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Economic aspects of prolonged home video-EEG monitoring: a simulation study

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Abstract

Introduction Video EEG monitoring (VEM) is an important tool for characterizing clinical events suspected as seizures. It is also used for pre-surgical workups in patients with drug-resistant epilepsy (DRE). In-hospital VEM high cost, long admission waiting periods and some other inconveniences led to an interest in home VEM (HVEM). However, because antiseizure medications cannot be reduced at home, HVEM may require longer monitoring. While the economic aspect is one of the main motivations for HVEM, the cost of HVEM lasting several weeks has not been assessed.

Methods We modeled the cost of HVEM for 8 weeks and compared it to the cost of 1-week in-hospital VEM. Additionally, we modeled the per-patient cost for a combination of HVEM and in-hospital VEM, considering that if in a proportion of patients HVEM fails to achieve its goal, they should undergo in-hospital VEM with drug reduction.

Results The average cost of HVEM up to 4–6 weeks of monitoring was lower than that for the 1-week in-hospital VEM. Combining the 3-week HVEM with 1-week in-hospital VEM (if needed) reduced the per-patient cost by 6.6–28.6% as compared to the situation when all the patients with DRE were referred to the in-hospital VEM.

Conclusions A prolonged intermittent HVEM can be cost-effective, especially if the minimal seizure frequency is about one seizure per week. The study findings support directing efforts into clinical trials and technology development.

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Introduction

Video-EEG monitoring (VEM) is one of the most important diagnostic tools in epileptology. It has three main indications [32]: differentiation between epileptic and non-epileptic events; characterization of seizure type and epilepsy syndrome classification; and it is a crucial part of the pre-surgical workup in patients with drug-resistant epilepsy (DRE) (Noachtar and Borggraefe [21]). To achieve the goals of VEM, often several seizures should be recorded. When several epileptogenic zones are suspected, it is recommended that each seizure type will be recorded separately, at least 1 month apart from other seizure types [32]. The current standard practice for obtaining VEM in patients undergoing epilepsy surgery workup is by admission to an epilepsy monitoring unit for about 1 week. The alternative home VEM (HVEM) option has recently gained



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attention [17]. Among other reasons, a putatively reduced financial cost compared to the in-hospital procedure made it an attractive potential alternative. During the COVID-19 pandemic, this option became even more appealing [7].

Slater et al. [30], demonstrated that the average cost of HVEM per patient is substantially lower than that of the in-hospital VEM (4098 USD vs. 13,821 USD) when the duration of both procedures is up to 1 week. In the hospital, anti-seizure medications (ASM) are often withdrawn to increase the likelihood of capturing seizures during a relatively short hospitalization. However, this practice cannot be safely carried out at home. In a previous study, we demonstrated that 6 weeks for adults and 5 weeks for children are sufficient to record three seizures on different days in 80% of the patients. While during 1 week of HVEM, at least one seizure can be captured in 68% of adults and 74% of children with DRE, three seizures on different days occur in only 23.4% of adults and 29% of children [33]. We used "three seizures on different days" as the goal of HVEM for patients with DRE since the seizures occurring on the same day can represent a seizure cluster originating from the same epileptogenic zone. Thus, for patients with DRE, the cost of 1-week in-hospital VEM should be compared to a longer duration of HVEM.

The use of HVEM for pre-surgery workup in DRE is far from consensus. In most publications on HVEM, the recordings were limited to several days, mainly due to technical challenges in attaching the electrodes to the scalp [3, 11]. Nurse et al. [20] recently reported a novel water-soluble glue for EEG electrode attachment. This allows prolonged EEG recording of up to six days without the need for whole EEG array reconnection. The patient's caregivers are instructed on how to reattach single EEG electrodes. Moreover, the same group reported high event capturing (94.9%) by video recording using a video camera placed on a telescopic pole [23]. Performing cycles of 6 days of recording, followed by a rest period, may enable HVEM for several non-consecutive weeks.

Repeated HVEM sessions were reported in less than 6% of cases by Klein et al. [17]. In the current study, we aimed to evaluate the economic viability of such prolonged studies. We constructed an economic model of HVEM lasting from 1 to 8 weeks, considering the expenses of professional medical resources, disposables, and technological and administrative costs.

We present our model's results for two VEM indications: (1) the differentiation between epileptic vs. none-pileptic events and (2) DRE pre-surgical workup. Seizure type and epilepsy syndrome classification are not considered separately since their economic aspects are similar to the abovementioned indications.

The waiting period for in-hospital VEM can be long, and postpone surgical treatment for DRE patients. If HVEM achieves its goals, it can shorten the pre-surgery workup and ultimately lead to an earlier surgery. Patients with DRE, who did not reach the diagnostic goal of HVEM, should be admitted to the hospital for VEM with ASM reduction. Thus, one of the questions of our study is whether the HVEM for patients with DRE is economically justified, considering that for some of these patients, the cost of in-hospital VEM is added to the cost of HVEM.

While we consider the clinical application of prolonged HVEM in the intermittent form, in our model, we used continuous time flow for simplicity. This does not change substantially the HVEM cost, since other patients can use the same EEG system during the off time.

In the present study, we calculated the direct cost of HVEM. Therefore, the indirect costs (expenses related to work or school absence of patients and their caregivers, patient transportation expenses, etc.), while important, are not within the scope of this study.

Methods

HVEM procedure modelling

The model was constructed using MATLAB 2022a (Math Works). The MATLAB code of our model is publicly available at https://github.com/marikmedv/Virtual_Video_EEG. The file name is HVEM_cost_calculator_080724.m. The user guide for this code is located in the Supplementary Materials (Appendix 5).

We modeled the HVEM procedure lasting from 1 to 8 weeks. Based on the report of Nurse et al. [20], we assumed that continuous HVEM could be performed with the assistance of a patient's caregiver in time segments of 6 days without electrode array reconnection. We included in the model daily online supervision by an EEG technician who reviews the electrodes' performance and gives instructions to the patient/caregiver. The model assumes that on the first day of HVEM and every new 6-day monitoring period, an EEG technician will meet the patients for EEG-array reconnection. Our model includes the option of data screening by an EEG technician.

We modeled the neurologist/epileptologist's work, as one working day per patient, including patient visits, HVEM data analysis, and reporting. We assumed that 8 h are sufficient for analysis of most HVEM recordings, even the long-lasting ones, providing that EEG technicians prescreened the data presented to the neurologist. In our model, patients with frequent clinical events require shorter HVEM than patients with infrequent events. We decided not to reduce the required time for short-lasting HVEM analysis, since these cases

are not necessarily clinically simple nor include a lower number of seizures.

