | na |
| 100 | 51 | .04 | 9 | 5 | 4 | 5 | 1 | 1 |
| — | — | — | na | na | na | na | na | na |
| — | — | .02 | 10 | 9 | 7 | 2 | .93 | .93 |
| 50 | 25 | 0 | 0 | 1 | 6 | 4 | 1 | 1 |

**TABLE 2** (Continued)

| | Characteristics, child | | | | | Recorded data | | |
|---|---|---|---|---|---|---|---|---|
| Subject | Sex | Age, years | Epilepsy etiology | Learning disabilities, yes/no) | ASMs, *n* | Recorded nights, *n* | Major motor seizures, *n* | Type of seizures |
| 41 | M | 4 | Unknown | No | 3 | 53 | 0 | — |
| 42 | F | 9 | Structural | Yes | 2 | 17 | 0 | — |
| 43 | F | 8 | Structural | Yes | 3 | 42 | 0 | — |
| 44 | M | 7 | Unknown | Yes | 2 | 55 | 0 | — |
| 45 | M | 4 | Genetic | Yes | 1 | 58 | 4 | OM |
| 46 | M | 12 | Genetic | Yes | 5 | 95 | 1 | OM |
| 47 | M | 10 | Structural | No | 1 | 60 | 0 | — |
| 48 | F | 6 | Structural | Yes | 1 | 47 | 0 | — |
| 49 | M | 12 | Unknown | Yes | 2 | 4 | 2 | TC, T > 30 |
| 50 | F | 7 | Unknown | No | 3 | 27 | 9 | TC, OM |
| 51 | M | 9 | Genetic | Yes | 4 | 38 | 10 | TC, OM |
| 52 | F | 10 | Unknown | No | 1 | 60 | 2 | TC |
| 53 | M | 5 | Unknown | No | 4 | 108 | 15 | OM |
| Total | 55% M | | Genetic: 20 (38%), unknown: 19 (36%), structural: 13 (24%), infectious: 1 (2%) | 68% yes | | 2310 | 552 | 204 TC, 30 T > 30, 48 HK, 270 OM |
| Mean | | 9.7 ± 3.6 | | | 2.5 ± 1.2 | 45 | | |
| Median (range) | | | | | | | 2 (1–147) | |

Abbreviations: ASM, antiseizure medication; CSI, Caregiver Stress Index; F, female; FAR, false alarm rate; HK, hyperkinetic; M, male; na, not available; OM, other major; PPV, positive predictive value; PSQI, Pittsburgh Sleep Quality Index; QoL, quality of life; Sens, sensitivity; T > 30, tonic > 30 s; TC, tonic–clonic.

[a]Overall seizure sensitivity for all seizure types combined.

[b]All recorded data of this participant was excluded due to insufficient video data.

seizures in children (median sensitivity = 100%). Besides high sensitivity for the detection of convulsive seizures, NightWatch also showed good performance in detecting HK and OM motor seizures in children. NightWatch was well tolerated and easy to use. Caregivers reported a positive effect on their experienced stress during NightWatch use, whereas their quality of sleep and QoL did not change significantly.

## 4.1 | Strengths and limitations

Strengths of the PROMISE trial include the prospective, home-based, video-controlled design, long-term follow-up, and many recorded nights and seizures. The long-term follow-up helped to estimate the performance reliably. Contextual conditions may significantly impact the seizure detection algorithm's performance. For instance, electrocardiography-based algorithms yielded poorer results in freely moving people than in those lying in bed.[19] The home environment allowed us to examine a realistic setting, but we could also evaluate user satisfaction. One of the challenges with a home-based approach is the risk of missing seizures due to the lack of continuous EEG supervision, which may inflate sensitivity. To reduce this bias, we applied different screening methods. First, we asked the caregivers to record all seizures. Second, trial nurses screened 5% of all video recordings. Third, we retrospectively ran an automated, previously validated video detection algorithm on all tracings.[16,17] During this process, we