Screening of video-EEG data by EEG technician was modeled for two scenarios: screening of 100% of the data and screening of only 50% of it. Since the main goal of VEM is recording seizures, we assume that substantial parts of the recorded interictal data may be redundant. Thus, manually screening only part of the HVEM data may be sufficient, especially when the whole data is screened by an automatic algorithm. For example, manual screening of the recordings obtained only on the days when seizures occurred can be considered a realistic scenario.

HVEM cost modelling

The HVEM cost was modeled based on the HVEM procedure model. We considered three types of interacting organizations, involved in the HVEM process:

- 1. Medical organization, is responsible for the HVEM as a clinical procedure, including data acquisition, analysis, and reporting.
- Technological organizations, such as the medical engineering unit of the medical center or external company, are responsible for technical support of hardware, software, and recorded data.
- 3. Administration, responsible for financial management, secretary work, insurance, and other non-clinical, non-technological activities.

Thus, we defined three main components of direct HVEM cost: basic, technical, and administrative costs.

$$\begin{aligned} & \textit{Direct HVEM cost} \\ &= \textit{Basic HVEM cost} + \textit{Technological cost} \\ &+ \textit{Administrative cost} \end{aligned} \tag{1}$$

Parameters of basic HVEM cost

The basic HVEM cost is comprised of the cost of medical professionals (neurologists and EEG technicians) and the cost of disposables:

- EEG-technician and Neurologist's salary-per-hour:
 The per hour average salary of EEG technician and neurologist were taken from the USA source (https://www.ziprecruiter.com/) and are equal to 31 USD and 134 USD, respectively.
- One electrode cost: Based on the approach described by Nurse et al. [20], we included the cost of the disposable Ag/AgCl electrode in our model. The total cost of the disposable electrode, the glue, and the

- conductive gel or paste used for one electrode was estimated to be 1 USD (taking the upper margin).
- Electrode number: We defined 42 electrodes: 32 regular EEG electrodes + 1 reference + 1 ground + 2 ECG electrodes + 4 EMG electrodes + 2 EOG electrodes. This was based on the recommendations of Tatum et al. [32] and Peltola et al. [25].
- Patient explanation time: The time needed for the EEG technician to give the patient the required directions and information before the HVEM. Based on the HVEM experience in Wolfson Medical Center, Holon, Israel, this was estimated as 1 h.
- Caregiver instructing time: The time required to instruct the caregiver before HVEM. This was estimated as 2 h: 1 h to explain how to detect seizures and another hour for providing instructions on how to reattach the electrodes (according to the approach, described by Nurse et al. [20]).
- Electrode attachment time: The time required for the EEG technician to attach an EEG array. This was estimated to be 90 min, considering the time needed to attach 34-electrode arrays on the scalp (including ground and reference electrodes) as well as other electrodes. The electrodes should be attached with low contact impedance to ensure high-quality recording at home.
- In-clinic testing time: The time for testing the recording in the clinic after the electrodes are attached and before the patient leaves the clinic to home. We defined this parameter as 20 min.
- HVEM duration: The total duration of the HVEM study. We set it to 1, 2, 3, 4, 5, 6, 7 and 8 weeks.
- Recording segment: The duration of the HVEM recording period from one electrode array attachment to the next. We set it as six days, according to the report of Nurse et al. [20].
- Online contact time: The time required for the EEG technician to perform a daily remote electrode check and communicate with the patient. We estimated it as 1 h. According to Syed et al. [31], the remote electrode check is performed for 3 min every 2 h. That means 36 min per day of HVEM. Since our model adopted the approach described by Nurse et al. [20], we added 24 min per day (completing 1 h) to enable the online instructing and control of the electrode reattachments by the patient's caregiver.
- Screening time: The time spent by the EEG technicians to screen the video-EEG data. We estimated it as 4 h for every 24-h-recording. According to [15], 19 min was required to review an EEG trace of 6 h duration. That means 1 h and 16 min per 24-h EEG trace.

However, an analysis of video recording was not included in that study. The standard time for 24-h video-EEG screening by an EEG technician in Hadassah University Medical Center is 2 h. According to Brunnhuber et al. [6], the EEG-technician time for data review is 2.7 h per 24 h of recording. Considering that home video-EEG screening can be more challenging due to the patient's movements and relocations inside the house, we doubled this time and defined it as 4 h.

- Screening percentage (SP): The percent of HVEM data that an EEG technician screens manually.
 We modeled two scenarios—100% of the recorded data screened or 50% of it.
- Neurologist time: The amount of time the neurologist dedicates to reviewing and analyzing the data, as well as writing the report. We estimated it to be 8 hours per study (regardless of the length). After data screening by an EEG technician, the main time-consuming contribution of a neurologist is the analysis of seizures. In our model, longer HVEM is associated with lower seizure frequency.

Therefore, the same number of seizures is recorded by HVEM studies of different duration.

Technological cost

Technological cost includes several components, including the cost of the device (hardware and basic software), the device's lifespan, external licensed software, data storage, expert support, and other fees. A long HVEM carries some higher expenses compared to a short HVEM. For example, the hardware is used by fewer patients (since each patient uses it for a longer period), and the cloud storage is more expensive since the amount of recorded data is larger. Therefore, the technological cost depends on HVEM duration, as reflected in our model. For example, assuming the device lifespan is 2 years, and the clinic can monitor four patients simultaneously for 50 working weeks per year, the approximate (about upper margin according to experience of the authors) hardware-software price per week per patient can be calculated as follows: hardware price (home video-EEG system with two video cameras and wireless real-time communication with the clinic: 40000 USD/(50*2) + external software annual license price (20,000 USD)/(50*4) = 500 USD. Since the same software package can be used for several patients recorded simultaneously, the price of external software is divided by the number of simultaneously recorded patients. In our model, we defined the technological cost to be 70% of the basic cost which is 1571 USD for the first week and 741 USD for every additional week. This leaves enough room to cover expert support, data storage, and additional technological expenses in our model.

It should be noted that the prices provided here are approximate. For exact prices, the reader should contact the companies that provide home video-EEG systems and software directly.

Since details of *Technological cost* can vary substantially in different situations, we defined this cost proportionally from basic HVEM cost. Considering the high probability of hardware damage at the patient's home, we defined the technological cost as 70% of the basic HVEM cost.

Administrative cost

We assume that the sum of technological and administrative costs should not exceed the basic cost and that the administrative cost should be substantially lower than the technological cost. Thus, we estimated the administrative cost to be 30% of the basic cost or 17.5% of the basic and technological costs combined. This, for example, corresponds to the standard administrative cost of medical service in Israel, which is defined in the range between 15 and 18% of all the other costs of the service.

We defined administrative costs as 30% of the basic cost (15% of the direct cost of HVEM). However, we are aware of the significant variations in healthcare administrative costs between countries in the and between different reports. According to Hagenaars et al. [14], the administrative costs in healthcare range between 1.3% in Iceland and 8% in the US. However, Chermew and Mintz [9] reported a much higher administration cost percentage in the US: 15–25%.

Thus, the Eq. (1) can be written as:

$$Direct\ HVEM\ cost\ =\ Basic\ HVEM\ cost\ +\ 0.7*Basic\ HVEM\ cost\ +\ 0.3*Basic\ HVEM\ cost,$$
 (2)

Or as:

$$Direct\ HVEM\ cost = 2*Basic\ HVEM\ cost$$
 (3)

HVEM simulations

The following calculations were used to simulate the different aspects of HVEM cost.

$$Basic\ HVEM\ cost = EEG\text{-}technician\ cost \\ + Neurologist\ cost \\ + Disposables\ cost$$
 (4)

 $Neurologist\ cost = Neurologist\ hours * Neurologist\ salary-per-hour$

(5)

EEG-technician hours = Electrode attachment hours

- + On-Line contact hours
- + Screening hours
- + $Patient\ explanation\ time$

Electrode at tachment hours

$$= ceil(HVEM length/recording segment)$$
 (8)

* Electrode attachment time

(ceil is a MATLAB command for upward rounding)

 $Screening\ hours = Screening\ time * HVEM\ length * SP$ (10)

(SP is screening proportion between 0 and 1.)

$$Disposables cost = One electrode cost * Electrode number * HVEM length (11)$$

To assess the influence of the *SP* reduction, the *Direct HVEM cost* and *EEG technician cost* was calculated first with *SP* set on *100% manual screening*, and second *on 50% manual screening*. Next, the *Direct HVEM cost* corrected for *SP 50% manual screening* was calculated in the following way:

Direct HVEM cost with 50% manual screening

- = Direct HVEM cost with 100% manual screening
- (EEG-technician cost with 100% manual screening
- EEG-technician cost with 50% manual screening)

(12)

According to Slater et al. [30], the mean cost of in-hospital VEM (up to one week) was 13,821 USD (95% confidence interval 12844–14873). This value was based on reimbursement records plus patients' payment records related to in-hospital VEM. Both medical and prescription costs were included.

Modeling HVEM cost for DRE pre-surgery workup (HVEM-DRE model)

Pre-surgical workup for DRE requires recording of epileptic seizures. Thus, our model assumed capturing three

seizures on different days [33]. Most DRE patients take ASM; some respond and have rare seizures. Therefore, in some patients, ASM should be withdrawn to record seizures in a reasonable time. Since it is not recommended to reduce ASM at home, some patients will not have enough seizures during HVEM and should be referred to in-hospital VEM.

The HVEM-DRE model takes into account that during HVEM, some patients do not achieve the diagnostic goal of the monitoring. Such patients are referred to the inhospital VEM for ASM reduction. If we consider a cohort of y patients, and P is the proportion (from 0 to 1) of patients who achieve the goal of monitoring then the cost for all patients who achieved the goal of HVEM is:

$$HVEM\ cost*y*P$$

and for all patients who did not achieve the goal of HVEM is:

$$(HVEM cost + in-hospital VEM cost) * y * (1 - P)$$

The cost for all patients (who either achieved or did not achieve the goal) is:

$$[HVEM cost * y * P]$$

+ $[(HVEM cost + in-hospital VEM cost)$
* $y * (1 - P)]$

Then the mean cost for the patient in the HVEM-DRE model is:

$$mean \, HVEM - DRE \, cost$$

$$= [HVEM \, cost * y * P]$$

$$+ [(HVEM \, cost + in-hospital \, VEM \, cost)$$

$$* y * (1 - P)]/y$$
(13)

or:

$$mean\ HVEM - DRE\ cost$$

$$= y*(HVEM\ cost*P)$$

$$+ [(HVEM\ cost+in-hospital\ VEM\ cost)$$

$$*(1-P)]/y$$

$$(14)$$

$$mean \ HVEM - DRE \ cost$$

$$= [HVEM \ cost * P]$$

$$+ [(HVEM \ cost + in-hospital \ VEM \ cost)$$

$$* (1-P)]$$
(15)

In the last formula (15), we can observe two opposite duration-dependent tendencies:

1. With time, HVEM cost rises, increasing the mean HVEM-DRE cost.

 With time, the proportion (P) of patients achieving the diagnostic goal of the HVEM rises, and therefore, the (1 − P) value decreases (fewer patients require a referral for in-hospital VEM), lowering the mean HVEM-DRE cost.

In our model there are two criteria for HVEM cessation: the first is when the patient achieves the diagnostic goal of HVEM, and the second is when the duration of HVEM achieves a predefined limit. For example, if the HVEM duration limit is 3 weeks, then all patients who had an HVEM for 3 weeks but did not achieve the diagnostic goal are referred to in-hospital VEM. However, some patients achieve the diagnostic goal in less than 3 weeks. Those patients may discontinue the HVEM early. Therefore, we should calculate the mean cost of all patients who achieve the goal of HVEM within 3 weeks as follows: [HVEM cost1 * P1]+[HVEM cost2 * (P2 - P1)] + [HVEM cost3 * (P3 - P2)]. HVEM cost1, HVEM cost2, and HVEM cost3 are the HVEM cost after 1, 2, and 3 weeks of monitoring respectively; P1, P2, and P3 are the proportions of patients who achieve the diagnostic goal after 1, 2, and 3 weeks respectively.

Therefore, the mean HVEM-DRE cost was calculated as follows:

Mean HVEM-DRE cost 1

*(1-P2)

$$= HVEM cost1 * P1$$

$$+ (HVEM cost1 + In-hospital VEM cost)$$

$$* (1 - P1)$$

$$Mean HVEM-DRE cost2$$

$$= HVEM cost1 * P1$$

$$+ HVEM cost2 * (P2-P1)$$

$$+ (HVEM cost2 + In-hospital VEM cost)$$

$$(16)$$

$$Mean \, HVEM \, cost1 * P1$$

$$= HVEM \, cost1 * P1$$

$$+ HVEM \, cost2 * (P2-P1) + \dots$$

$$+ HVEM \, costn * (Pn-Pn-1)$$

$$+ (HVEM \, costn + In$$

$$-hospital \, VEM \, cost) * (1-Pn)$$

$$(18)$$

Mean HVEM_DRE cost1 and HVEM cost1 are the costs of the HVEM-DRE and HVEM, when the HVEM was stopped at the end of week 1; HVEM-DRE cost2 and HVEM cost2—when HVEM was stopped at the end of week 2 and HVEM-DRE costn and HVEM costn—when HVEM was stopped at the end of week n.