| Primary outcome: NightWatch performance[a] | | | Secondary outcomes: Parental stress, sleep, and QoL | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sens, % | PPV, % | FAR/h | CSI score T1 | CSI score T2 | PSQI score T1 | PSQI score T2 | QoL score T1 | QoL score T2 |
| — | — | 0 | 12 | na | 12 | na | .47 | na |
| — | — | .05 | 0 | na | 4 | na | .93 | na |
| — | — | .01 | 6 | 3 | 4 | 2 | 1 | 1 |
| — | — | .05 | 7 | 3 | 2 | 2 | .86 | .86 |
| 75 | 5 | .05 | 10 | na | 10 | na | 1 | na |
| 100 | 3 | .05 | 11 | na | 18 | na | .61 | na |
| — | — | .01 | 6 | na | 8 | na | 1 | na |
| — | — | .24 | na | na | na | na | na | na |
| 100 | 33 | .01 | 11 | na | 14 | na | .93 | na |
| 78 | 54 | .01 | 10 | na | na | na | .90 | na |
| 100 | 22 | .06 | 9 | na | 12 | na | .91 | na |
| 100 | 6 | .03 | 7 | na | 7 | na | .89 | na |
| 67 | 37 | .02 | 11 | 11 | 15 | na | .83 | .45 |
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| | | | | | | | | |
| 90% ±4.5% | 31% ±8.3% | .07 ± .03 | 8.0 | 7.1 | 7.9 | 6.7 | .9 | .9 |
| 100% (46%–100%) | 24% (3%–94%) | .04 (.00–.53) | | | | | | |

found that the frame rate of the video recordings was not constant, hampering performance of the method compared to previous work.[16,17] Nonetheless, the video algorithm accounted for 67% of all false negative detections. In the randomly selected 5% of all data that we visually reviewed, we found 25 seizures in total (NightWatch detections + detected false negatives). If this number is representative for the complete dataset, we would expect 25 × 20 = 500 seizures in total. However, we found 552 seizures with our approach, suggesting that our method probably detected most of the seizures. Another challenge of our home- and video-based approach concerns the observer reliability. We expect that the reliability depends on the seizure type, with likely high accuracy for the identification of TCs and longer tonic seizures, whereas other seizure types (e.g., certain types of HK seizures and the seizures that we classified as "OM") can be more challenging to distinguish from normal or sleep-related behavior. Nevertheless, in our previous NightWatch trial in adults we found a substantial interobserver agreement for the different seizure types used in this study.[14] A significant advantage of our approach over conventional phase 4 studies includes the video-controlled design that allowed us to verify user feedback. Users may recognize nonepileptic events as seizures or label seizure-related alarms false if the caregiver arrives late and the seizure is short-lasting. Another strength includes the detection of a broad range of motor seizures.

A limited number of caregivers completed the online questionnaires, which may have biased results. This bias

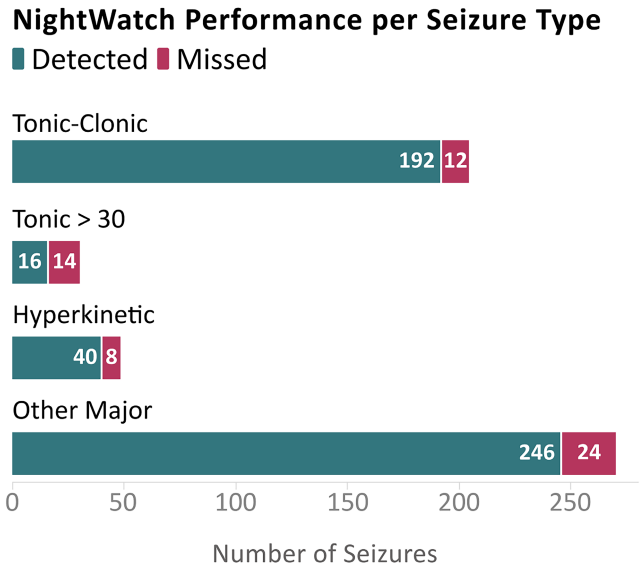


**FIGURE 4** NightWatch performance per seizure type. Overview is presented of number of seizures correctly detected (green bars) and number of seizures missed (red bars) by NightWatch for the different seizure types.

could work both ways; people who are either satisfied or unsatisfied may doubt the usefulness of the questionnaires, which reflects a realistic scenario of adherence in practice. Children of caregivers who did not complete the full questionnaire had on average fewer recorded nights during the intervention period compared to children of caregivers who did. This difference was not statistically significant but may have caused bias. The questionnaires provide some indicators but fall short of understanding the experienced value of NightWatch given the many interfering contextual factors (e.g., fluctuating disease course and parental coping). We addressed this limitation by conducting qualitative, in-depth interviews with 23 parents of 19 children, including dropout cases. We found that the experienced value of NightWatch resulted from an interplay of contrasting factors: on the one hand, the amount of assurance it could offer to reduce their fear of losing their child and the associated protective behavior, and conversely, their resilience to handle the potential extra burden of care (e.g., false alarms).[8]