P1, P2, Pn—are the proportions of patients who achieved the goal of pre-surgical workup HVEM (three recorded seizures on different days) at the end of weeks 1, 2 and n, respectively. These proportions were taken from our previous work [33].

Statistical analysis

To apply statistical inference for comparison between the HVEM-DRE cost and in-hospital VEM cost we should know the distribution of the cost in these two populations. Some idea about cost distribution in HVEM-DRE population can be based on the distribution of HVEM required duration for the recording of three seizures on different days [33]. However, we did not find a direct source describing the in-hospital VEM cost distribution. We assume that in-hospital VEM cost distribution at least partially depends on monitoring duration and, therefore, day-to-day cost distribution can represent some idea about the general cost distribution of in-hospital HVEM. We modeled day-to-day in-hospital cost distribution based on the report of Slater et al. [30] which describes the group of 5271 patients (38% children) and provides the mean value of in-hospital VEM cost, confidence interval (two standard deviations from the mean to each direction), and distribution of duration of in-hospital VEM in days up to one week. The modeling of inhospital VEM cost day-to-day distribution is described in detail in Appendix 1 in Supplementary Materials. We compared the modeled cost distribution of in-hospital VEM to the modeled HVEM-DRE cost of the same population (described by Slater et al. [30]), when 50% of the data are manually screened. This comparison was done using a two-sample Student T-test. The mean values of the HVEM-DRE cost of this population are shown in Fig. 2 as a yellow line.

A One-tailed paired Student T-test was used to compare the direct cost of HVEM in two situations: when 100% and 50% of data were manually screened with different values of HVEM length.

Sensitivity analysis

We performed a sensitivity analysis studying the influence of variation in the following parameters:

- (1) The minimal seizure frequency of the patient referred to HVEM.
- (2) The proportion of manual data screening.
- (3) The proportion of technological cost.
- (4) The proportion of administrative cost.
- (5) The EEG technician's screening time.
- (6) The distribution of adult and pediatric patients.

(7) The different numbers of recorded seizures as a criterion for HVEM goal achievement.

The minimal seizure frequency of the patients referred to HVEM: In our calculations described above this subsection, we used the HVEM model described in our previous study [33]. It is based on epilepsy patients with seizure frequency ranging from one per day to one per month. However, when considering a seizure frequency of one per month, it becomes impractical to record 3 seizures on different days, because it would take about 3 months. One practical approach would be to consider conducting HVEM over 3 nonsequential weeks. In that scenario, we should select the patient population with seizure frequency that enables recording 3 seizures in different days within 3 weeks. Such frequency should be no less than approximately one seizure per week or about 4 seizures per month. Therefore, we included the minimal seizure frequency as one of the parameters for the sensitivity analysis.

We calculated the HVEM-DRE model for patient populations with minimal seizure frequency of 1, 2, 3, and 4 seizures per month (Fig. 4, Tables S4–S7).

The proportion of manual data screening: We performed the HVEM-DRE model calculations using different proportions of manual data screening, ranging from 0% (completely automatized) to 100% (completely manual) at 20% intervals (0%, 20%, 40%, 60%, 80%, 100%). This is in addition to the modeling of 50% manual data screening, which is presented in Fig. 2. The calculations were performed separately for children and adults and patient populations with minimal seizure frequency of 1 per month and 4 per month (Fig. 5, Tables S8–S11),

The proportion of technological cost: In the main calculations, we considered the technological cost as 70% of the basic cost. Herein we added calculations of the HVEM-DRE model at different proportions of technological cost: 80%, 80%, and 100% for patients with a minimum of 1 seizure per month and with a proportion of 100% for patients with a minimum of 4 seizures per month (Fig. S3, Tables S12–S15).

The proportion of administrative cost: The proportion of administrative cost was defined as 30% of the basic cost in the main calculations. In a sensitivity analysis, we performed additional calculations with different proportions of technological cost, ranging from 40 to 60% in patients with a minimum of 1 seizure per month and with a proportion of 100% in patients with a minimum of 4 seizures per month (Fig. S4, Tables S16–S19).

The EEG technician's screening time: In the main calculations, the EEG reviewer's screening time was defined as 4 h per 24 h of recording. We added HVEM-DRE model calculations using different values for the EEG reviewer's

screening time: 2, 3, 5, and 6 h per 24 h of recording in patients with a minimum of 1 seizure per month, and with 6 h for patients with a minimum of 4 seizures per month (Figure S5 and S6, Tables S20–S24).

The distribution of adult and pediatric patients: In a sensitivity analysis, the HVEM-DRE model was calculated with different proportions of adult and pediatric patients: 0, 20, 40, 60, 80, and 100% for patients with a minimum of 1 seizure and patients with 4 seizures per month (Figure S7, Tables S25-S26).

The different numbers of recorded seizures as a criterion for HVEM goal achievement: We calculated the HVEM-DRE model with different numbers of recorded seizures on different days required for HVEM goal achievement: 1, 2, 3, and 4 seizures when the minimum seizure frequency is 1 seizure per month (Fig. S8, Tables S27–S30); and 4 seizures when the minimum seizure frequency is 4 seizures per month (Fig. S9, Tables S31).

Results

HVEM cost

The cost of an HVEM of up to 4 weeks was lower than that of an in-hospital VEM, assuming that EEG technicians manually screened 100% of the data. HVEM cost for up to 6 weeks was lower than that of an in-hospital VEM, assuming that 50% of data were manually screened. When an EEG technician manually screens 50% of the data, the direct HVEM cost is significantly lower ($p\!=\!0.0008$) than when 100% of the data is manually screened.

Table 1 presents the different components of the perpatient cost. Figure 1 depicts the cost of the HVEM procedure depending on its duration compared to the inhospital VEM cost.

The modeled costs of home VEM over the weeks of monitoring, when the data were manually screened for 50% and 100% of recording time—red and green lines, respectively. The blue line represents the actual cost of the in-hospital VEM for up to one week, as reported by Slater et al. [30]. Note that the points at which the two lines intersect correspond to the duration of HVEM, for which its cost is no longer less than in-hospital VEM. Here and hereafter, the costs are in USD.

Cumulative costs of HVEM followed by an in-hospital VEM (if needed): HVEM-DRE

The cost of HVEM-DRE at the end of the first week was higher than that of an in-hospital VEM. From the second week, the HVEM-DRE cost dropped below that of an in-hospital VEM (Fig. 2, Table S1 in Supplementary Material, Appendix 2). This trend was more prominent in children than adults, as well as when only 50% of data was manually screened. The reduced

 Table 1 Constituents of the cost for HVEM over the weeks of monitoring, USD

Costs/weeks	1 Week	2 Weeks	3 Weeks	4 Weeks	5 Weeks	6 Weeks	7 Weeks	8 Weeks
Direct HVEM Cost, 100% manual screening	4647	6952	9258	11,563	13,869	16,174	18,615	20,921
Direct HVEM Cost, 50% manual screening	4275	6146	8018	9889	11,761	13,632	15,639	17,511
Technician Cost, 100% manual screening	1168	2278	3389	4500	5610	6721	7858	8968
Technician Cost 50% manual screening	759	1472	2149	2856	3502	4179	4882	5558
Neurologist cost	1072	1072	1072	1072	1072	1072	1072	1072
Disposables cost	84	126	168	210	252	294	378	420
Basic cost, 100% manual screening	2342	3476	4629	5782	6934	8087	9308	10,460
Basic cost 50% manual screening	1952	2670	3389	4108	4826	5545	6332	7050
Technological cost	1626	2433	3240	4047	4854	5661	6515	7322
Administrative cost	697	1043	1389	1735	2080	2426	2792	3138

USD United States Dollar, HVEM home video-EEG monitoring

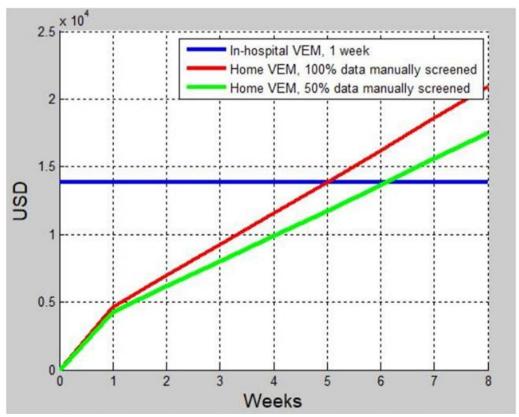


Fig. 1 Duration-dependent cost of home video-EEG monitoring

per-patient cost of HVEM-DRE with increasing duration of HVEM can be explained by the outcome of two

opposite duration-dependent trends: Longer HVEM led to an increase in HVEM cost, but the longer the HVEM

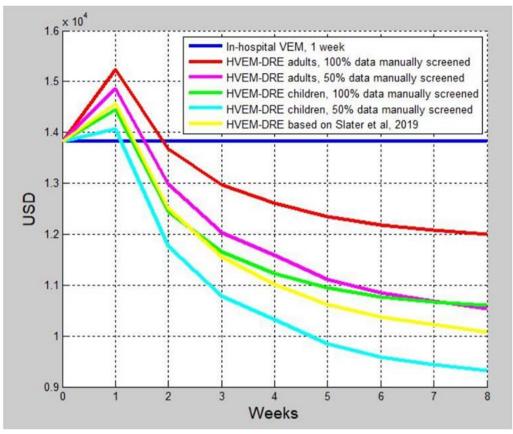


Fig. 2 HVEM-DRE model: the cost of HVEM (USD) until 3 seizures on different days are recorded, including in-hospital VEM (if needed)

was, the more patients achieved the diagnostic goals and escaped the need for an expensive in-hospital HVEM.

After 2 weeks of HVEM, the per-patient expenditure for the HVEM-in-hospital-VEM combination was lower than that of a one-week in-hospital VEM, assuming all patients with DRE who did not have enough seizures when monitored by HVEM underwent an in-hospital VEM. The savings yielded a 2–23% reduction in average per-patient cost. After 3 weeks of HVEM, the cost reduction was 6.6% and 14.8% for adults with 100% and 50% manual data screening, respectively. For children, the corresponding savings were even higher: 22.6% and 28.3% for 100% and 50% of manually screened data, respectively (Table S1 in Supplementary materials, Appendix 2).

The difference between costs of in-hospital VEM and HVEM-DRE was significant: the p-value was less than 0.001 from the 1st to the 8th week (both when HVEM was more expensive than in-hospital VEM at the first week and when HVEM was cheaper, between the 2nd and 8th weeks). The mean cost dynamics of the 5271 patients, based on the report of Slater et al. [30], is demonstrated in Fig. 2 (yellow line) and in Table S1 in Supplementary Material, Appendix 2.

Figure 3 and Table S2 (Supplementary Material, Appendix 2) demonstrate that the maximum cost reduction rate for patients with DRE is achieved during the second and third weeks of HVEM-DRE. HVEM longer than 3 weeks yielded less than 5% additional savings per week.

The modeled duration-dependent cost of HVEM-DRE depends on whether the diagnostic goal (recording of three seizures on different days) was achieved by HVEM alone. If not, and a patient still needs hospitalization, the cost of HVEM-DRE is a summated cost of HVEM and in-hospital VEM. The "week 0" represents a case that the HVEM is not performed, and all patients are referred to in-hospital VEM. The yellow line corresponds to the HVEM-DRE cost of the population described by Slater et al. [30]: 5271 patients (38% children), when 50% of data are manually screened; see "Statistical analysis" in "Methods" and "Results".

The cost of HVEM-DRE is calculated as a percentage of change in its cost relative to the previous week of monitoring. "Week 0" is when HVEM is not performed, and all patients are referred to in-hospital VEM. Of note, the cost of HVEM-DRE rises in the first week. However, a longer HVEM-DRE leads to decreases in the total cost.

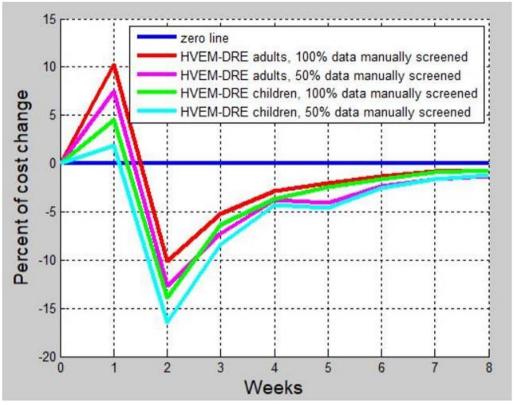


Fig. 3 The weekly change in the modeled duration-dependent cost of HVEM-DRE

Sensitivity analysis

The minimal seizure frequency of the patient referred to HVEM (Fig. 4, Tables S4–S6). With the increase in the minimum seizure frequency in patients referred to the HVEM, the HVEM-DRE model demonstrates improved cost-efficiency in both adult and pediatric populations. With a minimum of 4 seizures per month, all groups of patients (even adults with 100% manually screened data) demonstrate cost efficiency beginning from the first week (Fig. 4D).