## 4.2 | Related research

Unlike other commercially available SDDs, NightWatch demonstrated relatively high sensitivity and a slightly lower FAR.[1,11,20] A recent meta-analysis on the performance of wearable SDDs yielded a mean sensitivity of 91% for detecting convulsive seizures and an overall FAR of .08/h.[21] However, it is hard to compare our results with other devices, because almost none provides phase 4 studies or focuses on children or people with learning disabilities. Other devices usually include only small datasets with short-term follow-ups and recordings in a hospital or epilepsy monitoring unit. Another critical contrast with previous SDD trials consists of the seizure types; most trials focused on convulsive seizures only, whereas we included a broader range of significant motor seizure types. Previous surveys indicated that incorporating a broader range of seizures other than TCs may better meet the users' needs.[22–24]

Unlike our previous video-controlled trial in adults, NightWatch sensitivity in this pediatric cohort is slightly higher, but so is the FAR.[14] The FAR is partly explained by a high seizure burden, as almost one third of false alarms are related to seizures that did not meet our criteria for clinically urgent. The remainder is related to arousals or nonepileptic rhythmic movements. NightWatch algorithm corrects for individual baseline HR, but HR fluctuations and nonepileptic rhythmic movements may trigger false alarms. HR profiles of children differ from adults and are characterized by higher resting values and more significant variability.[25,26] Children, particularly those with developmental disorders, may also present with challenging behavior and sleep-related rhythmic movements.[27] Children with comorbid movement disorders were excluded from the trial, yet we did encounter some children with excessive or restless movements and body rocking. Accordingly, our post hoc analysis indicated that children with learning disabilities had higher FARs. We expect lower FAR in older cohorts and cohorts with less challenging behavior. Approximately one third of the participants did not experience a significant seizure during the intervention period. In parallel to this trial, children were treated by their neurologist and in 15 cases higher doses of antiseizure medications were given during the intervention compared to baseline, which might explain the lower seizure frequency. Possible other reasons for this include the reflection of a natural course of seizure frequency, or perhaps even a protective effect of SDD usage providing reassurance. Clinical trial simulations with time running forward and in reverse revealed that the placebo response is almost entirely attributable to the natural variability of epilepsy.[28]

Prospective, real-time, video-controlled performance studies in a home environment are scarce. Only two other phase 4 SDD studies have been performed, including the previous NightWatch study assessing its performance in adults living in a residential care facility.[1,14,29] NightWatch scored high on user-friendliness, and caregivers indicated that implementation facilitated a timelier response and more freedom. In contrast, the burden

of care remained unchanged.[14] This is in line with our results of lower stress scores following NightWatch usage. The second in-field study examined the applicability and usability of a wearable accelerometer device (Epi-Care) for detecting focal to bilateral convulsive seizures.[29] Most users were overall satisfied with the device, many indicated that the use of the device had resulted in fewer seizure-related injuries, and only a small group stopped using the device due to reasons related to it (e.g., high FAR, irritation or discomfort, low effectiveness). The study included a large population and long-term follow-up, but device performance data were based only on seizure diaries. Nearly all people with epilepsy included in these phase 4 studies lived in residential care facilities, reflecting a different ambulatory setting and possibly different user needs than in our study.[14,29]

A pilot study on 10 adolescents with epilepsy and their families showed an insignificant increase in QoL (Quality of Life in Epilepsy Inventory for Adolescents 48) while using a wearable SDD (SmartWatch) for 6 months.[30] A larger survey study found that most SDD users experienced reduced anxiety from device usage. At the same time, there was no significant difference in overall HR-QoL between SDD users and nonusers.[31] In a second large survey study, the majority of SDD users (including one third of users of NightWatch) agreed that using the device improved their QoL (median = 6 on a 7-point Likert scale).[32] Another large study followed families of children with newly diagnosed epilepsy. Those who wanted to use an SDD (approximately half of the families) were randomly allocated to the Epi-Care or an audio baby monitor.[33] QoL improved significantly over time in all parents, suggesting that QoL increases independently of SDD usage.

We recently performed an economic assessment of NightWatch. We found no significant changes in quality-adjusted life years after NightWatch intervention. Nonetheless, we demonstrated a decrease in societal costs (€775 reduction during the 2-month intervention period), suggesting that NightWatch might be a cost-effective addition to usual care for children with severe epilepsy living at home.[34] We found a small but significant reduction in caregiver stress, possibly partly explained by the short intervention period. The latter might also explain why we could not find a considerable change in caregivers' quality of sleep and life. Caregivers were optimistic about the practical use of NightWatch. Nonetheless, not all wanted to continue NightWatch, mainly due to cost (NightWatch is not yet reimbursable in the Netherlands), FAR, or seizure remission, thus emphasizing that SDD implementation is a multifactorial process. Acceptance of a device into a family home depends on device performance and even more on contextual factors like the burden of care[8] and taking time to trust the device.[35,36]

Future SDD studies should focus on ways to reduce FAR, which could facilitate implementation. Possible avenues include validating multiple algorithms that improve performance in specific subgroups (e.g., by focusing more on HR parameters than movement) and applying machine learning techniques to create individual-specific algorithms.[37,38] These approaches also have the potential of addressing the varying needs among users regarding the trade-off between true positives and FAR.[21]

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## CONFLICT OF INTEREST STATEMENT

R.D.T. has received speaker or consultancy fees from Theravance Biopharma, Arvelle, Medtronic, Zogenix, Xenon, Angelini, UCB, NewLife Wearables, and Novartis. None of the other authors has any conflict of interest to disclose. The authors are part of the Dutch TeleEpilepsy Consortium; no one from the TeleEpilepsy consortium, including the authors, has any direct financial links with LivAssured, or holds shares.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Dutch Tele–Epilepsy Consortium. Data availability is limited by exclusive rights for LivAssured with regard to commercial applications. Requests for analyses will require approval by the Medical Research Ethics Committee of the University Medical Center Utrecht and the Dutch Tele–Epilepsy Consortium with the permission of LivAssured.