The proportion of manual data screening (Fig. 5, Tables S7–S10). The decrease in the proportion of manually screened data results in improved cost-efficiency of the HVEM-DRE model. The combination of the increase in minimal seizure frequency in patients referred to HVEM (4 seizures per month) and the decrease in the proportion of manually screened data significantly improves the cost-efficiency of the HVEM-DRE model (Fig. 5C, D).

The proportion of technological cost (Fig. S3, Tables S11–S14). The HVEM-DRE model is sensitive to an increase in the technological cost if the seizure frequency is defined as 1 per month (Fig. S3A–C). In that case, the increase in the technological cost leads to a decrease in the cost efficiency of the model. However, the HVEM-DRE model is much less sensitive to an

increase in the technological cost if the minimal seizure frequency is defined as 4 per month.

The proportion of administrative cost (Fig. S4, Tables S15–S18). The same is true for the administrative cost. If the minimal seizure frequency is defined as 1 per month, then the HVEM-DRE model is sensitive to the increase in administrative cost (Fig. S4A–C). However, it is much less sensitive if the minimal seizure frequency is defined as 4 per month (Fig. S4D).

The EEG technician's screening time (Figs. S5 and S6, Tables S19–S23). An increase in the EEG technician screening time reduces the cost-efficiency of the HVEM-DRE model, especially if a minimum seizure frequency is defined as 1 per month (Fig. S5A–D). The cost-efficiency reduction is much less prominent with a minimum seizure frequency of 4 per month (Fig. S6).

The distribution of adult and pediatric patients (Fig. S7, Tables S24–S25). In a group of patients with a minimum seizure frequency of 1 per month, the HVEM-DRE model is less cost-efficient with a higher proportion of adult patients (Fig. S7A). If the minimum seizure frequency is defined as 4 seizures per month, then the change in the distribution of adult and pediatric patients makes no substantial difference (Fig. S7B).

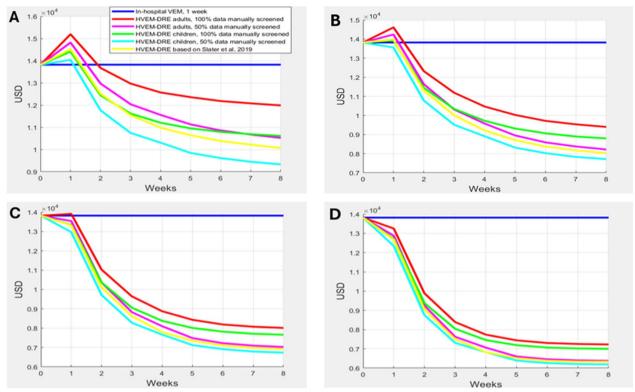


Fig. 4 The minimal number of seizures in patients referred to HVEM. A 1 seizure per month (Equal to Fig. 2.). B 2 seizures per month. C 3 seizures per month. D 4 seizures per month

The different numbers of recorded seizures as a criterion for HVEM goal achievement (Figs. S8 and S9, Tables S26–S29.). In a group of patients with a minimum seizure frequency of 1 per month, the HVEM-DRE model was sensitive to an increase in the number of required seizures (Fig. S8, Table S26–S38), while in the group of patients with a minimum of 4 per month, the cost-effectiveness was preserved except for the first week (Fig. S9, Table S29).

Discussion

In this simulation study, we demonstrated that the cost of an HVEM lasting five weeks is equivalent to a one-week in-hospital VEM. If 50% of the data is automatically screened, the cost of up to six weeks of HVEM is lower than that of a one-week in-hospital VEM. We calculated the direct cost of a one-week HVEM to be 4647 USD, similar to the 4098 USD reported by Slater [30] when considering the inflation rates. Furthermore, we have shown that for patients with DRE needing recording of at least three seizures on different days, the perpatient direct cost of HVEM lasting 2 to 8 weeks is lower than the mean direct cost of an in-hospital VEM. This is true even when the cost of the in-hospital VEM is added to the HVEM cost in those who failed to achieve

the diagnostic goal. This is due to the dropping of a proportion of patients every week from HVEM, when they achieve the HVEM goal, while the in-hospital VEM cost is added for other patients.

HVEM reduces the monitoring cost for patients with DRE mainly in the second to third weeks of recording. Longer HVEM reduces the cost by no more than 5% per week. Therefore, considering the present technological limitations, the economic advantage of a longer than three weeks HVEM is questionable. It is important to note that the cost reduction for the average patient can be expected when HVEM precedes in-hospital VEM; if HVEM is performed after in-hospital VEM, the cost of the whole procedure is not reduced compared to in-hospital VEM alone. According to our results, HVEM limited to one week is economically unjustified for patients with DRE. However, many patients do not achieve the diagnostic goal within one week of HVEM and therefore need to be referred to an in-hospital VEM. It is possible that for a selected category of patients with DRE who have several seizures per week, a one-week HVEM can be economically justified.

Our study showcases that the approach of HVEM followed by in-hospital VEM (if the goal of HVEM was not achieved) is economically justified from the healthcare

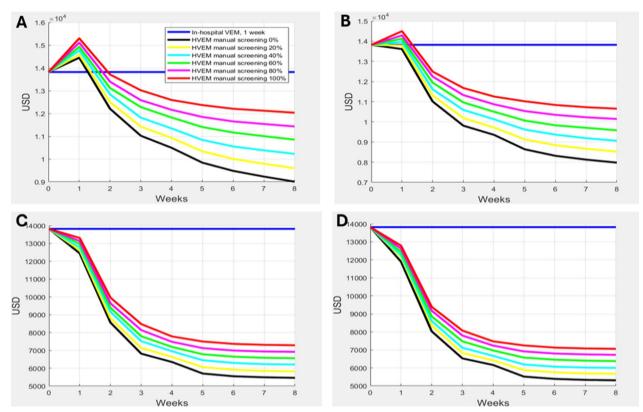


Fig. 5 Proportion of manual data screening by EEG technician. **A** adults, minimum 1 seizure per month. **B** children, minimum 1 seizure per month. **C** adults, minimum 4 seizures per month. **D** children, minimum 4 seizures per month

system position. However, it may increase the individual expenditure of a self-paying patient. This can happen in the case of uninsured patients in both low-resource [2, 12] and high-resource [8] countries. Regarding the different types of healthcare systems [5, 34], the HVEM-DRE model can be suitable for several healthcare system types providing that the procedure is covered by the insurance. The HVEM service provider can be governmental, public, or private. However, governmental, or public regulators should define the criteria for admission to HVEM and ensure adherence to these criteria. We believe that the final decision regarding the admission of the patient to HVEM should be made by the treating physician.

Due to the limited availability of in-hospital services in low-resource countries, HVEM presents an appealing alternative. However, HVEM does require resources, including trained personnel. Volunteer involvement in the education of local medical personnel and collaboration with medical centers in high-resource countries can help establish efficient medical services in low-resource countries [20].

At present, HVEM longer than one week (even divided into repeated sessions), is not a part of the common clinical practice. HVEM in repeated sessions has been reported only in a minority of cases [17]. However, for patients with DRE long-lasting HVEM has not only economic benefits but also clear clinical advantages: It is valuable in proving or excluding that the patient has more than one seizure type. This is based on the recordings of implanted responsive neurostimulation devices that discovered bilateral independent temporal seizures in patients previously believed to have unilateral seizures [10]. Another advantage of HVEM is avoiding the risks of ASM reduction.

According to Schulze-Bonhage et al. [27], ASM reduction is associated with approximately four-fold increase in risk for bilateral tonic-clonic seizures.

On the other hand, self-discontinuation of ASM by epilepsy patients is not uncommon [29]. Patients undergoing prolonged HVEM may decide on their own to reduce medications, to trigger seizures and thus shorten the recording time. To minimize this risk, the prolonged HVEM recording should be done intermittently with continuous recording segments lasting possibly up to one week. The cumulative time of HVEM should probably be no longer than three weeks. The patients should be educated on the risk of medication withdrawal. To avoid financial incentives to reduce ASM and shorten the

monitoring, no discount should be given if the HVEM is finalized before the scheduled date.

Another issue of prolonged HVEM is that longer device-per-patient use increases the technological cost, which can be a substantial burden for developing countries. The hardware and software may be too expensive for the healthcare system to pay. This can be partially solved by large monitoring units, where several patients are simultaneously monitored, using the same software license, and by longer device lifespan [13]. We suggest that the technological cost of HVEM in developing countries should be adjusted to the local salaries and, therefore, to the basic cost of HVEM.

We conducted a sensitivity analysis to evaluate the robustness of the HVEM-DRE model. We modified various input parameters and then compared the model's cost efficiency. One of the parameters that had the most significant impact on the model was the minimum seizure frequency required for referral to HVEM. If we consider a 3-week period as the optimal length for HVEM due to indirect costs and convenience limitations, and, if we expect to record three seizures, the seizure frequency should be about one seizure per week or more, or at least about four seizures per month. We demonstrated that by limiting the minimum seizure frequency to 4 seizures per month, the HVEM-DRE model became robust and generally insensitive to increases in technological or administrative costs or other challenges. Automated data analysis provides additional robusticity to the HVEM-DRE model by reducing the manually analyzed data. Setting the minimum to 4 seizures per month would limit the number of patients who can be referred to HVEM. Based on our previous work [33], 44.5% of adult patients and 40.6% of pediatric patients would meet the referral criteria with the minimal seizure frequency of 4 seizures per month. In that work [33] the maximal frequency of seizures was limited to one seizure per day.

The HVEM-DRE model demonstrates stable cost-efficiency when the criterion for HVEM goal achievement is capturing 3 seizures on different days in patients with a minimum seizure frequency of one to four per month. If the criterion for HVEM goal achievement is 4 seizures on different days, then the HVEM-DRE system is cost-efficient (except for the first week) if the minimal seizure frequency is 4 seizures per month, but is not cost-efficient if the minimal seizure frequency is 1 seizure per month.

The appropriate goal of long-term HVEM in patients with DRE undergoing a pre-surgical assessment is to record three seizures on different days. However, there are situations where capturing just one seizure may be sufficient. For instance, recording a single event can help determine whether the events reported by the patient or caregiver are truly epileptic seizures, helping to clarify

an uncertain diagnosis. Recording a single event can also aid in evaluating the patient's response to medication and serve as a supplementary assessment to an in-hospital VEM that captured only two seizures.

Our study has several limitations. It is based on a simulation, and we may have missed some real-life factors influencing the HVEM cost. The model cannot foresee all possible circumstances that can appear in clinical practice. Additionally, the cost of hardware, software, and administrative workload may vary in different situations, leading to uncertainty surrounding the exact definition of technological and administrative costs. In this study, we defined the technological and administrative costs as a proportion (70% and 30%, respectively) of the basic cost. However, later, with real-life experience, these definitions can change. To avoid underestimation of HVEM expenses, we used high costs for hardware, software, and labor in this model. The indirect HVEM cost and the patient's compliance may affect the frequency of electrode array reattachments as well. This may increase the direct and indirect costs of the HVEM. Furthermore, in our model, we used the published data based on the US sources (e.g., [30]).

It should be noted that there is a wide variation in inhospital VEM costs worldwide. According to [30], the mean cost of in-hospital VEM (both medical and prescription costs) in the US was 13,821 USD, while according to [6], in the UK the cost was 1639 £ (for 3 days of monitoring). Kobulashvili et al. [18] reported different costs of in-hospital VEM throughout Europe that ranged from less than 500€ per day to over 2000€ per day. Thus, while our study can be applicable to some regions of the world, we suggest using a region-specific model, which may render various degrees of HVEM benefit. For this purpose, readers can utilize our free online MATLAB code. The scarcity of published data on the components of in-hospital VEM cost is another challenge. We are aware of only one study [6] that elaborated on the components of in-hospital VEM.

The in-hospital VEM and HVEM costs have different structures. According to Brunnhuber et al. [6], 55.9% of 3-day in-hospital VEM cost is the cost of the in-hospital stay, while the cost of EEG-technician work is 19%. In contrast, the cost of EEG technician work in prolonged HVEM (3 weeks) is 36.6%, according to our model. This is due to the large quantity of data resulting from long home recordings. Another substantial expense of the prolonged HVEM is the technological cost (35.0% for 3 weeks of HVEM), explained by a low number of patients monitored by the same video-EEG device per unit of time. Therefore, the main strategies to reduce the HVEM cost are automatic data screening and the reduction of technological cost.

Reduced patient compliance can be associated with electrode detachments, leading to more frequent clinic visits for electrode reattachment. This increases the EEG-technician workload and the direct cost of HVEM. In addition, missing seizures due to electrode detachment lengthen the HVEM procedure, resulting in higher direct and indirect costs. It seems reasonable for medical personnel to monitor the patients' compliance. In cases of non-compliance, early transfer from HVEM to in-hospital HVEM should be considered to improve diagnostic and economic efficiency. HVEM can pose some technical problems that are not a part of in-hospital HVEM, e.g., the security of the data transfer from the patient's home to the hospital.