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## REFERENCES

1. Beniczky S, Wiebe S, Jeppesen J, Tatum WO, Brazdil M, Wang Y, et al. Automated seizure detection using wearable devices: a clinical practice guideline of the international league against epilepsy and the International Federation of Clinical Neurophysiology. Epilepsia. 2021;62(3):632–46.
2. Maguire MJ, Jackson CF, Marson AG, Nevitt SJ. Treatments for the prevention of sudden unexpected death in epilepsy (SUDEP). Cochrane Database Syst Rev. 2020;4(4):CD011792.
3. Thijs RD, Ryvlin P, Surges R. Autonomic manifestations of epilepsy: emerging pathways to sudden death? Nat Rev Neurol. 2021;17(12):774–88.
4. Sveinsson O, Andersson T, Mattsson P, Carlsson S, Tomson T. Clinical risk factors in SUDEP: a nationwide population-based case-control study. Neurology. 2020;94(4):e419–29.
5. van der Lende M, Hesdorffer DC, Sander JW, Thijs RD. Nocturnal supervision and SUDEP risk at different epilepsy care settings. Neurology. 2018;91(16):e1508–18.
6. Lamberts RJ, Thijs RD, Laffan A, Langan Y, Sander JW. Sudden unexpected death in epilepsy: people with nocturnal seizures may be at highest risk. Epilepsia. 2012;53(2):253–7.
7. Ryvlin P, Ciumas C, Wisniewski I, Beniczky S. Wearable devices for sudden unexpected death in epilepsy prevention. Epilepsia. 2018;59(Suppl 1):61–6.
8. van Westrhenen A, de Lange WFM, Hagebeuk EEO, Lazeron RHC, Thijs RD, Kars MC. Parental experiences and perspectives on the value of seizure detection while caring for a child with epilepsy: a qualitative study. Epilepsy Behav. 2021;124:108323.
9. Jones C, Reilly C. Parental anxiety in childhood epilepsy: a systematic review. Epilepsia. 2016;57(4):529–37.
10. Elger CE, Hoppe C. Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. Lancet Neurol. 2018;17(3):279–88.
11. Beniczky S, Jeppesen J. Non-electroencephalography-based seizure detection. Curr Opin Neurol. 2019;32(2):198–204.
12. Beniczky S, Ryvlin P. Standards for testing and clinical validation of seizure detection devices. Epilepsia. 2018;59(S1):9–13.
13. Shum J, Friedman D. Commercially available seizure detection devices: a systematic review. J Neurol Sci. 2021;428:117611.
14. Arends J, Thijs RD, Gutter T, Ungureanu C, Cluitmans P, Van Dijk J, et al. Multimodal nocturnal seizure detection in a residential care setting: a long-term prospective trial. Neurology. 2018;91(21):e2010–9.
15. Lazeron RHC, Thijs RD, Arends J, Gutter T, Cluitmans P, Van Dijk J, et al. Dutch tele-epilepsy consortium. Multimodal nocturnal seizure detection: do we need to adapt algorithms for children? Epilepsia Open. 2022;7(3):406–13.
16. van Westrhenen A, Petkov G, Kalitzin SN, Lazeron RHC, Thijs RD. Automated video-based detection of nocturnal motor seizures in children. Epilepsia. 2020;61(Suppl 1):S36–40.
17. Geertsema EE, Thijs RD, Gutter T, Vledder B, Arends JB, Leijten FSS, et al. Automated video-based detection of nocturnal convulsive seizures in a residential care setting. Epilepsia. 2018;59(Suppl 1):53–60.
18. Kalitzin S, Petkov G, Velis D, Vledder B, Lopes da Silva S. Automatic segmentation of episodes containing epileptic clonic seizures in video sequences. IEEE Trans Biomed Eng. 2012;59:3379–85.
19. Jahanbekam A, Baumann J, Nass RD, Bauckhage C, Hill H, Elger CE, et al. Performance of ECG-based seizure detection algorithms strongly depends on training and test conditions. Epilepsia Open. 2021;6(3):597–606.
20. Kuradaa AV, Srinivasanb T, Hammondc S, Ulate-Camposd A, Bidwell J. Seizure detection devices for use in antiseizure medication clinical trials: a systematic review. Seizure Eur J Epilepsy. 2019;66:61–9.
21. Naganur V, Sivathamboo S, Chen Z, Kusmakar S, Antonic-Baker A, O'Brien TJ, et al. Automated seizure detection with noninvasive wearable devices: a systematic review and meta-analysis. Epilepsia. 2022;63(8):1930–41.
22. van Westrhenen A, Wijnen BFM, Thijs RD. Parental preferences for seizure detection devices: A discrete choice experiment. Epilepsia. 2022;63(5):1152–63.
23. Bruno E, Viana PF, Sperling MR, Richardson MP. Seizure detection at home: do devices on the market match the needs of people living with epilepsy and their caregivers? Epilepsia. 2020;61(S1):S11–24.
24. Patel AD, Moss R, Rust SW, Patterson J, Strouse R, Gedela S, et al. Patient-centered design criteria for wearable seizure detection devices. Epilepsy Behav. 2016;64:116–21.
25. Fleming S, Thompson M, Stevens R, Heneghan C, Plüddemann A, Maconochie I, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. Lancet. 2011;377:1011–8.
26. Schumann A, Bär KJ. Autonomic aging – a dataset to quantify changes of cardiovascular autonomic function during healthy aging. Sci Data. 2022;9(1):95.
27. Prihodova I, Skibova J, Nevsimalova S. Sleep-related rhythmic movements and rhythmic movement disorder beyond early childhood. Sleep Med. 2019;64:112–5.
28. Goldenholz DM, Strashny A, Cook M, Moss R, Theodore WH. A multi-dataset time-reversal approach to clinical trial placebo response and the relationship to natural variability in epilepsy. Seizure. 2017;53:31–6.
29. Meritam P, Ryvlin P, Beniczky S. User-based evaluation of applicability and usability of a wearable accelerometer device