Another issue is the criterion for HVEM clinical goal achievement. As such criterion, we used in the present study as well as in our previous study [33] the recording of three seizures on different days. This is slightly different from the criteria recommended by Tatum et al. [32]: recording of three seizures in uncomplicated cases; and more than 1-month separation between recorded seizures if several seizure onset zones are suspected. Our criterion can be considered an adaptation of the recommendation of Tatum et al. [32] and applying them to prolonged HVEM in patients with DRE. On the other hand, since prolonged HVEM should be done intermittently, the intervals between the recordings can provide enough temporal separation between recorded seizures. This may be an advantage when more than one seizure onset zone is suspected.

Furthermore, while here we estimated the direct cost of HVEM, the indirect cost assessment was beyond the scope of this study. The indirect cost includes school or work absence (of both patient and caregivers) and psychological burning-out, among others. Libby et al. [19] state that a significant portion of the societal impact of epilepsy stems from its indirect expenses. While the availability of an HVEM can be higher than that of an in-hospital VEM, and the direct cost is lower, it needs to be clarified whether the indirect cost of a several-week HVEM would be lower as well. Indeed, staying at home for several weeks may lead to high indirect costs and can be challenging for patients. Compliance may decline over time due to fatigue and boredom.

The patient's transportation is an important indirect cost, especially when the distance between the patient's home and the clinic is significant. To minimize the need for repeated patient transportation, a long, continuous (up to 6 days) self-assisted HVEM can be helpful [22].

The indirect cost of HVEM is an important factor to consider in HVEM planning that should be done in two aspects: the first is to shorten the HVEM study (e.g. no more than three non-sequential weeks) and the second

is to select for HVEM patients with appropriate seizure frequency (e.g., no less than one seizure per week). On the other hand, however, a long waiting period for VEM is also associated with indirect costs. For example, poorly controlled seizures can lead to work and school absences, trauma, and impact the patient's and their family's quality of life. While HVEM requires resources, it is not restricted by the number of beds in epilepsy monitoring units and therefore it can reduce the waiting time for inhospital VEM. Thus, the whole picture of HVEM-associated costs is composed of three components: (1) the direct cost of HVEM (or HVEM-DRE), (2) the indirect cost of HVEM (or HVEM-DRE) and (3) the sparing indirect cost of waiting for in-hospital VEM. The modeling of all three components requires further study.

Total HVEM cost
= direct HVEM cost
+ indirect HVEM cost
- spared indirect cost of waiting for in

(19)

- hospital VEM

Moreover, some patients may have technical difficulties with the HVEM device. One possible way to reduce the indirect cost of HVEM and improve patient compliance is to allow a flexible recording schedule. For this to be possible, it is necessary that the EEG array can be effortlessly positioned and detached by the patient or caregiver. Some promising directions are the implementation of EEG systems with dry [28] or semidry [16] electrodes. Future technological developments may achieve this goal. Furthermore, given the relatively fast decreasing costs of technologies nowadays, patients may be able to purchase a private HVEM system. This may allow them to use it on an as-needed basis. Another option is to employ prolonged home video-audio monitoring without EEG [24] as a complementary tool for intermittent prolonged HVEM. The indirect cost of HVEM should be further assessed in clinical trials.

To efficiently supervise the HVEM, it is preferable to use the home VEEG systems with the ability to transfer the data online. Another important aspect of HVEN is the performance of video recording at home. Video cameras should be preferably placed under the online supervision of EEG technicians. We recommend using home VEEG systems with more than one video camera, if possible, to enable patients' mobility at home during HVEM without video recording interruptions. The patients' and their caregiver's education is valuable for efficient HVEM. Patient support groups that involve other patients, their families, and professionals can assist in mitigating the challenges of HVEM.

We demonstrated that reducing the need for manual data screening from 100 to 50% significantly reduced HVEM cost. Automated spike detecting [26] and seizure detecting [4] software may increase the technological cost but can be efficient in reducing manual workload, thus decreasing the total cost of HVEM. Abdelhameed and Bayoumi [1], reported deep learning-based seizure detector with sensitivity and specificity both about 99%. Further studies are required to assess the role of automated EEG analysis software in HVEM. Above and beyond automated EEG analysis, future algorithms may predict the most suitable VEM schedule for each patient based on their seizure frequency, cycling, and clustering data extracted from their individual seizure diaries. Automated EEG analysis software has the potential to reduce workload and decrease the overall cost of the procedure. This can be especially important in prolonged HVEM since long recordings produce large quantity of data. However, the development of artificial intelligence-based automated algorithms requires substantial resources, particularly an annotated EEG dataset. While there are several EEG datasets available, standardization of these datasets is challenging [35]. Additionally, the cost of clinically approved EEG analysis software is likely to be high, limiting its use in low-resource countries. Future development of low-cost clinically approved automated EEG analysis software based on the large publicly available EEG dataset is warranted.

Our research shows that prolonged intermittent HVEM can be cost-effective, especially when the minimum seizure frequency is about one seizure per week. These findings support the need to start clinical trials and further develop HVEM technology. Due to significant variations in healthcare systems, we recommend creating a cost-efficiency model for HVEM in specific regions and utilizing our MATLAB code for this purpose (https://github.com/marikmedv/Virtual_Video_EEG. The file name is HVEM_cost_calculator_080724.m). The user guide for this code is located in the Supplementary Materials (Appendix 5).

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12962-024-00568-7.

Supplementary Material 1.
Supplementary Material 2.
Supplementary Material 3.
Supplementary Material 4.
Supplementary Material 5.

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Author contributions

TV conceptualized the study, drafted and critically read the manuscript. RB drafted the manuscript and critically read the manuscript. NF critically read the manuscript. TS participated in drafting the manuscript and critically read the manuscript. AN contributed to constructing the model and critically read the manuscript. TG participated in editing and proofing the manuscript and critically read it. DEI contributed to constructing the model and critically read the manuscript. DEk drafted and critically read the manuscript. MM conceptualized the study, drafted the manuscript, wrote the simulation code, and supervised its final version.

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Data Availability

Not applicable.

Availability of materials

No original datasets were analyzed in present study. Our computer simulations were based on the results of already published articles that are mentioned in the reference list of this article. The average salaries for home video-EEG cost estimation were taken from https://www.ziprecruiter.com/. The MATLAB code of our model that was used in the present study is publicly available at https://github.com/marikmedv/Virtual_Video_EEG. The name of the file is HVEM_cost_calculator_030624.m.

Declarations

Ethics approval and consent to participate

The present work is a computer simulation study. No human or animal studies were performed. No human subject's data were included into this work except of the data taken from the already published articles that are mentioned in the reference list of this article.

Competing interests

Authors MM and DEk are the inventors of patents related to HVEM development, and author NF is the contributor to one of these patents. Authors MM. DEk and DEl are involved with VIRDA startup company, which develops HVEM systems.

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