for detecting bilateral tonic–clonic seizures: a field study. Epilepsia. 2018;59(S1):48–52.
30. Thompson ME, Langer J, Kinfe M. Seizure detection watch improves quality of life for adolescents and their families. Epilepsy Behav. 2019;98:188–94.
31. Chiang S, Moss R, Patel AD, Rao VR. Seizure detection devices and health-related quality of life: a patient-and caregiver-centered evaluation. Epilepsy Behav. 2020;105:106963.
32. Hadady L, Klivényi P, Fabó D, Beniczky S. Real-world user experience with seizure detection wearable devices in the home environment. Epilepsia. 2022. Online ahead of print. https://doi.org/10.1111/epi.17189
33. Borusiak P, Bast T, Kluger G, Weidenfeld A, Langer T, Jenke ACW, et al. A longitudinal, randomized, and prospective study of nocturnal monitoring in children and adolescents with epilepsy: effects on quality of life and sleep. Epilepsy Behav. 2016;61:192–8.
34. Engelgeer A, van Westrhenen A, Thijs RD, Evers SMAA. An economic evaluation of the NightWatch for children with refractory epilepsy: insight into the cost-effectiveness and cost-utility. Seizure. 2022;101:156–61.
35. van Westrhenen A, Souhoka T, Ballieux ME, Thijs RD. Seizure detection devices: exploring caregivers' needs and wishes. Epilepsy Behav. 2021;116:107723.
36. Sivathamboo S, Nhu D, Piccenna L, Yang A, Antonic-Baker A, Vishwanath S, et al. Preferences and user experiences of wearable devices in epilepsy: a systematic review and mixed-methods synthesis. Neurology. 2022;99(13):e1380–92.
37. Tang J, El Atrache R, Yu S, Asif U, Jackson M, Roy S, et al. Seizure detection using wearable sensors and machine learning: setting a benchmark. Epilepsia. 2021;62(8):1807–19.
38. Beniczky S, Karoly P, Nurse E, Ryvlin P, Cook M. Machine learning and wearable devices of the future. Epilepsia. 2021;62(Suppl 2):S116–24.

## SUPPORTING INFORMATION

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

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## APPENDIX 1 A

### A.1 | Contribution of authors.

| Name | Organization | Contribution |
|---|---|---|
| Anouk van Westrhenen, MD | Stichting Epilepsie Instellingen Nederland (SEIN), Heemstede, The Netherlands | Trial coordinator; collected, analyzed, and interpreted data, drafted the manuscript for intellectual content |
| Richard H. C. Lazeron, MD, PhD | Academic Center of Epileptology Kempenhaeghe, Heeze, the Netherlands | Principal investigator at Kempenhaeghe; designed and conceptualized study, major role in the acquisition of data, revised the manuscript for intellectual content |
| Johannes P. van Dijk, PhD | Academic Center of Epileptology Kempenhaeghe, Heeze, the Netherlands | Designed and conceptualized study, major role in the acquisition of data, revised the manuscript for intellectual content |
| Frans S. S. Leijten, MD, PhD | Utrecht University, Utrecht, the Netherlands | Principal investigator at University Medical Center Utrecht; designed and conceptualized study, major role in the acquisition of data, revised the manuscript for intellectual content |
| Roland D. Thijs, MD, PhD, FEAN, FRCP | Stichting Epilepsie Instellingen Nederland (SEIN), Heemstede, the Netherlands | Principal investigator of the trial; designed and conceptualized study, major role in the acquisition of data, interpreted data, revised the manuscript for intellectual content |

## APPENDIX 2 B

### B.1 | Coinvestigators of the TeleEpilepsy consortium.

| Name | Organization | Role | Contribution |
|---|---|---|---|
| F. Jansen | UMC Utrecht | Child neurologist | Collaborated in discussions about study design and implementation |
| C. Donjacour | SEIN, Zwolle | Neurologist | Collaborated in discussions about study design and implementation |
| J. van Hoey Smith | SEIN, Zwolle | Neurologist | Collaborated in discussions about study design and implementation |
| B. Kuijper | Maasstad Ziekenhuis | Neurologist | Collaborated in discussions about study design and implementation |
| J. Arends | Kempenhaeghe | Neurologist | Collaborated in discussions about study design and implementation |
| F. Tan | Kempenhaeghe | Physician | Collaborated in discussions about study design and implementation |
| P. Cluitmans | Technical University Eindhoven | Signal processing expert | Collaborated in discussions about study design and implementation |
| L. M'Rabet | Epilepsie NL | Patient representative | Collaborated in discussions about study design and implementation |
| M. Ballieux | Stichting ZIE | Patient representative | Collaborated in discussions about study design and implementation |
| M. de Groot-Schokker | Stichting Dravetsyndroom | Patient representative | Collaborated in discussions about study design and implementation |

Abbreviations: NL, Netherlands; SEIN, Stichting Epilepsie Instellingen Nederland; UMC, University Medical Center; ZIE, Zorg Intensief en Epilepsie.